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Canada's Guidance on Alcohol and Health: Final Report

January 2023



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- Sam Churchill, Tim Naimi and Adam Sherk: Lifetime Risk of Alcohol-Attributable Death and Disability: Shadow Analysis (Appendix 1)
- Tim Naimi: Per occasion alcohol use
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- Nancy Poole and Lorraine Greaves: Specific Messages for Girls and Women to Supplement the Guidance on Alcohol and Health (see Appendix 3)
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Conflict of Interest

The list of potential conflicts of interest for all participants in the project is available on CCSA's website: <u>Disclosure of Affiliations and Interests</u>.

About this Document

This report contains three documents produced for three different target groups.

Public Summary

The Public Summary is a one-page summary intended for the general public.

Technical Summary

The Technical Summary is intended for health organizations, health professionals (e.g., physicians, nurses, counsellors) and people who would like to learn about the update of the Low-Risk Alcohol Drinking Guidelines, its key takeaways, the risks associated with alcohol and the implications.

Technical Report

The Technical Report is intended for alcohol scientists, policy makers and healthcare professionals who are interested in understanding the detailed process followed, the types of evidence and the way they were used to update the Low-Risk Alcohol Drinking Guidelines.

The three documents in this report were made available for public consultation from Aug. 29 through Sept. 23, 2022. The report has been modified in response to that consultation. For details on the comments made during the consultation and the response to those comments, see Appendix 4.

Notes on Sex and Gender Terminology

Alcohol use has risks, effects, influences and consequences specific to sex and gender. In real life experience, sex and gender interact with each other, and with other intersectional characteristics to shape the impacts of alcohol use.

The effects and impacts of sex and gender on alcohol use among sub-populations such as Indigenous Peoples, older people, sexual minorities and gender minorities remain under-researched or unknown. As evidence about alcohol and social patterns of drinking evolves, it will be important to continuously reassess the impact of alcohol on all populations, and to create appropriate public health and health promotion advice for all populations.

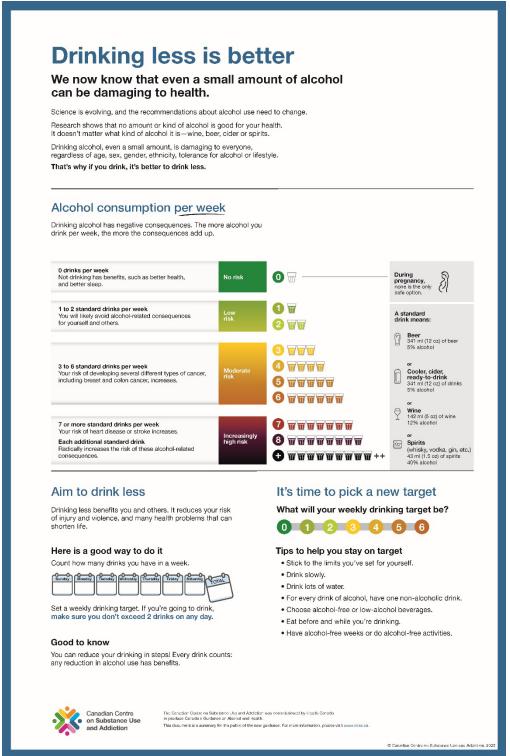
Throughout this report, when presenting sex-related risks, the terms female and male are used. When presenting gender-related risks, the terms women and men are used. When a section or topic involves the entanglement of sex and gender, the terms women and men are used.

Notes on a Standard Drink

In Canada, a standard drink is 17.05 millilitres or 13.45 grams of pure alcohol, which is the equivalent of:

- A bottle of beer (12 oz., 341 ml, 5% alcohol)
- A bottle of cider (12 oz., 341 ml, 5% alcohol)
- A glass of wine (5 oz., 142 ml, 12% alcohol)
- A shot glass of spirits (1.5 oz., 43 ml, 40% alcohol)

Public Summary



Note. For a PDF of this image, visit https://ccsa.ca/canadas-guidance-alcohol-and-health-public-summary-drinking-less-better-infographic

Technical Summary

Alcohol is a psychoactive substance used by about three-quarters of people living in Canada. It is often used in connection with social events or to mark special occasions. However, alcohol can cause harm to the person who drinks and sometimes to others around them. Alcohol is a leading preventable cause of death, disability and social problems, including certain cancers, cardiovascular disease, liver disease, unintentional injuries and violence. In 2017, alcohol caused 18,000 deaths in Canada. That same year, the costs associated with alcohol use in Canada were \$16.6 billion, with \$5.4 billion of that sum spent on health care.

To make more informed decisions about alcohol use, people living in Canada must be aware of important information about alcohol and health, assess their personal risk and consider reducing their alcohol use. Taken together, overwhelming evidence confirms that when it comes to drinking alcohol, less consumption means less risk of harm from alcohol.

Canada's Guidance on Alcohol and Health

To reduce the risk of harm from alcohol, it is recommended that people living in Canada consider reducing their alcohol use.

The reasons to do so derive from the following facts:

- a. There is a continuum of risk associated with weekly alcohol consumption where the risk of harm from alcohol is:
 - Low for individuals who consume 2 standard drinks or less per week;
 - Moderate for those who consume between 3 and 6 standard drinks per week; and
 - Increasingly high for those who consume 7 standard drinks or more per week.
- b. Consuming more than **2** standard drinks per drinking occasion is associated with an increased risk of harms to self and others, including injuries and violence.
- c. When pregnant or trying to get pregnant, there is no known safe amount of alcohol use.
- d. When breastfeeding, not drinking alcohol is safest.

Sex and Gender

Above the upper limit of the moderate risk zone for alcohol consumption, the health risks increase more steeply for females than males.

Far more injuries, violence and deaths result from men's alcohol use, especially in the case of per occasion drinking.

