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Lifetime Risk of Alcohol-Attributable Death and Disability

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Conflict of Interest

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Executive Summary

Key Messages

- Consuming alcohol can lead to death and disability from many diseases and injuries. However, alcohol's effects on health differ by disease, leading to confusion on what constitutes low-risk drinking. Accordingly, estimates of the effects of alcohol use on all causes mortality and disability at the individual level are needed to best advise individuals about their long-term risk.
- Since the publication in 2011 of Canada's Low-Risk Alcohol Drinking Guidelines, numerous diseases have been found to be causally related to alcohol use. Additional research has been published on how alcohol affects the risk of disease and injury. Based on this new information, this study updates the lifetime risk estimates for death and disability for people in Canada who consume alcohol.
- The lifetime risk of death and disability increases as alcohol consumption increases. As men and women experienced a similar risk of death and disability caused by alcohol for all levels of alcohol use examined, one guideline can be used for men and women.
- Based on risk thresholds of 17.5 years of life lost attributable to alcohol per 1,000 lifetimes, the alcohol use risk threshold should be set at 4 g/day for men and women in Canada. However, based on the same number of years of life lost but per 100 lifetimes, the threshold should be set at 11 g/day.
- The previous low-risk alcohol drinking guidelines recommended that men drink no more than 15 standard drinks per week (about 29 g/day) and women drink no more than 10 standard drinks per week (about 19 g/day). Based on the new estimations, these levels of alcohol use are not consistent with the evidence and acceptable risk thresholds (1 in 100 or 1 in 1,000 lifetime deaths attributable to alcohol). People who used these guidelines as a marker of risk may have experienced substantially more harm than originally thought.

Aims

With a view to update Canada's Low-Risk Alcohol Drinking Guidelines (LRDGs), published in 2011, this report addresses guideline biases and limitations, and provides the lifetime risk of death and disability for various levels of average alcohol consumption as measured in grams per day.

Methods

A lifetime risk approach was taken to estimate the lifetime risk of death, premature death (before 75 years of age), years of life lost (YLL) and disability-adjusted life years (DALYs) lost. The lifetime risk approach is based on the risk of death and disability among people who engaged in lifetime abstention (LA) multiplied by corresponding relative risks (RR). The risk of death and disability among lifetime abstainers was estimated using a comparative risk assessment that combined data on death, disability, exposure to alcohol and corresponding RRs. RRs were obtained from meta-analyses of cohort and case-control studies. Data on death and disability from 2017 to 2019 were obtained from Statistics Canada and the Institute for Health Metrics and Evaluation's Global Burden of Disease study. Alcohol exposure data were obtained from the Canadian Alcohol and Drug Use Monitoring Survey and the Canadian Tobacco, Alcohol and Drugs Survey. Survey data were corrected for total consumption in Canada (adult per capita consumption) using data from Statistics Canada and the World Health Organization's Global Information System on Alcohol and Health. Two risk

thresholds were assessed: 1 in 1,000 deaths attributable to alcohol (or 17.5 YLL/DALYs lost per 1,000 lifetimes) and 1 in 100 deaths attributable to alcohol (or 17.5 YLL/DALYs lost per 100 lifetimes).

Results

Thresholds for alcohol use among males and females were estimated to range from 4 to 6 g/day when using the outcomes of deaths, YLL and DALYs lost at a risk threshold of 1 in 1,000 deaths and 17.5 YLL or DALYs lost per 1,000 lifetimes. When using a risk threshold of 1 in 100 deaths and 17.5 YLL or DALYs lost per 100 lifetimes attributable to alcohol, the threshold for alcohol use was estimated to range from 11 to 12 g/day using the outcomes of deaths, YLL and DALYs lost. For premature deaths, the alcohol use threshold was 5 and 4 g/day among males and females, respectively, when using a risk threshold of 1 in 1,000 alcohol-attributable premature deaths. The threshold increased to 20 and 22 g/day among males and females, respectively, when using a risk threshold of 1 in 100 premature deaths attributable to alcohol. Alcohol use thresholds were similar for males and females for all outcomes and risk thresholds. These thresholds were even lower when the lowest risk of health loss from alcohol (2 g/day) was used as a reference point.

Conclusion

As the lifetime risk of death and disability is similar for males and females, one guideline for alcohol consumption can be used for Canada. The optimal outcome for the measurement of health loss attributable to alcohol is DALYs lost. Based on the risk thresholds of 17.5 DALYs lost attributable to alcohol per 1,000 and 100 lifetimes, risk thresholds for alcohol use should ideally be set at either 4 or 11 g/day for both males and females in Canada.

Introduction

Drinking alcohol causes a substantial burden of death and disability in Canada (Canadian Substance Use Costs and Harms, 2020). To reduce the burden of disease attributable to alcohol use, many countries have implemented drinking guidelines (Butt et al., 2011; National Health and Medical Research Council, 2020; Santé publique France, 2019; Shield et al., 2017; U.K. Chief Medical Officers, 2016). Over time, the aim of drinking guidelines has changed from the designations of "safe" or "sensible" guidelines to the designation of "low-risk" guidelines. The change in designation comes as research has shown that for numerous health outcomes, such as gastrointestinal diseases, cancer and injuries, there is no safe level of alcohol consumption (Hurst et al., 1994; Rehm, Baliunas, et al., 2010; Rehm et al., 2014; World Health Organization, 2014). Implementing low-risk drinking guidelines fits with well-informed consumers changing their behaviour based on advice from governmental, research and professional sources (Room & Rehm, 2012). The Canadian Low-Risk Alcohol Drinking Guidelines (LRDGs) (Butt et al., 2011) assessed three different risks of drinking:

- Increased long-term risk of serious diseases caused by drinking alcohol over numerous years (e.g., liver disease, some cancers);
- Increased short-term risk of injury or acute illness due to overconsuming alcohol on a single occasion; and
- situations and Individual circumstances that are particularly hazardous (e.g., females who are pregnant or planning to become pregnant, teenagers, people on medication) and for which abstinence or only occasional light intake is advised.

Since the 2011 publication of the LRDGs, numerous meta-analyses have been published. Based on published mechanistic, animal and epidemiological studies, diseases that were not considered to be causally related to alcohol use are now thought to be so. Furthermore, the LRDGs considered the risk of serious medical conditions associated with various levels of alcohol use and the risk of all-cause mortality as measured by high-quality meta-analyses (Butt et al., 2011). This approach has several limitations.

First, all-cause mortality relative risks (RRs) are estimated based on large, nonrepresentative cohort studies. These cohort studies are constructed for ease of follow-up, and their findings may be biased when applied to the general population. In particular, cohort studies are biased by the over-representation of deaths that occur among middle-class individuals compared with other segments of the general population, including deaths due to cardiovascular diseases where alcohol has a protective effect at low doses (Rehm, 2000; Rehm et al., 2003).

Second, RR estimates are derived from large cohort studies that took place in one or multiple countries. However, country-specific factors are needed to determine the effect on health of the average volume of alcohol consumed, contributing to country variations in cause-of-death structures (Shield et al., 2020). In particular, the effects of alcohol are affected by genetics, behavioural risk factors (such as smoking and drug use) and environmental factors (such as highway traffic laws that modify the impact of alcohol on traffic injuries). The interaction between alcohol and these factors helps determine the effect alcohol has on health at both the individual and country levels (Brooks et al., 2009; Kuper et al., 2000; Lieber, 1990; Rehm, Baliunas, et al., 2010; Roerecke et al., 2015).

Lastly, competing risks (i.e., mortality that occurs before an alcohol-attributable death would be observed) modify the impact of alcohol on health. For example, dying from alcohol-attributable cancer, which generally occurs later in life, is strongly affected by competing risks.

To address these limitations, guidelines in Australia and the United Kingdom have taken a mathematical modelling approach using disease-specific RRs applied to country-specific data on mortality (National Health and Medical Research Council, 2020; U.K. Chief Medical Officers, 2016). Studies have shown that the effect of alcohol on health is not limited to death as alcohol causes a substantial amount of disability (Rehm et al., 2017; Shield et al., 2020). Furthermore, alcohol is the leading risk factor for death and disability among people aged 15 to 49 years (Canadian Substance Use Costs and Harms Scientific Working Group, 2020; Shield & Rehm, 2015). Therefore, the assessment of additional health measurements, including the burdens of disease attributable to premature death and disability, may be critical for setting new low-risk drinking guidelines.

To help update Canada's LRDGs, the purpose of this report is twofold. First, it addresses the above-noted biases and limitations of the guidelines by implementing a lifetime risk methodology. Second, it provides up-to-date research evidence to update the guideline's main recommendation and help reduce the effects of alcohol use on the long-term risk of death and disability. This report is intended for public health practitioners and scientific researchers.

This report is part of the GRADE-ADOLOPMENT (Grading of Recommendations Assessment, Development and Evaluation- Adaptation, Adoption, De Novo Development) process being followed to update the guidelines, which will use the underlying evidence base supporting the United Kingdom and Australia's alcohol guidelines. For more information, visit the LRDG Project 2022 web page.

Methods

The lifetime risk of death and disability attributable to alcohol was estimated using a life-course risk method (National Health and Medical Research Council, 2020; Santé publique France, 2019; Shield et al., 2017; U.K. Chief Medical Officers, 2016). Lifetime risk curves were based on the average grams of pure alcohol (that is, ethanol) consumed per day. Life-course risk methodology estimates were based on four outcomes: death, death of people ages 74 years and younger, years of life lost (YLL), and disability-adjusted life years (DALYs) lost. DALYs lost are a summary measure of YLL and years lived with disability (YLD). YLD represents the prevalence of disabling conditions multiplied by the disability (that is, state of health) associated with the condition (0 being no disability and 1 being similar to death). All risk curves were produced for people who drank (D) by sex based on the average alcohol consumption of one to 100 grams of alcohol per day. People who drank were defined as people who consumed at least one standard drink of alcohol (14 grams of alcohol) in the past year. Risk curves were estimated for four different alcohol consumption reference categories: a reference group of lifetime abstention (LA), and an average of 2 g/day, 5 g/day and 14 g/day.

Definitions of Acceptable Risk

An acceptable level of risk is defined differently for voluntary behaviours, such as alcohol drinking, smoking and so on (Starr, 1969), compared with risks from involuntary exposures, such as air pollution (Hunter & Fewtrell, 2001; National Health and Medical Research Council, 2004; Rifkin & Bouwer, 2007). (For more about the distinction between voluntary and involuntary risk, see Fischhoff et al., 1984; Kahneman, 2011; Slovic, 1987; Starr, 1969). The analysis by Starr (1969, p. 1237) has been used to estimate acceptable voluntary risks about 1,000 times greater than involuntary risks (Rehm et al., 2014). A one in 1,000,000 lifetime mortality risk has been used as a gold standard definition of acceptable involuntary risk. It has been used for the assessment of different risk exposures in various jurisdictions, including for water safety in Australia and the United States (Hunter & Fewtrell, 2001; National Health and Medical Research Council, 2004) and increases in exposure to carcinogens in the air, sediment or soil (Rifkin & Bouwer, 2007). Dividing this risk by 1,000 (the ratio from Starr [1969] for acceptable levels of involuntary versus voluntary risk) leads to an acceptable voluntary risk threshold of one death in 1,000 lifetimes.

However, other definitions of acceptable voluntary risk have been used (Rifkin & Bouwer, 2007). For the guidelines from Australia, France and the United Kingdom, a standard of one death in 100 lifetimes was used (National Health and Medical Research Council, 2020; Santé publique France, 2019; U.K. Chief Medical Officers, 2016).

The acceptable risk for a lifetime death can also be stated based on the average YLL per death of 17.5 YLL based on data from the Institute of Health Metrics and Evaluation's (2021) Global Burden of Disease study. As DALYs lost are on an equivalent scale to YLL, the same threshold of 17.5 DALYs lost per 1,000 lifetimes can also be used (Murray, 1994).

This report reviewed the following modelled thresholds for levels of acceptable risk:

- For premature mortality: 1 in 1,000, and 1 in 100 premature deaths attributable to alcohol
- For lifetime mortality: 1 in 1,000, and 1 in 100 deaths attributable to alcohol
- For YLL: 17.5 YLL attributable to alcohol per 100 and 1,000 lifetimes
- For DALYs lost: 17.5 DALYs attributable to alcohol per 100 and 1,000 lifetimes

Diseases and Injuries Included in the Modelling of Alcohol-Attributable Deaths and Disability

The inclusion of diseases and injuries in the modelling of alcohol-attributable deaths and disability was based on three criteria. The first criterion was that the disease or injury had to be causally related to alcohol use. Causality was assessed by whether it was included in the World Health Organization's Global Status Report on Alcohol and Health (2018), the Institute of Health Metrics and Evaluation's Global Burden of Disease study (2021) or both. The World Health Organization and the Institute of Health Metrics and Evaluation assess causality for the inclusion of diseases and injuries in their studies. Causality was also assessed by whether the diseases and injuries were included in the low-risk drinking guidelines for Australia and the United Kingdom (National Health and Medical Research Council, 2020; U.K. Chief Medical Officers, 2016).

The second criterion was the availability of a dose-response risk function for the relationship between alcohol consumption (measured in grams per day) and the disease or injury that also passed the GRADE criteria (Canadian Centre on Substance Use and Addiction, 2021).

The third criterion was that either death or disability needed to be measured specifically for the disease or injury causally related to alcohol use.

Based on these criteria, the diseases and injuries included in the modelling of alcohol-attributable deaths and disability are listed in Table 1. They are listed in the table as coded by the International Classification of Diseases, Tenth Revision (ICD-10-CA).

Table 1. Alcohol-related diseases, conditions and injuries

Cause category	ICD-10-CA codes
Communicable, maternal, perinatal and nutritional conditions	A00–B99, D50-53, D64.9, E00-02, E40–46, E50–64, G00–04, G14, H65–66, J00–22, N70–73, O00–99, P00–96, U04
Infectious and parasitic diseases	A00–B99, G00–04, G14, N70–73, P37.3, P37.4
Tuberculosis	A15-19, B90
Respiratory infections	H65–66, J00-22, P23, U04
Lower respiratory infections	J09–22, P23, U04
Noncommunicable diseases	C00–97, D00–48, D55–64 (minus D64.9), D65–89, E03–07, E10–34, E65–88, F01–99, G06–98 (minus G14), H00–61, H68–93, I00–99, J30–98, K00–92, L00–98, M00–99, N00–64, N75–98, Q00–99, X41–42, X44, X45, R95
Malignant neoplasms	C00–97
Mouth and oropharynx cancers	C00–14
Lip and oral cavity	C00–08
Other pharyngeal cancers	C09–10, C12–14
Oesophagus cancer	C15
Colon and rectum cancers	C18–21
Liver cancer	C22
Breast cancer	C50
Larynx cancer	C32
Diabetes mellitus	E10–14 (minus E10.2–10.29, E11.2–11.29, E12.2, E13.2–13.29, E14.2)

Cause category	ICD-10-CA codes
Mental and substance use disorders	F04–99, G72.1, Q86.0, X41–42, X44, X45
Alcohol use disorders	F10, G72.1, Q86.0, X45
Neurological conditions	F01–03, G06–98 (minus G14, G72.1)
Degeneration of nervous system due to alcohol	G31.2
Epilepsy	G40–41
Alcohol polyneuropathy	G62.1
Alcohol myopathy	G72.1
Cardiovascular diseases	I00–99
Hypertensive heart disease	I10–15
Ischaemic heart disease	I20–25
Stroke	I60–69
Ischaemic stroke	G45–46.8, I63–63.9, I65–66.9, I67.2–67.848, I69.3–69.4
Intracerebral haemorrhage	I61–I62, I62.9, I69.0–I69.298
Subarachnoid hemorrhage	I60–I60.9, I67.0–I67.1
Cardiomyopathy, myocarditis, endocarditis	I30–33, I38, I40, I42
Alcohol cardiomyopathy	I42.6
Atrial fibrillation and flutter	I48
Digestive diseases	K20–92
Alcoholic gastritis	K29.2
Cirrhosis of the liver	K70, K74
Pancreatitis	K85–86
Fetus and newborn affected by maternal use of alcohol	P04.3
Injuries	V01–Y89 (minus X41–42, X44, X45)
Unintentional injuries	V01–X40, X43, X46–59, Y40–86, Y88, Y89
Road injury	V01–04, V06, V09–80, V87, V89, V99*
Poisonings	X40, X43, X46–48, X49
Falls	W00–19
Fire, heat and hot substances	X00–19
Drowning	W65–74
Exposure to mechanical forces	W20–38, W40–43, W45, W46, W49–52, W75, W76
Other unintentional injuries	Rest of V, W39, W44, W53–64, W77–99, X20–29, X50–59, Y40–86, Y88, Y89
Intentional injuries	X60–Y09, Y35–36, Y870, Y871
Self-harm	X60–84, Y870
Interpersonal violence	X85–Y09, Y871

Data Sources

Burden of Disease

Data on the number of deaths that occurred in Canada by cause, sex and age were obtained from Statistics Canada, Canadian Vital Statistics database (Statistics Canada, 2021a). Data on YLD by cause, age, and sex were obtained from the Institute of Health Metrics and Evaluation's Global Burden of Disease study (2021). Population data by age and sex were obtained from Statistics Canada (2021d). Deaths, YLL and population data were obtained for 2017, 2018 and 2019, and such data were used to estimate a three-year average for deaths, YLD and population estimates. Deaths and YLD were grouped into the following age groups: <1, 1 to 4, 5 to 9, 10 to 14 .... 80 to 84, 85 to 89, and >90 years of age. The YLL were estimated based on life tables by sex obtained from Statistics Canada (2021b) and the age at death.

Relative Risk Estimates

The sources for the RR estimates are outlined in Table 2. These RRs used the reference group of people who engaged in LA from alcohol and were corrected for people who engaged in past drinking (PD) (i.e., people who have consumed at least one standard drink of alcohol in their lifetime, but who have not consumed at least one standard drink of alcohol in the past year).

Table 2. Relative risk estimates by disease category

Cause category	RR source
Communicable, maternal, perinatal and nutritional conditions	
Infectious and parasitic diseases	
Tuberculosis	Imtiaz et al., 2017
Respiratory infections	
Lower respiratory infections	Samokhvalov, Irving, Mohapatra et al., 2010
Noncommunicable diseases	
Malignant neoplasms	
Mouth and oropharynx cancers	
Lip and oral cavity	Bagnardi et al., 2015
Other pharyngeal cancers	Bagnardi et al., 2015
Oesophagus cancer	Bagnardi et al., 2015
Colon and rectum cancers	Vieira et al., 2017
Liver cancer	World Cancer Research Fund & American Institute for Cancer Research, 2018
Breast cancer	Sun et al., 2020
Larynx cancer	Bagnardi et al., 2015
Diabetes mellitus	Knott et al., 2015
Mental and substance use disorders	
Alcohol use disorders	100% alcohol attributable
Neurological conditions	
Degeneration of nervous system due to alcohol	100% alcohol attributable

Cause category	RR source
Epilepsy	Samokhvalov, Irving, Mohapatra et al., 2010
Alcohol polyneuropathy	100% alcohol attributable
Alcohol myopathy	100% alcohol attributable
Cardiovascular diseases	
Hypertensive heart disease	Liu et al., 2020
Ischaemic heart disease	Zhao et al., 2017
Stroke	
Ischaemic stroke	Larsson et al., 2016
Intracerebral haemorrhage	Larsson et al., 2016
Subarachnoid hemorrhage	Larsson et al., 2016
Cardiomyopathy, myocarditis, endocarditis	
Alcohol cardiomyopathy	100% alcohol attributable
Atrial fibrillation and flutter	Larsson et al., 2016
Digestive diseases	
Alcoholic gastritis	100% alcohol attributable
Cirrhosis of the liver	Roerecke et al., 2019
Pancreatitis	Samokhvalov et al., 2015
Fetus and newborn affected by maternal use of alcohol	100% alcohol attributable
Injuries	
Unintentional injuries	
Road injury	Shape of the RR curve: Taylor & Rehm, 2012; Area under the RR curve: Brown et al., 2021
Poisonings	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Falls	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Fire, heat and hot substances	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Drowning	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Exposure to mechanical forces	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Other unintentional injuries	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Intentional injuries	
Self-harm	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010
Interpersonal violence	Shape of the RR curve: Taylor et al., 2010; Area under the curve: Canadian Institute for Health Information, 2010

The increased risk of death and disability for causes that are 100% attributable to alcohol was not modelled (see below, Alcohol Use, Addiction and Executive Functioning, for further details).

Relative Risk Estimates for Injuries

The risk of injuries depends on the acute consumption of alcohol and the context of this consumption. This risk will differ by country, as the context of alcohol use will differ by country. Similar to the guidelines for Australia and United Kingdom (National Health and Medical Research Council 2020; U.K. Chief Medical Officers, 2016), the estimation of the RR for injuries is based on a two-step process. The first step was to determine the shape of the risk curve between alcohol use and the risk of injuries. Based on the GRADE criteria, the risk relationship from Taylor et al., 2010, and Taylor & Rehm, 2012, was determined to be linear on the natural logarithmic scale.