Aim and Approach

Canada's Guidance on Alcohol and Health is informed by a public health perspective. It is intended to replace Canada's Low-Risk Alcohol Drinking Guidelines. It provides accurate and current information about the risks and harms associated with the use of alcohol. The guidance should help people make well-informed and responsible decisions about their alcohol consumption.

The guidance is based on the principle of autonomy in harm reduction and a fundamental idea behind it is that **people living in Canada have a right to know.**

It is hoped that the guidance will be used to develop messaging that speaks directly to the unique concerns of people with diverse backgrounds and personal experiences. It should serve to improve alcohol literacy, providing information and suggestions so people are able to make their own choices about how much they drink. The guidance will support health professionals, family doctors and nurses who are crucial allies to help people assess their individual risk of harm from alcohol use.

The Guidance on Alcohol and Health is also intended to contribute to an evidence base for future alcohol policy and prevention resources, with a view to changing Canada's drinking culture and curbing the normalization of harmful alcohol use in society.

The production of the Guidance on Alcohol and Health followed a rigorous and transparent approach to assess the impact of various levels of alcohol use on deaths and disabilities. The analyses were based on the most recent data and methods, which have evolved since the Low-Risk Alcohol Drinking Guidelines were released in 2011. Analyses were supplemented by additional reviews on specific topics and consultations with the public and experts.

Risk Associated with Weekly Levels of Alcohol Use

Throughout the life course, there are established thresholds of mortality risk that people are willing to accept. For example, for involuntary risks such as air pollution, a 1 in 1,000,000 lifetime mortality risk has been used as a gold standard. That is, people are willing to accept a negligible 1 in 1,000,000 risk of premature death when exposed to these risks.

- For risks associated with activities that people undertake deliberately and by choice, such as unprotected sexual practices, smoking and so on, people may accept a level of risk that is about 1,000 times greater than the one for involuntary risk. Hence, advice and recommendations made to people about voluntary activities generally use a low risk level, equivalent to a 1 in 1,000 risk of premature death.
- However, for drinking alcohol, it is not unusual for guidelines to be based on a higher risk threshold, 10 times that of voluntary activities. Recommendations for alcohol use have often used a moderate risk level, equivalent to a 1 in 100 risk of premature death.

Using these different thresholds, this project's estimates make it possible to put forward a clear continuum of risk whereby the risk for those who consume 2 standard drinks or less per week is low, it is moderate for those who consume between 3 and 6 standard drinks per week, and it is increasingly high for those who consume above 6 standard drinks per week, with increasing risk conferred by every additional drink.

Figure 1. Continuum of risk associated with average weekly alcohol consumption



People should not start to use alcohol or increase their alcohol use for health benefits. Any reduction in alcohol use is beneficial. This applies even for those who are unable or unwilling to reduce their risk to low or moderate levels. In fact, those consuming high levels of alcohol have even more to gain by reducing their consumption by as much they are able.

Figure 2. Illustration of examples standard drinks



Risk Associated with Alcohol Use Per Occasion

On any drinking occasion, the risk of acute outcomes such as unintentional injuries and violence is strongly associated with cognitive and physical impairment from consuming too much alcohol. The risk of negative outcomes begins to increase with any alcohol use and consuming more than 2 standard drinks per occasion is associated with a significant increased risk of harms to self and others.

Binge drinking, usually defined as consuming five or more standard drinks in one setting for men, or four or more standard drinks in one setting for women, is a pattern of consumption that results in legal impairment for most people. It is a well-established risk factor for death from any cause,

including unintentional injuries, violence, heart disease and high blood pressure, and inflammation of the gastrointestinal system, and for developing an alcohol use disorder (i.e., alcohol dependence).

Many of the complications arising from acute impairment and binge drinking involve second-hand effects that affect someone other than the person who drinks alcohol (e.g., violence, road crashes, child abuse and neglect).

Risk when Pregnant, Trying to Get Pregnant or Breastfeeding

Alcohol is a teratogen or agent that can cause malformation of the fetus. It can lead to learning, health and social effects with lifelong impacts on the fetus as well as brain injury, birth defects, behavioural problems, learning disabilities and other health problems typically referred to as fetal alcohol spectrum disorder (FASD). These adverse effects are also observed at low levels of exposure or short-term exposure to high levels of consumption. For this reason, when pregnant or trying to get pregnant, there is no known safe amount of alcohol use. Reproductive health is compromised by alcohol use. Possible impacts of alcohol on pregnancy and delivery outcomes include increases in miscarriage, hypertensive disorders of pregnancy and placental abnormalities.

Alcohol consumption can also negatively impact breastfeeding by causing a decrease in milk production, early cessation of breastfeeding and effects on infant sleep patterns. Moreover, alcohol enters breast milk through passive diffusion meaning that breastfeeding infants, who are less able to metabolize alcohol, can be exposed to it. Therefore, when breastfeeding, no alcohol use is safest for the baby. Consuming a standard drink on occasion can be okay, as long as it is planned. It takes about two hours for the alcohol contained in a standard drink to be eliminated from the body and leave the breastmilk.

Sex and Gender

Alcohol use and harms are influenced by both sex-based physiological differences, as well as many gender-related factors, including alcohol marketing tactics, and gender roles, attitudes and expectations. Many harms from alcohol use are gender-related, including stigma, sexual assault and intimate partner violence.

Risk for Women

The physiological differences between females and males at low levels of alcohol use have only a small impact on lifetime risk of death. However, it is unequivocal that **above the upper limit of the moderate risk zone for alcohol consumption (above 6 standard drinks per week), the health risks increase more steeply for females than for males.** Enzymes, genes, lean body weight and size, organ function and metabolism are important in processing alcohol and are affected by sex-related factors. These biological factors enhance the impact of alcohol on females, causing higher blood alcohol levels, faster intoxication, more risk for disease, including breast cancer, and more long-term harm, such as liver damage and injury.