The second step in the estimation of the RR for people who drink (i.e., people who consumed alcohol in the past year; RR_D) was based on the average amount of alcohol consumed per day (operationalized as x). The process used to estimate the RR_D is based on data about the population-attributable fractions (PAFs) of road injuries for Canada (using toxicology reports on blood alcohol content [BAC] as a proxy) and data on the alcohol use of Canadians. PAFs for road traffic injuries were obtained for 2016 from Brown et al., 2021, and PAFs for other unintentional injuries and intentional injuries were obtained for 2009 from the Canadian Institute for Health Information (2010). These data represent the most recent data published on BAC for injuries in Canada. PAFs were based on injuries that occurred among people with a BAC above 0.08 g/dL. Injuries that occur at and above a BAC of 0.08 g/dL have been shown to be strongly associated with alcohol use. While a proportion of injuries that occur among people who have a BAC below 0.08 g/dL may also be causally associated with alcohol (especially people with a BAC between 0.05 to 0.08 g/dL), these injuries were not modelled due to uncertainty as to whether they were attributable to alcohol use.

Alcohol use statistics were based on multiple data sources. The prevalence of people who drink, by age and gender, were obtained for 2009 from the Canadian Alcohol and Drug Use Monitoring Survey for 2009 (Health Canada, 2010) and for 2016 from the Canadian Tobacco, Alcohol and Drugs Survey for 2017, used as a proxy for 2016 (Statistics Canada, 2018). For the analyses of alcohol-attributable health harms, alcohol use by gender was used as a proxy for alcohol use by sex. These data were analyzed to estimate the prevalence of people who engaged in LA (P_{LA}), PD (P_{PD}), and D (P_D). Among people who drink alcohol, relative average daily consumption of alcohol coefficients was also estimated. All survey analyses were performed by sex and age (15 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 75, and 75 years of age and older). All survey analyses were completed using a package of R code for analyzing complex surveys (Lumley, 2004).

Adult *per capita* alcohol consumption data for Canada were obtained for 2009 and 2016 from Statistics Canada (Statistics Canada, 2021c), and unrecorded and tourist *per capita* alcohol consumption data were obtained from the World Health Organization's Global Information System on Alcohol and Health (2021). When modelling the amount of alcohol consumed by people who drink, the *per capita* consumption of alcohol was adjusted using a correction factor of 0.8 (see below, Estimations of the Lifetime Risk of Death and Disability for People Who Have Never Consumed Alcohol). The distribution of alcohol use (measured in grams per day) was modelled based on the method outlined in Rehm, Kehoe et al., 2010, and Kehoe et al., 2012.

This method was developed using data from over 60 individual surveys conducted in both developing and developed countries. First, this method assumes that the average daily amount of alcohol consumed by people who drink can be accurately modelled using a gamma distribution, which was the case in the surveys examined by both Rehm and Kehoe and their colleagues. Second, this method assumes that the standard deviation of the gamma distribution of alcohol consumption can be predicted based on the mean consumption of alcohol. Rehm and Kehoe and their colleagues observed a strong correlation between the mean and the standard deviation of the gamma

distribution (an r of 0.971). Based on the mean alcohol consumed (μ) by age and sex, the standard deviation (σ) was estimated according to Formula 1. (The coefficient of sex is 1 for females and 0 for males in Formula 1.) The gamma distributions were then integrated to determine the prevalence estimates for the drinking categories of 0.037 to 5, 5 to 10, 10 to 15 … 145 to 150 g/day.

Formula 1

$$\hat{\sigma}_{shifted=}(1.171 + 0.087 \cdot sex) \cdot \hat{\mu}_{shifted}$$

The derivation of the RR_D is based first on the estimate of the population RR (compared to a counterfactual scenario of everyone in the population abstaining from alcohol for their lifetimes); such an estimation uses Formulas 2 and 3. The population RR can be modelled using Formula 3 based on the risk among people who drink RR_D, P_D, P_{LA} and P_{PD}. To solve for the RR_D in Formula 4, we transformed this formula (see Formula 5) and solved for the RR_D using the uniroot function of the statistical software package R (R Core Team, 2013).

Formula 2

$$PAF = (RR_{POP} - 1)/RR_{POP}$$

Formula 3

$$RR_{POP} = 1/(1 + PAF)$$

Formula 4

$$RR_{POP} = P_{LA} + P_{PD} + \sum_{x=1}^{xn} (P_{D_x} \cdot RR_{D_x})$$

Formula 5

$$0 = P_{LA} + P_{PD} + \sum_{x=1}^{xn} (P_{D_x} \cdot RR_{D_x}) - RR_{POP}$$

Latency Period for Death and Disability Attributable to Alcohol Use

No latency period was used in the estimation of the attributable fractions, except for cancer. For cancer mortality and morbidity attributable to alcohol consumption, a latency period of 10 years was chosen between the consumption of alcohol and the diagnosis or death from cancer, based on an observed approximate latency period of 11 to 12 years for breast, colorectal, oral cavity, oesophageal (squamous cell carcinoma) and pharyngeal cancers, and eight to nine years for laryngeal and liver cancers (Grundy et al., 2016).

Estimations of the Lifetime Risk of Death and Disability for People Who Have Never Consumed Alcohol

A comparative risk assessment method was used to estimate the burden of disease attributable to alcohol use in 2017, 2018 and 2019. These estimates were based on the theoretical minimum risk exposure level (TMREL) of LA. LA was used as a TMREL based on historical precedent. However, no assumption was made about the exposure to alcohol that resulted in the lowest risk of overall health loss (GBD 2016 Alcohol Collaborators, 2018). The PAF for alcohol use was estimated using a Levin-based method that combines data on alcohol exposure with corresponding RR estimates (Levin, 1953; Rehm et al., 2008b) (see Formula 6).

Formula 6

$$PAF = \frac{P_{LA} + P_{PD}RR_{PD} + \int_{0.037\ g/day}^{150\ g/day} P_D(x) \cdot RR_D(x)dx - 1}{P_{LA} + P_{PD}RR_{PD} + \int_{0.037\ g/day}^{150\ g/day} P_D(x) \cdot RR_D(x)dx}$$

The PAF estimations were based on alcohol consumption statistics from 2009 for cancer, and from 2019 for all other diseases and injuries causally associated with alcohol use. For diseases that were 100% attributable to alcohol, the PAF was assumed to be 1. The prevalence of people who consumed alcohol, by age and gender, for 2009 were obtained from Canadian Alcohol and Drug Use Monitoring Survey, used as a proxy for 2007 to 2009 (Health Canada, 2010), and for 2017 from the Canadian Tobacco, Alcohol and Drugs Survey, used as a proxy for 2017 to 2019 (Statistics Canada, 2018). For these analyses, alcohol use by gender was used as a proxy for alcohol use by sex. Adult *per capita* alcohol consumption data for Canada were obtained for 2009 and 2019 from Statistics Canada (2021c), and unrecorded and tourist *per capita* alcohol consumption data were obtained from the World Health Organization's Global Information System on Alcohol and Health (2021). Alcohol use was modelled using a gamma distribution.

A correction factor of 0.8 was applied to adult *per capita* alcohol consumption data to account for (i) alcohol that was not consumed, and (ii) the underreporting of alcohol consumption in medical observation studies from which the RR estimates were obtained (Gmel & Rehm, 2004). A study by Stockwell and colleagues found that cohort studies of the relationship between alcohol consumption and all-cause mortality had a coverage rate of 61.7%, when compared to *per capita* consumption, ranging from 29.2% for Russia to 96.5% for Japan (Stockwell et al., 2018).

The adjustment of survey data can be justified by the observation that the underreporting of alcohol consumption in medical epidemiology studies (Feunekes et al., 1999; King, 1994; Rehm, 1998a) is much less than in population surveys. Population-level surveys underestimate alcohol consumption because, on average, such surveys ask many fewer questions to measure alcohol consumption compared to the number of such questions asked in medical epidemiology studies (Feunekes et al., 1999; King, 1994; Rehm, 1998b). Furthermore, the undercoverage of population surveys is also affected by recruitment biases (Shield & Rehm, 2012). The method used to model alcohol consumption among people who drink assumes that the undercoverage of alcohol consumption is constant by age and sex.

The number of alcohol-attributable deaths (AA_Deaths) and alcohol-attributable years lived with disability (AA_YLD) were estimated by applying the PAFs to corresponding deaths and YLD estimates by sex, age and cause of death or disability. The risk of death for people who engaged in lifetime

abstention (Risk_D_LA) for a given cause of death (c) and age (a) was estimated by subtracting the total number of alcohol-attributable deaths (AA_Deaths) from the total number of deaths and dividing this number by the population (Pop in the formulas below) of Canada (see Formula 7). Similarly, the risk of disability for people who engaged in lifetime abstention (Risk_D_YLD) for a given cause of disability (c) and age (a) was estimated by subtracting the total number of AA_YLD from the total number of YLD and dividing this number by the population of Canada (see Formula 8).

Formula 7

$$Risk\_D\_LA_{a,s,c} = \left[Deaths_{a,s,c} - AA\_Deaths_{a,s,c}\right]/Pop_{a,s}$$

Formula 8

$$Risk\_YLD\_LA_{a,s,c} = \left[YLD_{a,s,c} - AA\_YLD_{a,s,c}\right]/Pop_{a,s}$$

Estimations of the Lifetime Risk of Death and Disability for People Who Consume Alcohol

The alcohol-attributable mortality and morbidity risk by cause, age and sex for people who consume alcohol was estimated by multiplying Risk_D_LA and Risk_YLD_LA for a given age and cause by the corresponding RR given an age, sex, cause and average daily alcohol consumption amount (see Formulas 9 and 10). These models assumed that people consume alcohol starting at 15 years of age and continue to consume alcohol until their death. It was assumed that there was no risk of an alcohol-attributable death for a person 0 to 14 years of age.

Formula 9

$$Risk\_D\_AA_{a,s,c} = Risk\_D\_LA_{a,c} \cdot (RR_{a,s,c}(x) - 1)$$

Formula 10

$$Risk\_YLD\_AA_{a,s,c} = Risk\_YLD\_LA_{a,c} \cdot (RR_{a,s,c}(x) - 1)$$

The total Risk_D_AA and Risk_YLD_AA by age and sex was then estimated by summing the cause-specific Risk_D_AA and Risk_YLD_AA by age and sex (see Formulas 11 and 12).

Formula 11

$$Risk\_D\_AA_{a,s} = \sum_{c=ci}^{cn} Risk\_D\_AA_{a,s,c}$$

Formula 12

$$Risk\_YLD\_AA_{a,s} = \sum_{c=ci}^{cn} Risk\_YLD\_AA_{a,s,c}$$

To estimate the lifetime risk of alcohol-attributable mortality and morbidity for a given average level of daily alcohol use, we first estimated the proportion of people expected to be alive in the

population at the end of a given age based on their sex and average daily alcohol consumption. This proportion was based on the proportion of people alive at the end of age a-1, as well as on the Risk_D_AA and the Risk_D_LA for a given age and sex (see Formula 13).