Risk for Men

Men drink more alcohol than women and are more likely to drink in excess. Consequently, they are more likely to be involved in alcohol-impaired driving collisions, to be treated in hospitals and hospitalized for alcohol-related medical emergencies and health problems, to be diagnosed with an

alcohol use disorder and to die from alcohol-related causes. Alcohol is also more strongly associated with perpetration of violence for men than for women.

Men are also more likely than women to take other risks (e.g., use other substances, drive under the influence) that when combined with alcohol further increase their likelihood of experiencing and causing alcohol-related harms. Overall, far more injuries, violence and deaths result from men's alcohol use, especially in the case of per-occasion drinking.

Youth

Alcohol use is a leading behavioural risk factor for death and social problems among youth and young adults, and alcohol is the most common psychoactive substance used by this age group. A high proportion of alcohol consumed by youth is in the form of binge drinking with its attendant risks of injuries, aggression, violence and other age-important consequences such as dating violence and worsening academic performance. In addition, even for the same number of drinks consumed per drinking occasion, the risk of adverse outcomes from alcohol consumption is greater for youth than for adults. This may be due to several factors, including greater impulsivity and less emotional maturity among youth, lower body mass on average, less experience doing complex tasks that are made more dangerous by alcohol (e.g., operating a motor vehicle) and faster drinking speeds.

For this reason, recommendations related to the risks associated with weekly levels of alcohol use and alcohol use per occasion do not apply to youth under the legal drinking age. For them, the main message should be to **delay alcohol use for as long as possible.**

When Zero's the Limit

There are circumstances when no alcohol use is safest. For example, when:

- Driving a motor vehicle;
- Using machinery and tools;
- Taking medicine or other drugs that interact with alcohol;
- Doing any kind of dangerous physical activity;
- Being responsible for the safety of others; and
- Making important decisions.

Reasons for the New Guidance on Alcohol and Health

Alcohol and Cancer

Cancer is the leading cause of death in Canada. However, the fact that **alcohol is a carcinogen that can cause at least seven types of cancer** is often unknown or overlooked. The most recent available data show that the use of alcohol causes nearly 7,000 cases of cancer deaths each year in Canada, with most cases being breast or colon cancer, followed by cancers of the rectum, mouth and throat, liver, esophagus and larynx. According to the Canadian Cancer Society, drinking less alcohol is among the top 10 behaviours to reduce cancer risk.

Alcohol and Heart Disease

After cancer, heart disease is the second leading cause of death in Canada. For many years, the commonly held belief that drinking in moderation offered protection against coronary artery disease

has been widely publicized. Research in the last decade is more nuanced with the most recent and highest quality systematic reviews showing that **drinking a little alcohol neither decreases nor increases the risk of ischemic heart disease, but it is a risk factor for most other types of cardiovascular disease,** including, hypertension, heart failure, high blood pressure, atrial fibrillation and hemorrhagic stroke.

Alcohol and Liver Disease

Statistics show that **liver disease is on the rise in Canada, and alcohol is one of its main causes.**Drinking a large amount of alcohol, even for just a few days, can lead to a build-up of fat in the liver. This is called alcohol-associated fatty liver. A more severe form of alcohol-related liver disease is called alcohol-associated hepatitis, which is generally caused by alcohol abuse or, less commonly, when people consume large amount of alcohol in a short period of time (binge drinking). Eventually, ongoing alcohol-related liver injury can lead to the development of scar tissue in the liver, termed fibrosis, which can lead to life-threatening cirrhosis and liver cancer.

Alcohol and Violence

Alcohol is frequently associated with violent and aggressive behaviour, including intimate partner violence, male-to-female sexual violence, and aggression and violence between adults. Alcohol can also increase the severity of violent incidents. No exact dose–response relationship can be established but consuming alcohol increases the risk of perpetrating alcohol-related violence. It is therefore reasonable to infer that individuals can reduce their risk of perpetrating aggressive or violent acts by limiting their alcohol use. Based on consistent evidence, it is highly likely that avoiding drinking to intoxication will reduce individuals' risk of perpetrating alcohol-related violence.

Policy Implications

To support people living in Canada who will want to drink less, governments, working in close collaboration with employers, healthcare providers and community stakeholders, need to implement policies that promote public health. Such policies include strengthening regulations on alcohol advertising and marketing, increasing restrictions on the physical availability of alcohol, and adopting minimum prices for alcohol.

As a priority, people living in Canada need consistent, easy-to-use information at the point of pour to track their alcohol use in terms of standard drinks. They also have a right to clear and accessible information about the health and safety of the products they buy. A direct consequence of the current project is that a particular effective policy change could be the mandatory labelling of all alcoholic beverages with the number of standard drinks in a container, Canada's Guidance on Alcohol and Health and health warnings.

Technical Report

Introduction

Canada's first Low-Risk Alcohol Drinking Guidelines (LRDGs) were originally published by the Canadian Centre on Substance Use and Addiction (CCSA) in November 2011 (Butt et al., 2011). The guidelines were developed by an independent expert working group, with members drawn from Canadian addiction research agencies. The 2011 LRDGs provided people living in Canada with advice on how to minimize relative long-term risk of serious diseases caused by the consumption of alcohol over a number of years (e.g., liver disease, some cancers) and relative short-term risk of injury or acute illness due to the overconsumption of alcohol on a single occasion (Stockwell et al., 2012). In addition, specific recommendations were provided for situations and individual circumstances that are particularly hazardous and for which abstinence or only occasional light intake was advised (e.g., just before or during pregnancy, teenagers, people on medication). The guidelines also included tips for safer drinking and the definition of a standard drink. The 2011 LRDGs were a significant step to providing consistent information and messaging for minimizing the risk associated with drinking alcohol. They have provided the cornerstone for undertaking a variety of health promotion, prevention and education initiatives across the country (Paradis, 2016).

Still, there were important limitations with the research evidence used to develop the 2011 LRDGs. In the LRDG technical report (Butt et al., 2011), the working group noted the under-reporting of personal alcohol use in self-reported surveys, the failure to take account of heavy drinking episodes in many epidemiological studies, the misclassification of former and occasional drinkers as lifetime abstainers, and the failure to control for confounding effects of personality and lifestyle factors independent of alcohol. In its quality appraisal, using the AGREE II instrument, the Public Health Agency of Canada (PHAC) further noted limitations, particularly with respect to the rigour of development and editorial independence, two domains that did not receive the minimum acceptable score of 60%. Consequently, the 2011 LRDGs received an overall assessment of 60.7% and so did not meet the criteria for high quality guidelines. They were recommended for use with modifications, and since then it has been known that careful consideration would need to be paid to these limitations when developing alcohol guidelines.

Awareness and Adherence to the 2011 LRDGs by People Living in Canada

Since their publication, the 2011 LRDGs have been promoted to varying degrees across the country and adopted differently by key demographics. In 2012, just a few months after the release of the guidelines, a national survey indicated that a quarter (26%) of people living in Canada had seen or heard of the LRDGs. Since then, a few provincial studies have recorded people's awareness of the LRDGs. In 2017, Public Health Ontario surveyed 2,000 adults in Ontario aged 19 and older who consume alcohol and found that less than a fifth (17%) were aware of the 2011 LRDGs (Public Health Ontario, 2017a). In 2019–2020, the new Canadian Postsecondary Education Alcohol and Drug Use Survey (CPADS) surveyed students in colleges and universities in Canada about their knowledge of the 2011 LRDGs (Health Canada, 2021). Not surprisingly, within this young group, awareness was negligible with only 16% reporting to have heard about the guidelines and less than a third of those (28%), being able to accurately report what the guidelines were.

In Quebec, significant resources have been invested to disseminate and promote the 2011 LRDGs (Paradis, 2016). No study has specifically surveyed Quebecers' knowledge of the guidelines, but a

study conducted by the Institut national de santé publique du Québec found that 55% of Quebecers thought the 2011 LRDGs were adequate, while 37% believed they were too high, that is, corresponded to larger amounts of alcohol than what they consider to be low-risk drinking (Bergeron et al., 2021).

According to the most recent data from the Canadian Alcohol and Drugs Survey (CADS, Health Canada, 2019), a majority of people living in Canada indicated drinking within the 2011 LRDGs. In 2019, 83% of the people aged 15 years and older who consumed alcohol in the past year reported to drink within the guidelines for shortterm risk and 77% within those for long-term risk. While more females than males reported to drink alcohol within the guidelines for short-term risk (85% vs 81%), the percentages were similar for the long-term risk guideline (76% for males vs. 78% for females). Young adults between the ages of 20-24 were less likely than other age groups to drink within the guidelines. In 2019, threequarters (74%) followed the guideline for shortterm risk of injury and harm while 69% reported to follow the guidelines for long-term health risk.

Canada's 2011 LRDGs

The 2011 LRDGs recommended people who consume alcohol to reduce:

- Long-term health risk by drinking no more than 10 standard drinks a week for women, with no more than two drinks a day most days, or 15 standard drinks a week for men, with no more than two drinks a day most days.
- Short-term risk of injury and harm by drinking no more than three standard drinks for women or four standard drinks for men on any single occasion.

While the percentages seem to indicate general adhesion to the 2011 LRDGs, the reality may be otherwise. The CADS estimates are based on the alcohol consumption in the previous seven days, meaning that people who consumed alcohol in the past year but did not have a drink in the week preceding the survey are automatically considered as not exceeding the 2011 LRDGs. This seems very unlikely given Canada's timeout culture where people drink to mark special occasions rather than on a regular daily basis. In fact, a study conducted in 2015 explored adherence to the LRDGs while attempting to adjust for the under-reporting of alcohol consumption (Zhao et al., 2015). It was found that 73% of people living in Canada over the age of 15 followed the weekly limits while 61% followed the daily limits recommended by the LRDGs. In Ontario, the Public Health Ontario survey found that 39% of people who used alcohol in the Ontario sample regularly exceeded the LRDG daily limits and 27% the weekly limits (Public Health Ontario, 2017a). According to CPADS, a majority (88%) of students who use alcohol reported following the guidelines for long-term risk, but only 36% indicated drinking within the recommendations for short-term risk (Health Canada, 2021). Zhao and colleagues (2015) also found that, after adjustment for under-reporting, more than 80% of all drinks consumed in Canada were consumed in a fashion inconsistent with the LRDGs.

Time to Update

There are no set criteria for updating health guidelines to ensure they remain current and evidence based, but an update is typically recommended when new evidence is identified that is relevant and important or could alter current guidelines (Vernooij et al., 2014). Over the last decade, several reasons that justify an update of the 2011 LRDGs have been identified.

First, knowledge on and estimates of relations between different dimensions of alcohol use and particular diseases, disorders or injuries have been evolving since 2011. Research now confirms the importance of alcohol use as a risk factor for an increasing number of diseases including at least seven types of cancers, dementia and sexually transmitted diseases (International Agency for Research on Cancer, 2012; Lu et al., 2017; Rehm et al., 2017). Second, a Canadian study showed

that more than 50% of alcohol-attributable cancer deaths in British-Columbia are among former alcohol users and people using alcohol within the 2011 LRDGs for long-term risks (Sherk et al., 2020). People living in British-Columbia who use alcohol within the LRDG's weekly limits also account for 65% of hospital stays due to unintentional injuries and a substantial percentage of deaths due to digestive conditions (18%) and injuries (40%), suggesting that reducing the burden of disease requires revising the 2011 LRDGs (Sherk et al., 2020). Third, countries like the United Kingdom, France, Denmark, Holland and Australia recently reviewed new evidence on alcohol and health and released updated guidelines with limits significantly different from the 2011 LRDGs, with weekly limits ranging from the equivalent of 5.2 to 8.3 Canadian standard drinks for women and men alike.² Finally, given recent reports on the extent to which alcohol use causes social problems for individuals other than the drinkers themselves (Laslett et al., 2019), there has been curiosity as to what alcohol guidelines would be if social and mental health harms were also included in addition to diseases, disorders and injuries.