Formula 13

$$Alive_{a,s,x} = Alive_{a-1,s,x} \cdot \left[1 - (Risk\_D\_AA(x)_{a,s} + Risk\_D\_LA_{a,s})\right]$$

The total lifetime risk of an alcohol-attributable death per 1,000 people was then estimated by summing the one-year age-specific alcohol-attributable mortality risks multiplied by the proportion of people alive in the population at the end of a given age based on their sex and average daily alcohol consumption (see Formula 14). The life risk of alcohol-attributable YLL per 1,000 people was estimated by summing the one-year age-specific alcohol-attributable mortality risks multiplied by the years of life lost for that death and the proportion of people alive in the population at the end of a given age based on their sex and average daily alcohol consumption (see Formula 15). The life risk of alcohol-attributable YLD per 1,000 people was estimated by summing the one-year age-specific alcohol-attributable YLD risks multiplied by the proportion of people alive in the population at the end of a given age based on their sex and average daily alcohol consumption (see Formula 16). The life risk of DALYs lost was estimated by summing the lifetime risks of alcohol YLL and YLD (see Formula 17).

Formula 14

$$Lifetime\_R\_Death(x)_s = \left[\sum_{a=15}^{n} Alive_{a,s,x} \cdot Risk\_D\_AA(x)_{a,s}\right] \cdot 1{,}000\ people$$

Formula 15

$$Lifetime\_R\_YLL(x)_s = \left[\sum_{a=15}^{n} Alive_{a,s,x} \cdot Risk\_D\_AA(x)_{a,s} \cdot YLL_{a,s}\right] \cdot 1{,}000\ people$$

Formula 16

$$Lifetime\_R\_YLD(x)_s = \left[\sum_{a=15}^{n} Alive_{a,s,x} \cdot Risk\_YLD\_AA(x)_{a,s}\right] \cdot 1000\ people$$

Formula 17

$$Lifetime\_R\_DALYs(x)_s = Lifetime\_R\_YLL(x)_s + Lifetime\_R\_YLD(x)_s$$

Uncertainty Estimations

The 95% uncertainty intervals were based on a set of 1,000 simulations of all lowest level parameters (that is, parameters sampled from their respective error distributions). These parameters were then used to estimate 1,000 simulated estimates of the alcohol-attributable burden of disease. From these simulations, the 2.5th and 97.5th percentiles were used for the 95% uncertainty intervals (UIs).

Results

Relative Risks for Diseases and Injuries by Sex

The RRs by cause of disease and average alcohol consumption are outlined in Table 3 for females and Table 4 for males (see the Appendix). For most diseases and injuries, alcohol had a net negative impact on health at all levels of alcohol use. However, for females only alcohol had a protective effect at lower alcohol use amounts for diabetes mellitus, ischemic heart disease, ischemic stroke, intracerebral hemorrhage, and pancreatitis. Furthermore, the leading causes of death among those causes related to alcohol were, for males, ischemic heart disease, followed by colorectal cancer and unintentional injuries (excluding road injuries) and, for females, breast cancer and unintentional injuries (excluding road injuries).

Lifetime Risk of an Alcohol-Attributable Death by Sex

The lifetime risk of an alcohol-attributable death and a premature alcohol-attributable death increased as alcohol consumption increased. Compared to people who engaged in lifetime abstention, males experienced a slight protective effect for premature deaths if they were consuming 2 to 3 g/day, while females did not experience a protective effect at any level of alcohol use. Compared to people who engaged in LA, males experienced a protective effect for overall deaths if they were consuming 1 to 5 g/day, while females experienced a protective effect if they were consuming 1 to 6 g/day. In all cases, the 95% UIs crossed the null hypothesis and the protective effects should be interpreted with caution. For premature deaths, the risk threshold, based on 1 in 1,000 premature deaths, would be 5 (95% UI: <1, 16) g/day for males and 4 (95% UI: <1, 10) g/day for females, and when based on 1 in 100 premature deaths, the risk threshold would be 20 (95% UI: 8, 25) g/day for males and 22 (95% UI: 10, 15) g/day for females (see Figure 1). For overall deaths, the risk threshold, based on 1 in 1,000 deaths, would be 6 (95% UI: <1, 24) g/day for males and 6 (95% UI: <1, 20) g/day for females, and when based on 1 in 100 deaths, the risk threshold would be 12 (95% UI: 1, 24) g/day for males and 12 (95% UI: 1, 24) g/day for females (see Figure 2). The risk thresholds varied based on the reference point chosen for the TMREL (see Figures 3 to 6).

Figure 1. Lifetime risk of a premature death attributable to alcohol use at varying levels of average alcohol intake

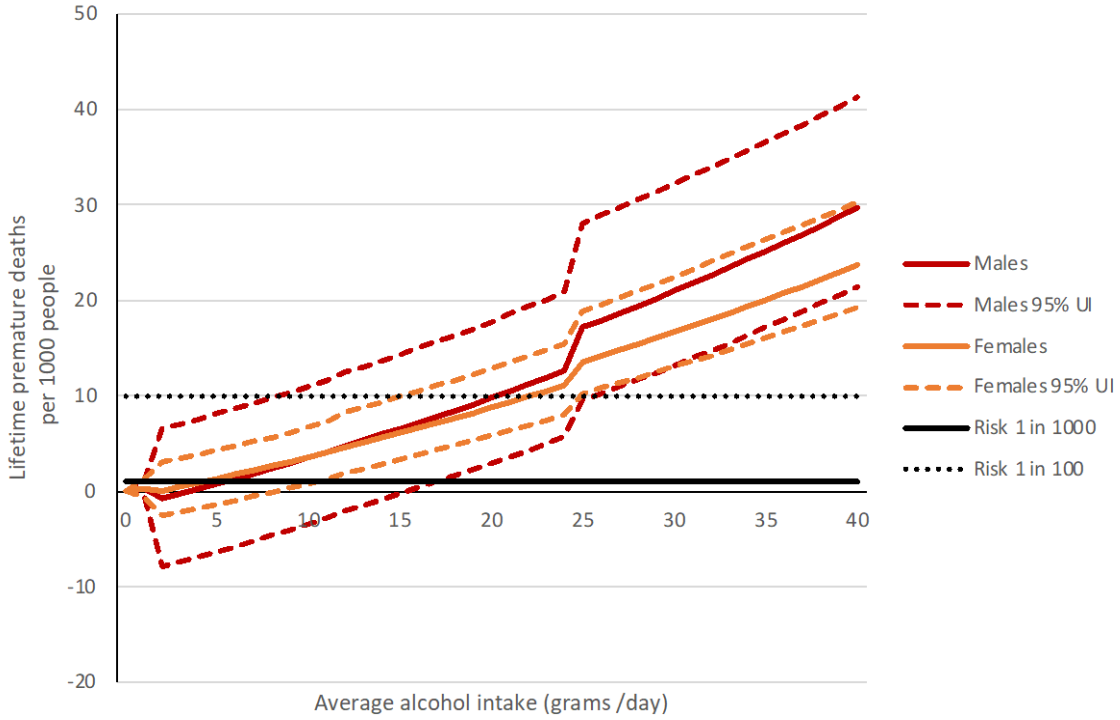


Figure 2. Lifetime risk of death attributable to alcohol use at varying levels of average alcohol intake

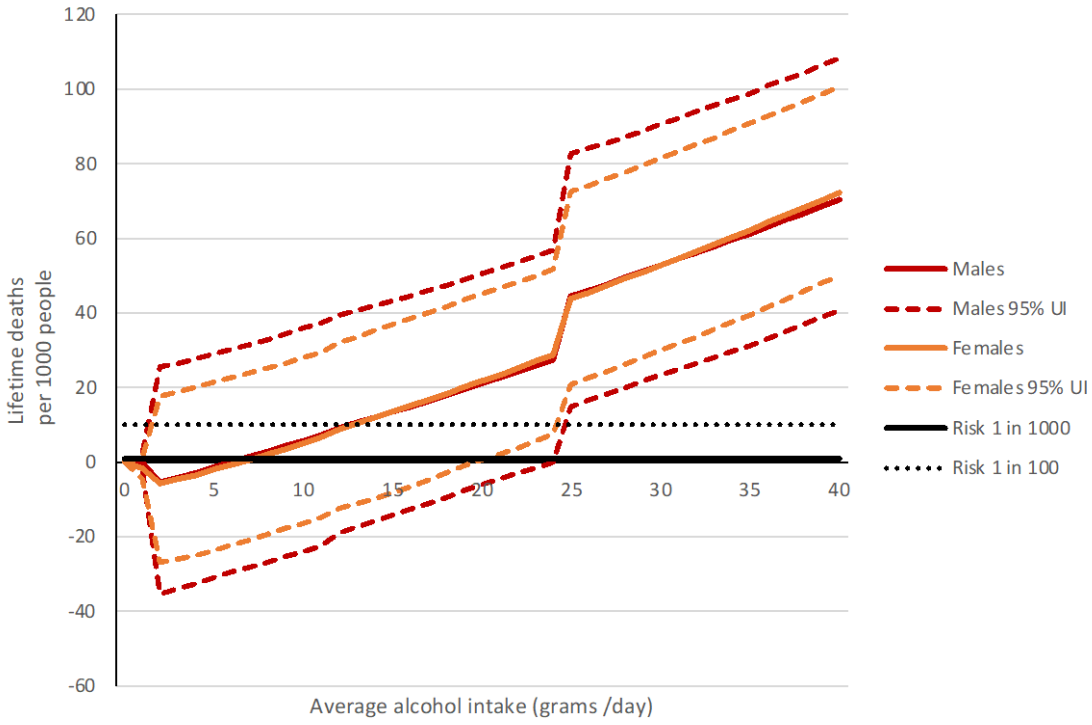


Figure 3. Lifetime risk of a premature death attributable to alcohol use at varying levels of average alcohol intake and risk references among males

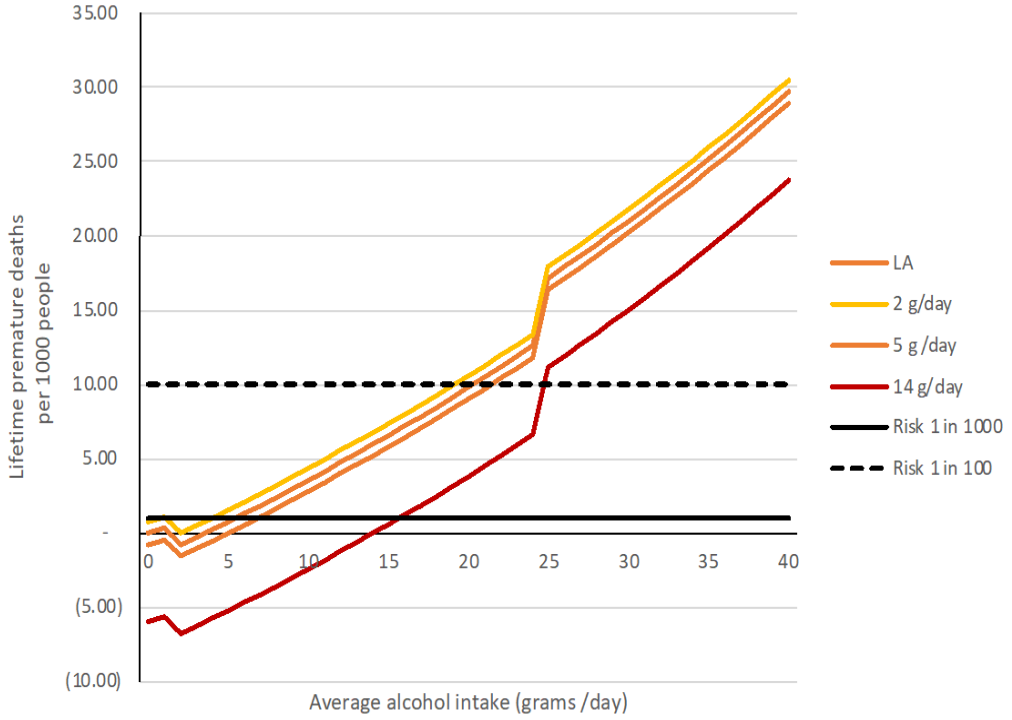


Figure 4. Lifetime risk of a premature death attributable to alcohol use at varying levels of average alcohol intake and risk references among females

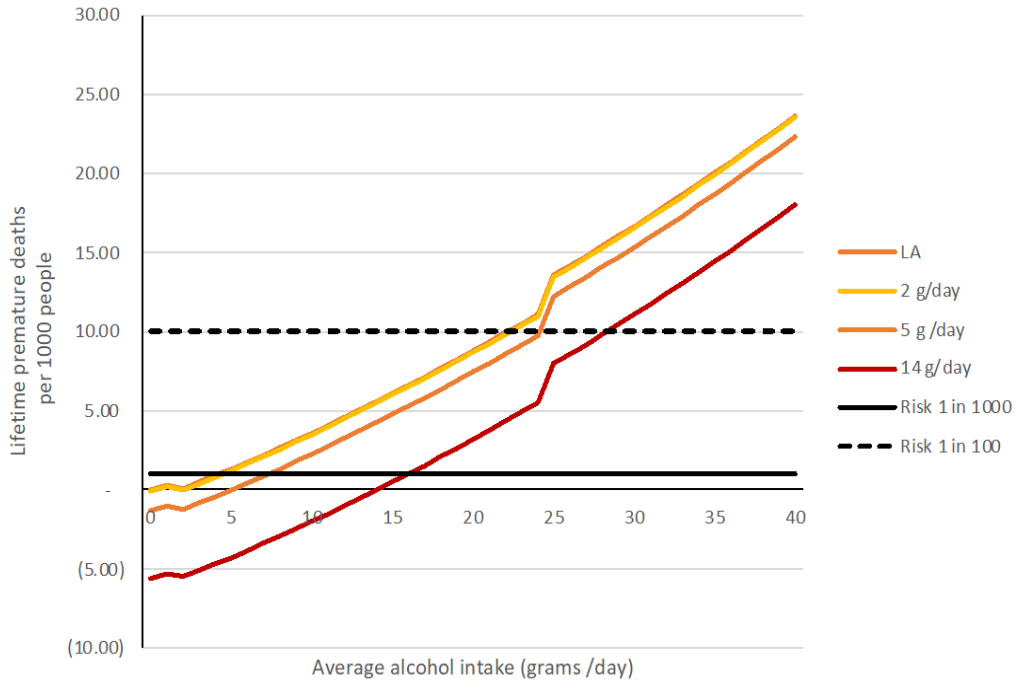


Figure 5. Lifetime risk of a death attributable to alcohol use at varying levels of average alcohol intake and risk references among males

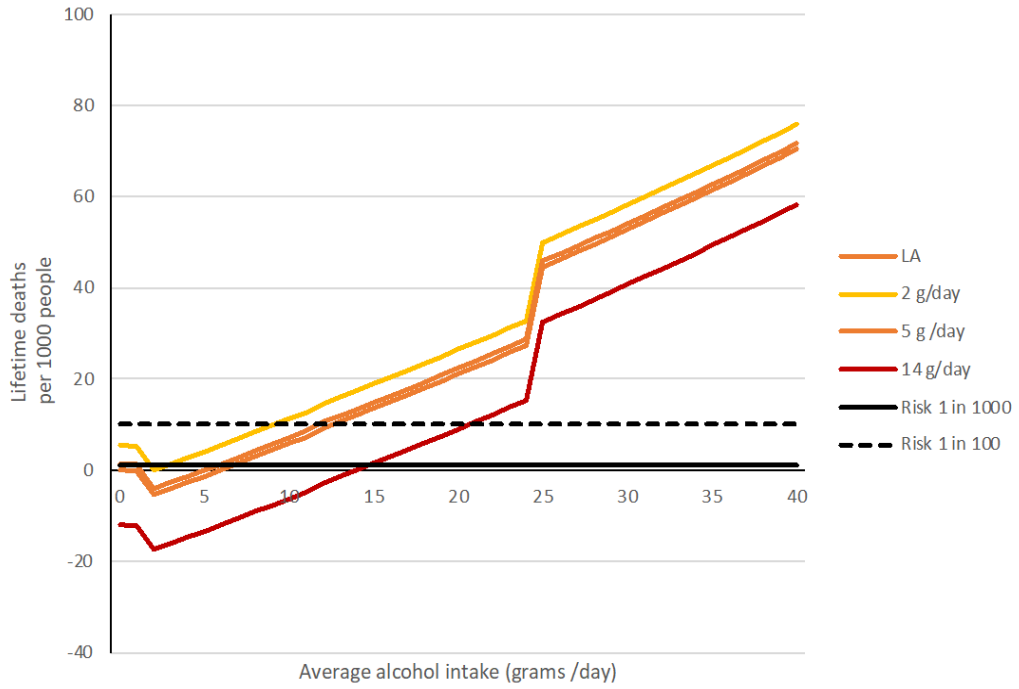
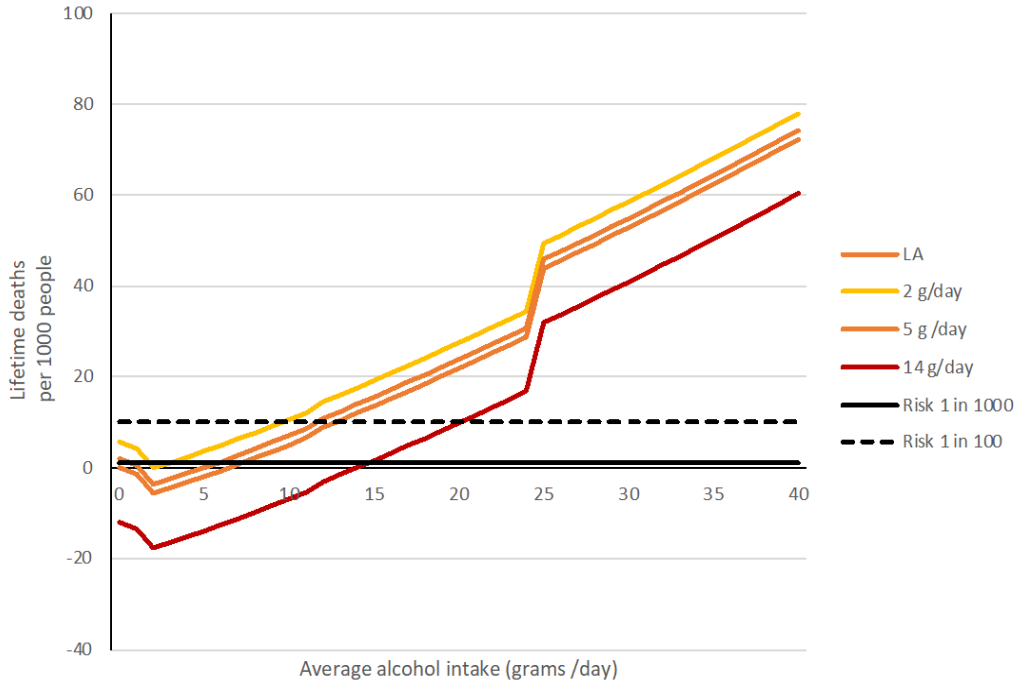


Figure 6. Lifetime risk of a death attributable to alcohol use at varying levels of average alcohol intake and risk references among females



Lifetime Risk of Alcohol-Attributable Years of Life Lost by Sex

The number of YLL increased as alcohol use increased among both males and females. Among males and females, a protective effect was observed for those consuming 2 to 3 g/day when compared to people who engaged in LA. In all cases, the 95% UIs crossed the null hypothesis and the protective effects should be interpreted with caution. The risk threshold based on 17.5 YLL in 1,000 lifetimes would be 4 (95% UI: <1, 16) g/day for males and 4 (95% UI: <1, 10) g/day for females, while the risk threshold based on 17.5 YLL in 100 lifetimes would be 11 (95% UI: 1, 22) g/day for males and 11 (95% UI: 1, 19) g/day for females (see Figure 7). The risk thresholds varied based on the reference point chosen for the TMREL (see Figures 8 and 9).