The Canadian 2011 LRDGs did not include an expiration date but given the limitations and in light of the new evidence, in early 2019, CCSA, Health Canada, PHAC and members of the Canadian 2011 LRDGs working group engaged in discussions to update the guidelines. In July 2020, Health Canada confirmed funding to CCSA to update Canada's LRDGs and make recommendations for knowledge mobilization to maximize dissemination and application of the updated guidelines. The mandate specified building on the guidelines from the United Kingdom (U.K. Chief Medical Officers, 2016) and Australia (National Health and Medical Research Council, 2020), which had provided access to the underlying evidence base supporting their alcohol guidelines. It was further agreed that CCSA would be responsible for overseeing and facilitating the updating process. Health Canada would provide advice, support and guidance through membership on the project's various committees, plus administrative support. PHAC would provide methodological advice and support.

Aim and Scope of This Report

Canada's Guidance on Alcohol and Health is intended to replace Canada's Low-Risk Alcohol Drinking Guidelines. It provides accurate and current information about the risks and harms associated with the use of alcohol. The guidance should help people make well-informed and responsible decisions about their alcohol consumption. The Guidance on Alcohol and Health is also intended to contribute to an evidence base for future alcohol policy and prevention resources, with a view to changing Canada's drinking culture and curbing the normalization of harmful alcohol use in society.

In the interests of transparency and because developing best practices for defining alcohol drinking guidelines remains a work in progress (Holmes et al., 2019), this report will describe the updating process, so that others can learn from the Canadian experience. The report is divided into three main parts:

- 1. The construction of experts' recommendations;
- 2. The evidence used by the experts; and
- 3. The experts' recommendations for updated alcohol guidelines in Canada.

² Around the world, what constitutes a standard drink ranges from 8 to 20 grams of pure alcohol. In Canada, it is defined as 13.45 grams (Paula et al., 2020). Some say that Canada's particular standard drink was chosen because it corresponds to the measure of whisky traditionally available in Canadian bars (Miller et al., 1991). A more probable reason is that it corresponds to the amount of pure alcohol contained in 341 ml bottles of 5% beer, which has traditionally been the alcoholic beverage of choice in Canada.

Part 1: Development of Experts' Recommendations

To update the 2011 LRDGs, four committees were convened. An executive committee with members from federal, provincial and territorial governments, and national organizations was established to provide project oversight and advice. Three scientific expert panels were established to review the evidence for updating the guidelines and making recommendations on how best to mobilize this new knowledge effectively. One panel focused on the impacts of alcohol consumption on physical health, a second one on the social and mental health effects, and a third on knowledge mobilization.

To provide scientific support to members of scientific expert panels (hereafter referred to as the experts), CCSA further established an internal Evidence Review Working Group responsible for evaluating and summarizing evidence, leading consultations and conducting new research as needed.

Members of the executive committee and the experts were required to disclose affiliations and interest, as per Schünemann et al. (2013). The list of potential conflicts of interest was published on CCSA's website in <u>Disclosure of Affiliations and Interests</u>.

1.1 Defining Research Questions

The general research question underlying the 2011 LRDGs update is as follows: To minimize the risk of developing alcohol-related physical and mental health disorders and social problems, which level or pattern of use should be recommended to people living in Canada?

For this question to lead to evidence-based guidelines, three more specific questions were developed, each one specifying a particular target population, the level of exposure to alcohol and the type of outcomes being considered. (For more information, see <u>Update of Canada's Low Risk Alcohol Drinking Guidelines: Development of Research Questions</u>.) It is these three specific research questions that have guided this project's evidence collection, analyses and conclusions:

- 1. What are the short-term risks and benefits (physical and mental health, and social impact) associated with varying levels of alcohol consumption (including no alcohol consumption), in different contexts, associated with a single episode of drinking in the general population?
- 2. What are the long-term risks and benefits (physical and mental health, and social impact) associated with varying levels and patterns of alcohol consumption (including no alcohol consumption) in the general population?
- 3. What are the risks and benefits (physical and mental health, and social impact) associated with varying levels and patterns of alcohol consumption (including no alcohol consumption) during pregnancy or breastfeeding, for fetal, infant and child development?

The specific questions were formulated to encompass all effects, so that studies focusing on both positive and negative effects could be identified.

1.2 Estimating the Lifetime Risk of Alcohol-Related Death and Disability in the Canadian Population

From the outset of this project, there was a common understanding among experts that to update the 2011 LRDGs, the specific research questions would be answered through mathematical modelling. Modelling had previously been used to establish the 2011 LRDGs as well as alcohol guidelines in Australia (National Health and Medical Research Council, 2020), the U.K. (U.K. Chief

Medical Officers, 2016) and France (Santé publique France & Institut national du cancer, 2017). Moreover, since 2016, the European Union Joint Action on Reducing Alcohol-Related Harm has recommended the use of cumulative lifetime risk of death from alcohol-related disease or injury as a common metric for assessing the risks from alcohol at the country level; the metric should also inform discussions by experts to establish alcohol guidelines (Broholm et al., 2016).

Modelling requires alcohol mortality risk functions for all disease or injury categories causally related to alcohol consumption. These risk functions can be found in meta-analyses that assess the dose-response relationship between alcohol and the risk of disease mortality. The quality of modelling depends upon the quality of the risk functions and therefore on the identification of the highest quality meta-analyses. Such identification is a complex and lengthy process that could have gone over the 21 months allocated to update the 2011 LRDGs. However, the project's mandate stipulated that the update should be informed by the 2016 alcohol guidelines from the U.K. (U.K. Chief Medical Officers, 2016) and the 2020 Australian guidelines to reduce health risks (National Health and Medical Research Council, 2020). Therefore, a quality assessment of these alcohol guidelines was performed. (For more information, see *Updating Canada's Low-Risk Alcohol Drinking Guidelines: Evaluation of Selected Guidelines.*) With regards to its methodology for identifying and selecting evidence on the risks and benefits associated with alcohol consumption, the Australian guidelines received top ratings.