Figure 7. Lifetime risk of a year of life lost (YLL) attributable to alcohol use at varying levels of average alcohol intake

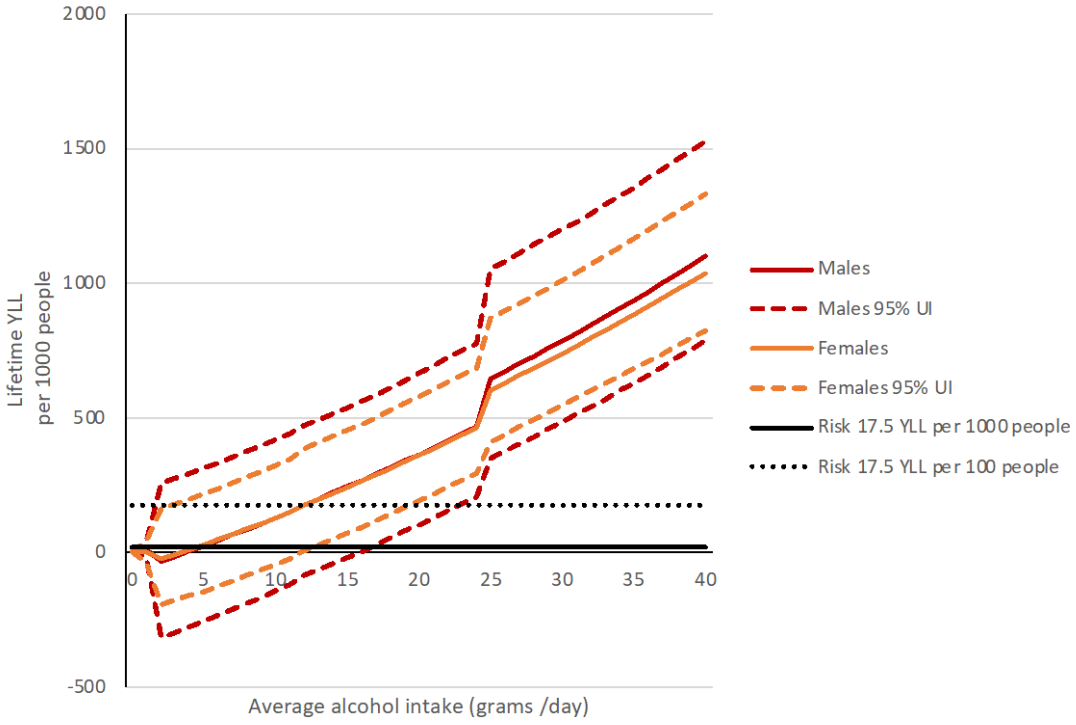


Figure 8. Lifetime risk of a year of life lost (YLL) attributable to alcohol use at varying levels of average alcohol intake and risk references among males

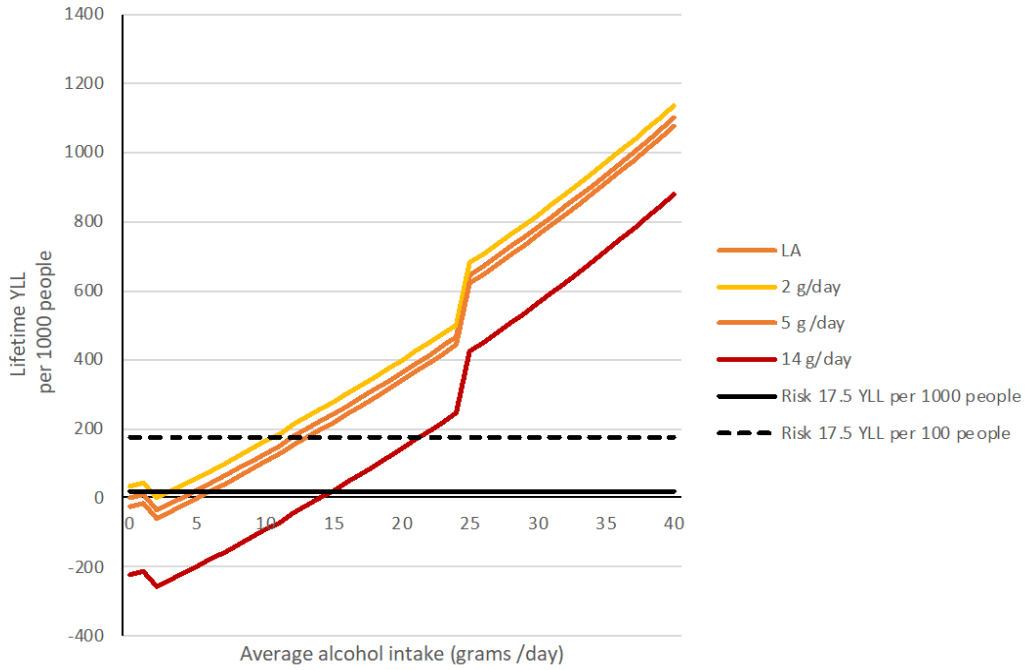
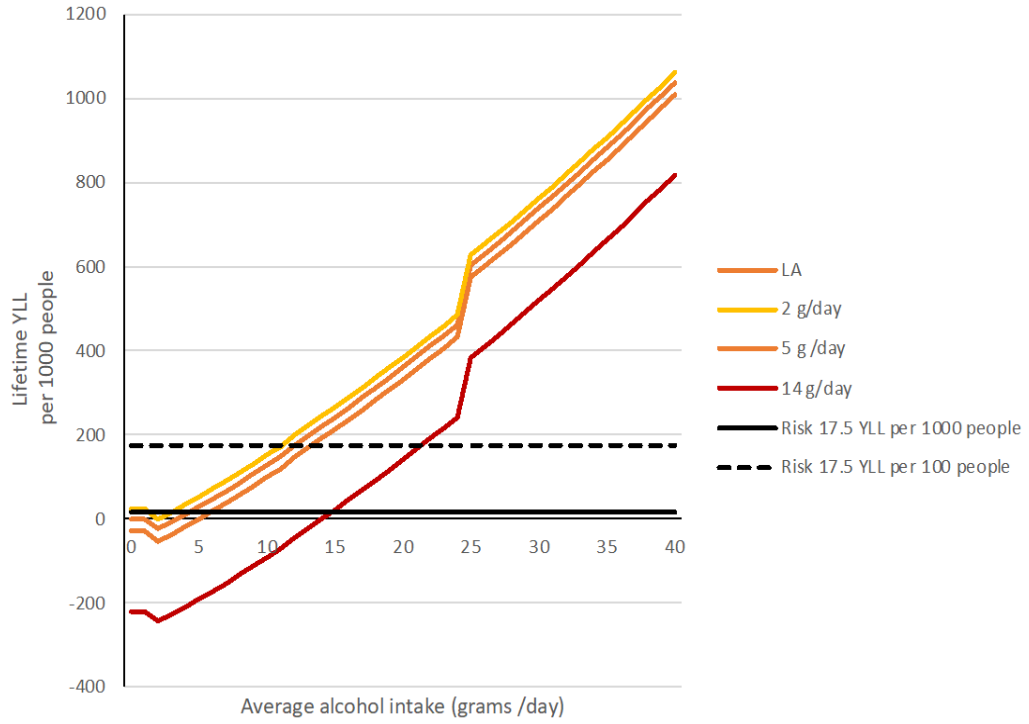


Figure 9. Lifetime risk of a year of life lost (YLL) attributable to alcohol use at varying levels of average alcohol intake and risk references among females



Lifetime Risk of Alcohol-Attributable Disability Adjusted Life Years Lost by Sex

The number of DALYs lost increased as alcohol use increased among both males and females. Among males and females, a protective effect was observed for those consuming 2 to 3 g/day for males and 1 to 3 g/day for females when compared to people who engaged in LA. In all cases, the 95% UIs crossed the null hypothesis and the protective effects should be interpreted with caution. The risk threshold based on 17.5 DALYs lost in 1,000 lifetimes would be 4 (95% UI: <1, 16) g/day for males and 4 (95% UI: <1, 12) g/day for females, while the risk threshold based on 17.5 DALYs lost in 100 lifetimes would be 11 (95% UI: 1, 22) g/day for males and 11 (95% UI: 1, 19) g/day for females (see Figure 10). The risk thresholds varied based on the reference point chosen for the TMREL (see Figures 11 and 12).

Figure 10. Lifetime risk of disability adjusted life years (DALYs) lost attributable to alcohol use at varying levels of average alcohol intake

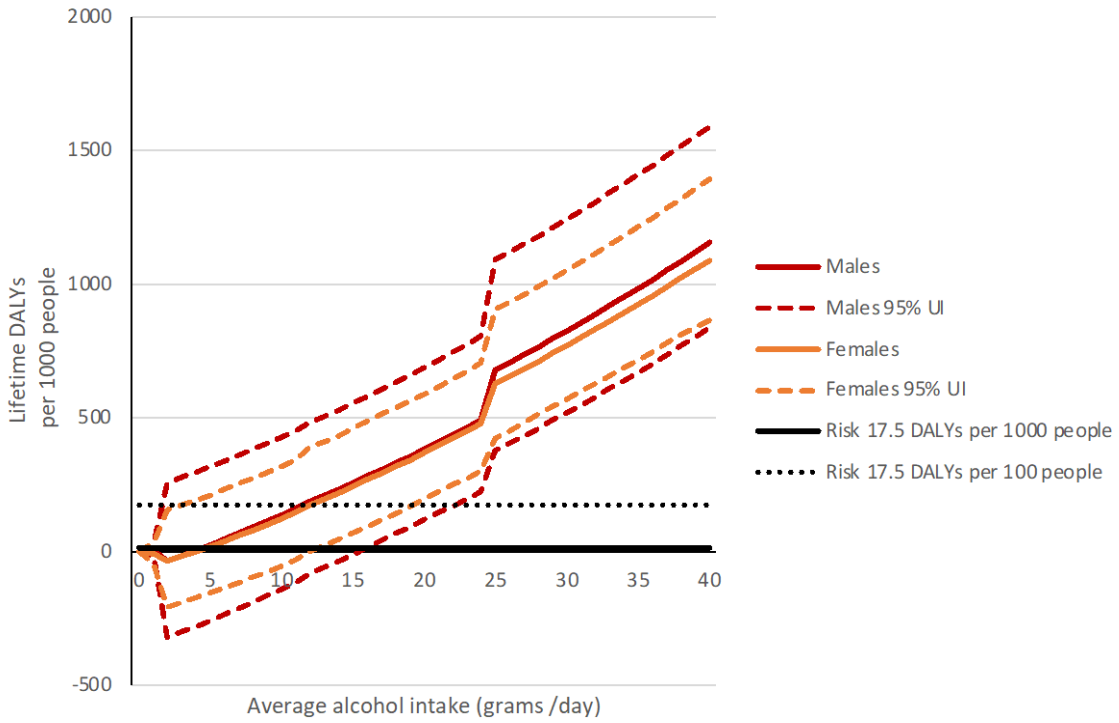


Figure 11. Lifetime risk of a disability adjusted life year (DALY) lost attributable to alcohol use at varying levels of average alcohol intake and risk references among males