Hence, to update Canada's LRDGs, the global evidence review did not start from scratch, but rather built upon the rigorous and systematic work previously done by the Australian Alcohol Working Committee (AAWC), which covered the January 2017 to February 2021 period. (The overall process is explained in section 2.1.) Besides ensuring the quality of the modelling, the global evidence review on the risks and benefits associated with alcohol consumption identified areas where high quality systematic reviews were missing; for these areas, the experts agreed to commission additional reviews to formulate the updated guidelines for Canada.

1.3 The Evidence Base for Updating the Guidelines

A range of inputs was considered in updating the 2011 LRDGs:

- Global evidence review of the effects of alcohol on health;
- Mathematical modelling of the lifetime risk of death and disability for various levels of average alcohol consumption;
- Rapid review on alcohol and mental health;
- Rapid review on alcohol and violence; and
- Comprehensive multi-part review of recent literature on women's health and alcohol.

This project's mandate also required recommendations for knowledge mobilization of the updated alcohol guidelines. To this end, a series of activities was undertaken to better understand people's views, preferences and expectations on alcohol guidelines. Discussions on formulation and presentation of the finalized guidelines were further informed by the following activities:

- Summary Evidence on Understanding and Response to Alcohol Consumption Guidelines;
- Public consultation to hear what alcohol, health and well-being issues matter most and what is most useful to people in Canada;

- Interviews with representatives from different health-related organizations that have an interest in alcohol-related issues; and
- Focused discussions with Indigenous People serving on the LRDG executive committee and scientific expert panels.

The overall process by which the recommendations were developed is illustrated in Figure 1.

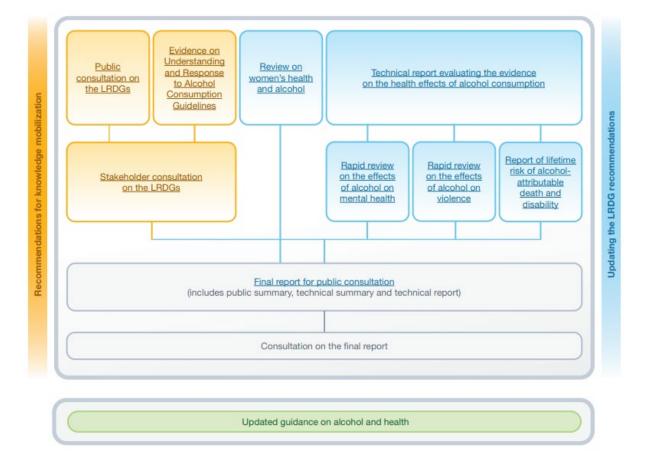


Figure 1: Process for updating Canada's LRDGs

Note. For a PDF of this image, visit https://ccsa.ca/sites/default/files/2023-01/CCSA-LRDG-Lower-Risk-Drinking-Guidelines-Process-and-Documentation-2023-en.pdf.

1.4 Reaching Conclusions and Formulating Recommendations

This project was conducted during the COVID-19 pandemic and its associated stay-at-home and travel restrictions. Therefore, all meetings held during this project were conducted online, except the last three-days meeting to review the results of the open consultation, which was held in-person. Despite the challenging context, the co-chairs of the scientific expert panels created an online environment that was conducive to respectful dialogue and the healthy exchange of ideas. The project comprised three scientific expert panels, but due to the overlap and interest in all the panel evidence-review activities, experts were invited to attend all panel meetings.

Between September 2020 and October 2022, members of the scientific expert panels met on 18 occasions to discuss the process and the evidence used to develop the recommendations. Efforts were deployed for panel members to engage in a dialogue and share information for the purpose of increasing the understanding of the issues and to provide a rationale for choosing a particular position. The main conclusions and agreement on final recommendations was reached through consensus.

Part 2: Evidence Used to Construct the Recommendations

The studies and evidence reviews informing the update to the 2011 LRDGs are available on the CCSA webpage dedicated to this project. Those interested in understanding in detail the types of evidence and the way they were used to update the guidelines are encouraged to visit the webpage to access the full reports. The following sections provide summaries of each report, to give readers an overview of the material reviewed by the experts to reach their conclusions.

2.1 Global Evidence Review on the Effects of Alcohol on Health

Several studies have quantified the risk relationships between alcohol use and the occurrence of and mortality from all disease or injury categories causally related to alcohol consumption. However, the quality of these studies varies greatly. To provide an answer to this project's <u>three research questions</u> and estimate the impact of alcohol consumption on individuals, a systematic search and review was performed of meta-analyses that reported alcohol dose-response curves between different average levels of alcohol use, disease and injuries. The aim was to identify the highest quality systematic reviews and meta-analyses using a standard set of quality criteria. (For the full report, see <u>Update of Canada's Low-Risk Alcohol Drinking Guidelines: Evidence Review Technical Report</u>.)

2.1.1. Methods

A systematic electronic search was performed using PubMed, PsycNET, Embase, Cochrane Library, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, International Health Technology Assessment Database, Joanna Briggs Institute, Database of Systematic Reviews of Effects, and Epistemonikos. The search was limited to articles published from Jan. 6, 2017, to Feb. 17, 2021. It provided an update to the AAWC systematic review for 2007 to 2017. All articles included in the Australian's systematic review were also included in this review (National Health and Medical Research Council, 2020).