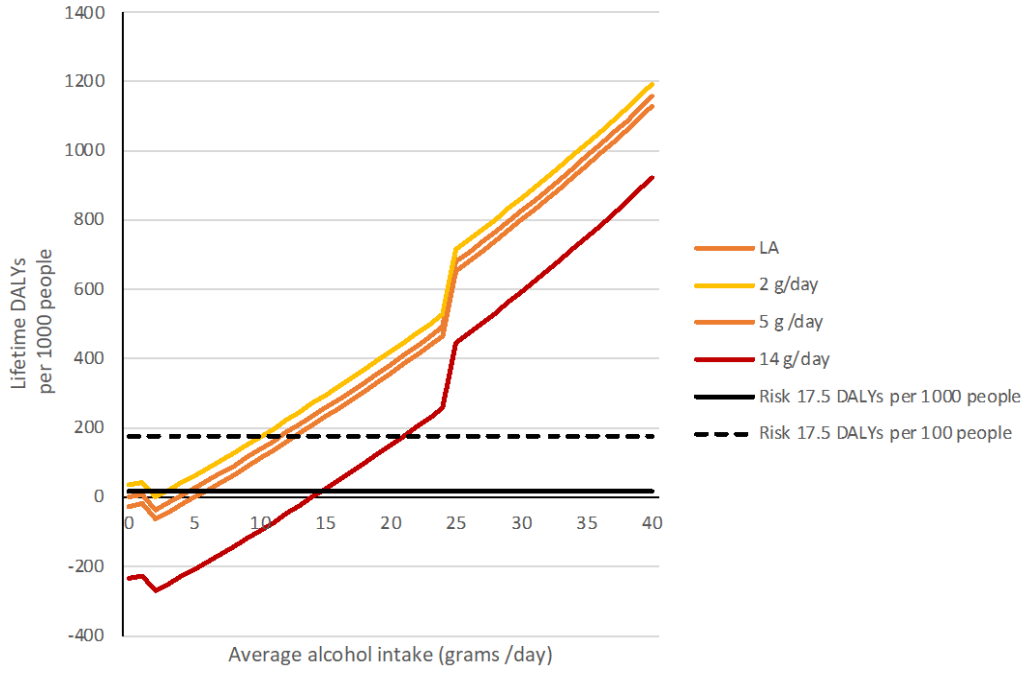
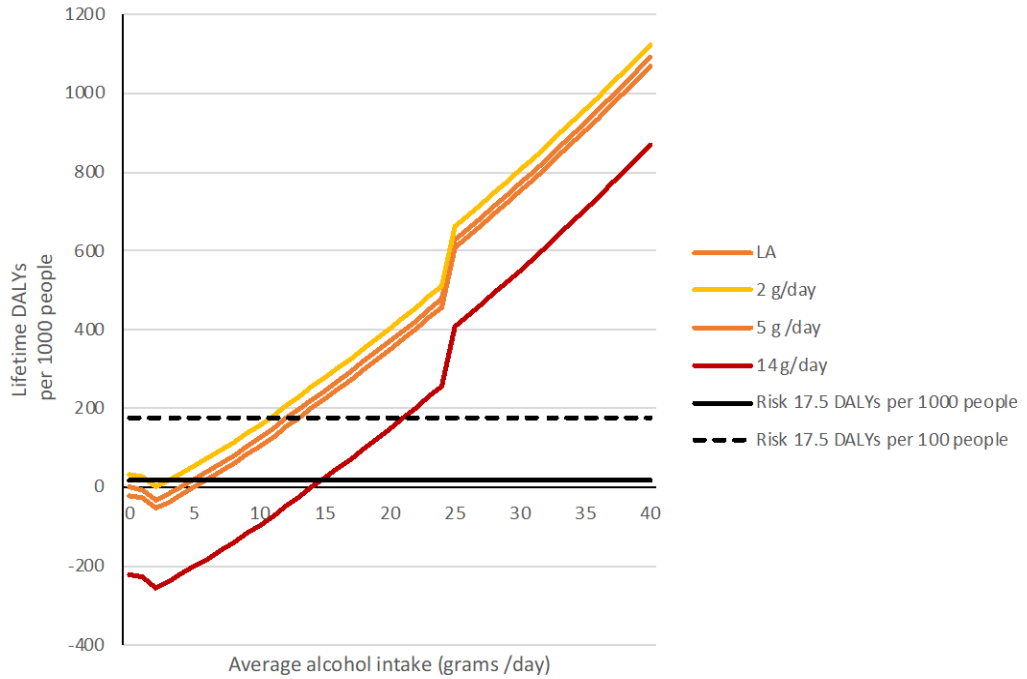


Figure 12. Lifetime risk of a disability adjusted life year (DALY) lost attributable to alcohol use at varying levels of average alcohol intake and risk references among females



Lifetime Deaths and Disability Under the 2011 LRDGs

Canada's 2011 LRDGs recommended consuming no more than 15 drinks a week for males (~29 g/day) and 10 drinks a week for females (~19 g/day). Consumption by males of 29 g/day would result in 51.1 (95%: 21.7, 88.8) deaths per 1,000 people, 20.2 (95%: 12.4, 31.4) premature deaths per 1,000 people, 756.7 YLL (95%: 457.6, 1,172.6) per 1,000 lifetimes, and 796.1 DALYs (95% UI: 492.4, 1,212.8) lost per 1,000 people. Consumption by females of 19 g/day would result in 20.1 (95%: -0.9, 43.4) deaths per 1,000 people, 8.2 (95%: 5.4, 12.3) premature deaths per 1,000 people, 335.8 (95%: 165.1,552.8) YLL per 1,000 lifetimes, and 344.5 DALYs (95% UI: 171.6, 563.6) lost per 1,000 people.

Discussion

The effects of alcohol use on health are numerous, with alcohol being causally related to over 200 codes for the international classification of disease (Rehm et al., 2017). Based on a systematic review of the published literature on the risk relationships between alcohol use and the occurrence of disease and injury, this study estimated that for people who live in Canada, the lifetime risk of death and disability attributable to alcohol use increases as the amount of alcohol use increases. The models did not demonstrate a significant protective effect at lower levels of alcohol use, so alcohol should not be promoted or used as a product to improve health.

The guidelines in this report were based on the health harms cause by ethanol in alcoholic beverages. They do not distinguish between harms caused by beer, wine, spirits and other alcoholic beverages. Harms caused by beer, wine, spirits and other alcoholic beverages are based mainly on ethanol content, regardless of the form in which ethanol is consumed. Alcohol poisonings, which are caused predominately by the consumption of spirits, are the one exception where the type of alcoholic beverage makes a difference (Rehm et al., 2017). Furthermore, the antioxidative and anti-carcinogenic properties of resveratrol have received media attention. However, it has been estimated that for every cancer prevented by resveratrol in red wine, the ethanol contained in red wine causes 100,000 cancer cases (Shield et al., 2016). The health benefits of resveratrol were not modelled as the effects of resveratrol on cancer prevention were considered to be negligible.

Alcohol Use, Addiction and Executive Functioning

The aim of this project is to estimate the risk of alcohol at different levels of consumption to help people who live in Canada make informed decisions about their alcohol use. However, numerous factors come into consideration when determining whether to consume alcohol. Alcohol is an addictive substance that provides positive and reinforcing effects (Brown et al., 1980; Cho et al., 2019). Furthermore, alcohol negatively impacts executive functioning at acute levels of intoxication and as a result of higher levels of chronic alcohol consumption (Guillot et al., 2010; Spinola et al., 2017). Therefore, the decision to limit alcohol consumption may be affected by the reinforcing effects of alcohol use and by impaired executive functioning.

Limitations

Our study is subject to limitations. First, the reported risks of alcohol use are based on average consumption and not on drinks consumed per drinking occasion. For instance, for people engaged in heavy episodic drinking (consuming ≥60 g on at least one occasion monthly), there is no protective effect of alcohol consumption on ischemic cardiovascular diseases (Roerecke & Rehm, 2010; Sundell et al., 2008). Drinking patterns can affect the risk of injury as this risk is lower for people who consume a consistent amount of alcohol over many days than for people who consume the same amount on fewer occasions. The mortality risk due to drinking patterns may also vary by country due to differences in, for example, road safety (World Health Organization, 2014). In this respect, our calculations are conservative: taking into account drinking patterns would lead to lower average guidelines as the alcohol-attributable mortality risk decreases at average moderate drinking levels and the more that consumption of the same amount of alcohol is spread out over time.

Second, statistical models are only as good as their input. The RRs were obtained from meta-analyses, which have been based on studies where participants may have underestimated their drinking, likely leading to higher guidelines. While there is literature on the average level of underestimation inherent in general population surveys (Midanik, 1982; Rehm et al., 2007), the

coverage rate of epidemiological studies is not that clear as different methods of assessment yield different results (King, 1994). Further, the standard is not clear, since sales or other administrative statistics for specific groups of people are not available. The use of food frequency questionnaires in more medical epidemiology settings may yield different results, as those questionnaires have been successfully validated and have yielded higher average consumption levels in experimental research (Giovannucci et al., 1991; King, 1994; Rehm, 1998b; Willett, 2012). Furthermore, the underlying RRs upon which the meta-analyses are based used as a reference category people who engaged in LA, leading to various biases (Rehm et al., 2008a), including a proportion of people who formerly drank alcohol being misclassified as people who engaged in LA, leading to an underestimation of the RRs (Zeisser et al., 2014). Additionally, the underlying cohort studies upon which the RRs are partially based typically follow middle-class participants who are middle aged, and so the cause-specific RRs from these studies may not apply to other segments of the population (Rehm, 2000; Rehm et al., 2003).

Third, as with other guidelines, alcohol-attributable health harms to others, such as low birth weight (Patra et al., 2011), traffic injuries (Hurst et al., 1994) and violence (Evans, 1980), were not accounted for, as guidelines are intended to inform people who drink alcohol about risks to themselves. This study was limited to alcohol's impact on mortality, and did not include (i) risk tolerance differences between countries and cultures (Weber & Hsee, 1998), (ii) alcohol's impact on society, the economy or morbidity, or (iii) the pleasure that people may obtain from drinking, which has been shown to be hard to quantify (Johansson et al., 2006), as guidelines for risk factors are set based on mortality alone (World Health Organization, 2014).

The mortality risks for alcohol-attributable diseases, other than alcohol use disorders, are based on RRs. This model could not be employed for alcohol use disorders as they are 100% alcohol-attributable by definition. In the case of alcohol use disorders, in some cases a method based on the prevalence of alcohol dependence among people with a given alcohol intake is used (Shield et al., 2017). However, this method may be flawed, especially at lower levels of alcohol use, as the risk of developing alcohol dependence would be very small for someone who consistently consumes two or fewer drinks per day.

The Long-Term Risk of Death and Disability Under the Proposed Updated Guidelines

The 2011 LRDGs recommended that males drink no more than 15 standard drinks per week (~29 g/day) and females drink no more than 10 standard drinks per week (~19 g/day) (Butt et al., 2011). The present analysis suggests that these thresholds are not consistent with the evidence and acceptable risk thresholds (1 in 100 or 1 in 1,000 lifetime deaths attributable to alcohol), and people who used these guidelines as a marker of risk may have experienced substantially more harm than originally hypothesized. The risks for long-term harm under the proposed updated guidelines also exclude numerous causes of death and disability where causality is not proven, such as for cancer of the stomach and pancreas (Rehm et al., 2017), or where an RR to model the relationship is not available from a high-quality cohort study, as for depression. Therefore, the presented lifetime risks may underestimate the harm caused by alcohol at lower consumption levels.

Risk Measurement

Guidelines, including the 2011 LRDGs, have been based on either total mortality or premature mortality attributable to alcohol use (Butt et al., 2011; National Health and Medical Research Council, 2020; Santé publique France, 2019; Shield et al., 2017; U.K. Chief Medical Officers, 2016).

However, the measurement of health outcomes using premature mortality ignores the deaths of older individuals (Lloyd-Sherlock et al., 2015). For Canada and other high-income countries, decreases in mortality risk at older ages have been credited as the main factor leading to improvements in life expectancies (Tarkiainen et al., 2012). Furthermore, the measurement of premature mortality gives equal importance to all premature deaths, regardless of the age at death, and so deaths at younger ages (15 to 30 years of age) and at older ages (older than 60 years of age) are weighted equally. Thus, if premature mortality or total mortality is the basis for establishing guidelines, the unequal health loss caused by deaths among people relatively young in age (Harris, 2006), which is the case with deaths attributable to alcohol use (Institute for Health Metrics and Evaluation, 2018; Rehm et al., 2017), will be ignored.

Summary health indicators, such as DALYs lost and health adjusted life expectancy (HALE), include non-fatal health outcomes. However, DALYs lost and HALE can be conceptually difficult to understand. Alcohol causes numerous disabling chronic illnesses that are not fatal (Rehm et al., 2017). Thus, summary health indicators are needed to measure the full health impact of alcohol. Furthermore, although it has been hypothesized that premature mortality is strongly correlated with YLL due to premature mortality and morbidity (Norheim et al., 2015), thereby justifying the use of premature mortality as a proxy measure of health loss, no analysis of this hypothesis exists to our knowledge. Thus, guidelines that use premature mortality or mortality as a measure of health may be flawed, and may lead to nonoptimal health strategies (Shield & Rehm, 2018).

The risk thresholds when based on YLL attributable to alcohol and DALYs lost attributable to alcohol were the same. Specifically, these thresholds result in low-risk drinking guidelines of 4 g/day to 11 g/day for both men and women using the health loss (YLL and DALYs lost) thresholds for 1,000 and 100 lifetimes, respectively. Therefore, the choice of YLL or DALYs lost as a risk outcome will not affect the low-risk threshold of alcohol use.

Conclusions

This report provides the information required to set thresholds for low-risk drinking guidelines based on the lifetime risks of death and disability associated with alcohol use. Although there are limitations to the modelling strategy, the presented risk estimates provide the most up-to-date knowledge on the risk relationship between alcohol consumption and health loss in Canada. As the lifetime risk of mortality and morbidity is similar for males and females in Canada, one guideline can be used. Based on the risk thresholds of 17.5 DALYs lost attributable to alcohol per 1,000 lifetimes or 100 lifetimes, alcohol use risk thresholds should ideally be set between 4 and 11 g/day for males and females in Canada.

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Appendix

Table 3. Increased risk of diseases and injuries for females based on average daily alcohol use

			Average alcohol intake (g/day)									
Disease or injury	Deaths per 100,000 people per year	Pre-mature deaths per 100,000 people per year	5	10	15	20	25	30	35	40	45	50
Ischemic heart disease	72.1	16.7	-5.0%	-5.0%	-5.0%	-5.0%	4.0%	4.0%	4.0%	4.0%	7.0%	7.0%
Breast cancer	28.3	17.3	4.7%	9.5%	14.7%	20.0%	25.6%	31.5%	37.6%	44.0%	50.7%	57.7%
Other un-intentional injuries	22.6	4.3	4.0%	8.1%	12.4%	16.8%	21.4%	26.3%	31.3%	36.5%	41.9%	47.5%
Lower respiratory infections	22.3	3.7	2.4%	4.9%	7.4%	10.0%	12.7%	15.4%	18.2%	21.0%	23.9%	26.9%
Colorectal cancer	21.0	9.2	3.4%	7.0%	10.7%	14.5%	18.4%	22.5%	26.7%	31.1%	35.6%	40.3%
Diabetes Mellitus	12.6	4.7	-21.6%	-26.9%	-30.0%	-31.9%	-33.2%	-34.0%	-34.4%	-34.6%	-34.6%	-34.4%
Hyperten-sion	11.3	1.9	3.0%	6.0%	8.9%	11.8%	14.9%	18.0%	21.4%	24.8%	28.4%	32.0%
Atrial fibrillation and flutter	10.4	0.6	3.3%	6.6%	10.1%	13.7%	17.4%	21.2%	25.2%	29.2%	33.5%	37.8%
Intra-cerebral hemor-rhage	8.6	2.4	-8.0%	-8.0%	-1.0%	-1.0%	25.0%	25.0%	25.0%	25.0%	25.0%	67.0%
Liver cirrhosis	6.9	5.5	109.5%	182.1%	254.9%	330.8%	411.2%	496.7%	588.0%	685.5%	789.6%	900.9%
Ischemic stroke	6.5	1.1	-10.0%	-10.0%	-8.0%	-8.0%	8.0%	8.0%	8.0%	8.0%	8.0%	14.0%
Liver cancer	6.0	3.2	2.0%	4.0%	6.1%	8.2%	10.3%	12.5%	14.7%	17.0%	19.3%	21.7%
Intentional injuries	5.8	5.9	13.3%	28.3%	45.4%	64.7%	86.6%	111.4%	139.4%	171.2%	207.3%	248.1%
Road injuries	2.8	2.5	4.9%	10.1%	15.5%	21.2%	27.1%	33.4%	39.9%	46.8%	54.0%	61.6%
Oesoph-agus cancer	2.6	1.5	6.8%	14.1%	21.9%	30.2%	39.0%	48.4%	58.5%	69.1%	80.5%	92.5%

Subarach-noid haemorr-hage	2.4	1.7	21.0 %	21.0%	11.0%	11.0%	39.0%	39.0%	39.0%	39.0%	39.0%	82.0%
Oral cavity and pharynx cancer	2.2	1.2	13.1 %	27.6%	43.6%	61.4%	81.0%	102.6 %	126.3 %	152.3 %	180.8 %	211.7 %
Pancreatitis	1.2	0.5	-12.7%	-22.7%	-28.3%	-28.4%	-23.9%	-15.0%	-2.0%	14.8%	34.9%	58.4%
Epilepsy	0.7	0.4	7.0%	13.8%	21.0%	28.6%	36.8%	45.5%	54.7%	64.5%	74.9%	86.0%
Larynx cancer	0.3	0.2	7.5%	15.5%	24.0%	32.9%	42.3%	52.3%	62.8%	73.8%	85.4%	97.6%
Tuber-culosis	0.2	0.1	9.4%	19.7%	30.9%	43.2%	56.7%	71.4%	87.6%	105.2 %	124.5 %	145.6 %

Dark red > 50%; light red 20% to 50%; yellow 10% to <20%; green <-10%

Table 4. Increased risk of diseases and injuries for males based on average daily alcohol use

			Average alcohol intake (g/day)									
Disease or injury	Deaths per 100,000 people per year	Pre-mature deaths per 100,000 people per year	5	10	15	20	25	30	35	40	45	50
Ischemic heart disease	104.1		-5.0%	-5.0%	-5.0%	-5.0%	4.0%	4.0%	4.0%	4.0%	7.0%	7.0%
Colorectal cancer	25.6	13.9	3.4%	7.0%	10.7%	14.5%	18.4%	22.5%	26.7%	31.1%	35.6%	40.3%
Other unin-tentional injuries	23.2	9.8	4.0%	8.1%	12.4%	16.8%	21.4%	26.3%	31.3%	36.5%	41.9%	47.5%
Lower respiratory infections	19.3	5.1	2.4%	4.9%	7.4%	10.0%	12.7%	15.4%	18.2%	21.0%	23.9%	26.9%
Intentional injuries	18.0	17.9	13.3 %	28.3 %	45.4%	64.7%	86.6%	111.4 %	139.4 %	171.2 %	207.3 %	248.1%
Diabetes Mellitus	16.8	9.0	0.0%	0.2%	0.4%	0.6%	1.0%	1.4%	1.9%	2.4%	3.0%	3.6%
Liver cirrhosis	12.2	10.3	15.5 %	32.9 %	52.8%	75.7%	102.0 %	132.3 %	167.1 %	207.1 %	253.2 %	306.1%
Liver cancer	11.1	7.5	2.0%	4.0%	6.1%	8.2%	10.3%	12.5%	14.7%	17.0%	19.3%	21.7%
Oesopha-gus cancer	9.0	6.2	6.8%	14.1 %	21.9%	30.2%	39.0%	48.4%	58.5%	69.1%	80.5%	92.5%
Hyper-tension	8.4	3.4	7.2%	15.0 %	19.0%	23.2%	27.5%	32.0%	34.0%	35.9%	38.0%	40.0%
Intra-cerebral hemor-rhage	8.2	3.3	-8.0%	-8.0%	-1.0%	-1.0%	25.0%	25.0%	25.0%	25.0%	25.0%	67.0%
Atrial fibrillation and flutter	6.6	1.0	3.3%	6.6%	10.1%	13.7%	17.4%	21.2%	25.2%	29.2%	33.5%	37.8%
Road injuries	6.0	5.6	7.6%	15.9%	24.7%	34.2%	44.5%	55.5%	67.4%	80.2%	93.9%	108.7%
Ischemic stroke	5.7	1.9	-8.0%	-8.0%	-8.0%	-8.0%	8.0%	8.0%	8.0%	8.0%	8.0%	14.0%
Oral cavity and pharynx cancer	5.2	3.6	13.1 %	27.6%	43.6%	61.4%	81.0%	102.6 %	126.3 %	152.3 %	180.8 %	211.7%
Larynx cancer	1.8	1.1	7.5%	15.5%	24.0%	32.9%	42.3%	52.3%	62.8%	73.8%	85.4%	97.6%

Subarach-noid haemorr-hage	1.6	1.2	21.0 %	21.0%	11.0%	11.0%	39.0%	39.0%	39.0%	39.0%	39.0%	82.0%
Pancreatitis	1.5	0.9	9.1%	18.9%	29.7%	41.5%	54.3%	68.3%	83.5%	100.1 %	118.3 %	138.0%
Epilepsy	0.7	0.6	7.0%	13.8%	21.0%	28.6%	36.8%	45.5%	54.7%	64.5%	74.9%	86.0%
Tuber-culosis	0.3	0.2	9.4%	19.7%	30.9%	43.2%	56.7%	71.4%	87.6%	105.2 %	124.5 %	145.6%

Dark red > 50%; light red 20% to 50%; yellow 10% to <20%