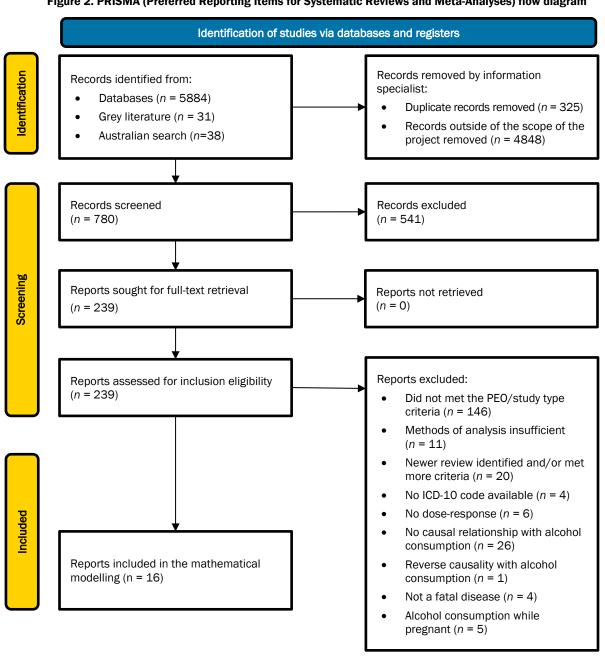
An information specialist screened the search results and removed duplicates and any articles that were clearly outside of the scope of the project based on titles and abstracts. Two independent investigators assessed articles for title and abstract, and subsequently for full-text eligibility against:

- The study design and the Population, Exposure, Comparator and Outcome (PECO) criteria;
- Methodological quality criteria selected from A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2; Shea et al., 2017) and Risk of Bias in Systematic Reviews (ROBIS; Whiting et al., 2013) tools;
- Methods of analyses criteria; and
- Mathematical modelling criteria.

If a particular disease or injury category was considered by more than one systematic review or meta-analysis, priority was given to the article that met the most methodological quality criteria. In the event that the same number of criteria were met, the most recent article was given priority.

Finally, the quality of each eligible systematic review and meta-analysis was assessed by two independent investigators using two international standard tools: A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2; Shea et al., 2017), and the Grading of Recommendations, Assessment, Development and Evaluations system (GRADE; Schünemann et al., 2013). Studies were also evaluated for the inclusion of sex- and gender-based analysis (Brabete et al., 2020).

Figure 2. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram



2.1.2 Results

In addition to the 38 systematic reviews already identified by the AAWC, a total of 5,915 systematic reviews were initially retrieved from the updated search. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram presented in Figure 2 illustrates that after removing duplicates and any articles that were outside of the scope of the project, a subset of 780 systematic reviews were screened for title and abstract and a total of 239 systematic reviews (37 identified by the AAWC and 202 identified by this update) were subsequently screened for full-text eligibility.

The 31 reports identified by the search of the grey literature were excluded as PECO and study design criteria were not met. Most of the grey literature items were found to be informative brochures, reports, fact sheets and books.

In the end, a total of 16 systematic reviews fulfilled all the inclusion criteria for this project for all three research questions and were selected for inclusion in the mathematical modelling.

Research Question 1: Short-Term Risks and Benefits

Twenty-nine systematic reviews on the short-term risks and benefits of alcohol were evaluated. **Two systematic reviews were selected for inclusion in the mathematical modelling.** One selected review focused on road injury (Taylor & Rehm, 2012) and the other on intentional and unintentional injuries (Taylor et al., 2010).

Research Question 2: Long-Term Risks and Benefits

A total of 154 systematic reviews across eight categories of diseases associated with the long-term health risks and benefits of alcohol were evaluated. Fourteen reviews were selected for inclusion in the mathematical modelling. The selected reviews assessed the relationship between alcohol use and liver cirrhosis (Roerecke et al., 2019), ischæmic heart disease (Zhao et al., 2017; for relative risks, see fully adjusted relative risks for people 19 to 55 years of age at baseline outlined in Table 3), hypertensive heart disease (Liu et al., 2020), breast cancer (Sun et al., 2020), liver cancer (World Cancer Research Fund International, 2018), pancreatitis (Samokhvalov et al., 2015), lower respiratory infections (Samokhvalov et al., 2010a), epilepsy (Samokhvalov et al., 2010b) ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage (Larsson et al., 2016), atrial fibrillation (Larsson et al., 2014), colon and rectum cancers (Vieira et al., 2017), diabetes mellitus (Knott et al., 2015), larynx cancer, mouth and oropharynx cancers, esophagus cancer (Bagnardi et al., 2015) and tuberculosis (Imtiaz et al., 2017). The relative risks obtained from systematic reviews were not adjusted for misestimation of alcohol use. Although there is a hypothesis of a slight underestimation of alcohol use in medical epidemiology studies (Stockwell, 2018), the direction of alcohol use measurement bias in cohort studies is unknown (Biemer et al., 2013; King, 1994).

Research Question 3: Pregnancy and Child Development Risks and Benefits

Twenty-five systematic reviews focusing on the risks and benefits associated with alcohol consumption during pregnancy or breastfeeding for fetal, infant and child development were evaluated. **None were selected for inclusion in the modelling** because none met the mathematical

modelling criteria. The studies focused on alcohol-attributable mortality and morbidity to others rather than the person who consumes alcohol.

2.1.3 Quality of Evidence

The quality of each retained systematic review was assessed with AMSTAR 2 and GRADE. (For the full AMSTAR and GRADE assessments, see <u>Update of Canada's Low-Risk Alcohol Drinking</u> Guidelines: Evidence Review Technical Report.)

The systematic reviews used PECO questions and clearly presented inclusion criteria. All were based on strong and rigorous methods for statistical combination of their results. Retained reviews also examined dose-dependent relationships through pooled analyses, which is indicative of high-quality methods. The majority of retained reviews also described the included studies with a good amount of detail justifying their inclusion. The review search strategies were detailed and many of the studies conducted the screening steps in duplicate. Most of the retained reviews had no imprecision and indirectness according to GRADE. However, many of the retained reviews did not assess risk of bias. Heterogeneity was also reported for many of the reviews and, despite conducting sensitivity analyses, the source for heterogeneity was seldom identified. Hence, the overall quality score of most retained reviews was low but this was expected.

Tools used to assess the quality of identified systematic reviews consider randomized clinical trials the gold standard. However, for examining the association between alcohol consumption and health, this study design is neither practical nor ethical. For example, it would be unethical to randomize one group of females to drink alcohol on a daily basis for 10 years and another one to abstain, and then test who develops breast cancer. In fact, in the field of alcohology most evidence is derived from cohort and observational studies that have inherent limitations that explain why many systematic reviews retained for this project did not receive a high-quality score. However, in no way does this mean that the quality of evidence is insufficient to provide guidance on alcohol and health to people living in Canada. In fact, there is a high level of confidence among members of the scientific expert panels and the Evidence Review Working Group that the identified reviews covered in this report are the latest and most high-quality evidence available to examine this public health issue.

2.1.4 Implications

The global evidence review identified the most recent and highest quality systematic reviews and meta-analyses available to examine the relationship between alcohol consumption and the various outcomes covered by this project's research questions. The methodology used to select these systematic reviews is based on the Australian guidelines, which received a top score according to a previous evaluation, further strengthening our certainty that our results are based on the highest quality evidence. (For more information, see Update of Canada's Low-Risk Alcohol Drinking Guidelines: Evaluation of Selected Guidelines.)

Through this work, we identified areas where high quality systematic reviews are currently missing (e.g., mental health, violence) and for which the experts agreed to commission additional reviews to complete the LRDG update (see section 2.4). A decision was also taken to commission a report on women's health and alcohol that would address, among other things, the issues of pregnancy.

2.2 Mathematical Modelling of the Lifetime Risk of Death for Various Levels of Average Alcohol Consumption

To establish alcohol guidelines, modelling the lifetime risk of death for various levels of average alcohol consumption has been recommended (Broholm et al., 2016; Rehm et al., 2014) and applied

(e.g., in Australia, the U.K., France and Canada). Modelling allows for the estimation of the "excess risk" of mortality and disability associated with various levels of average consumption and the specification of the level of risk from negligible to high associated with each level of consumption. The aim of modelling is not to set a "threshold" of consumption below which there is no risk, but to provide "benchmarks" based on which recommendations can be formulated.

For this project, the lifetime risk approach was adopted to estimate the lifetime risk of death, premature death (< 75 years of age), years of life lost (YLLs) and disability-adjusted life years (DALYs) lost. A full report presenting all analyses is available in <u>Lifetime Risk of Alcohol-Attributable Death and Disability</u>. Every estimation and result presented in the report was subsequently the object of a shadow analysis that confirmed the accuracy of the primary analyses (Appendix 1).

Discussions among experts led to a decision to use risk thresholds associated with YLLs. Compared to using lifetime risk of death or premature death, YLLs allows researchers to consider the deaths of older individuals and, more importantly, factors the unequal health loss caused by death among people relatively younger in age. While DALYs can be an optimal outcome for the measurement of health loss attributable to alcohol, there is limited data on the DALYs alcohol cause and this project's analyses resulted in identical risk thresholds whether they were based on YLLs or DALYs.³ Since DALYs is conceptually more difficult to understand than YLLs, the experts fixed their choice on YLLs estimations. Results are presented and discussed below, after a review of methodological principles.

2.2.1 Methodological Principles

Calculating Alcohol-Attributable Deaths

In epidemiology, the concept of an attributable fraction makes it possible to express the proportion of risk for a particular health event (in this case death), due to exposure to a particular cause (in this case alcohol consumption). An attributable fraction is classically calculated from the number of deaths that could be avoided if the exposure was eliminated.

The proportion depends on the risk of death according to sex and age but also on the "trajectory" of exposure, which is the history of alcohol consumption before the subject's death. Establishing alcohol-attributable deaths in the population requires access to the population's mortality rate and knowledge of the individuals' lifetime exposure to alcohol in standardized terms, such as average grams of alcohol per day. With this data, alcohol-attributable deaths can be calculated for various levels of consumption, provided that it is considered identical among individuals and constant over time for each of them until death. In this model, lifetime abstainers are the reference group in relation to which the risks associated with different average levels of alcohol consumption are calculated.

By varying the average level of consumption in such a scenario, it becomes possible to summarize the relationship between the risk due to alcohol and different levels of consumption. In return, this informs the benchmarks for different levels of risk.

³ For example, there is evidence that DALYs can be influenced by mental disorders such as depression but because the evidence search did not identify high-quality systematic reviews assessing the relationship between alcohol use and mental health, it is likely that the current project underestimates alcohol-related DALYs.

Diseases and Injuries Included in the Modelling

A total of 34 cause categories for alcohol-related diseases, conditions and injuries and more than 200 three-digit International Classification of Disease, version 10 (ICD-10-CA) codes were included in the modelling of alcohol-attributable deaths. To be included, there were three criteria:

- 1. The disease or injury had to be causally related to alcohol use;
- 2. A dose-response risk function needed to be available for the risk relationship between alcohol consumption (measured in grams per day) and the disease or injury of interest that also passed the GRADE criteria; and
- 3. Either death or disability needed to be measured specifically for the disease or injury causally related to alcohol use.

What Evidence Has Changed Since the Release of the 2011 LRDGs?

- Animal, mechanistic and epidemiological evidence published since the publication of the Canadian LRDGs in 2011 has led to changes in the diseases that are known to be causally related to alcohol use.
- Alcohol has been found to causally increase the risk of lower respiratory infections (Samokhvalov et al., 2010a).
- Systematic reviews on the risk relationship between alcohol use and the diagnosis of and death from cancer have observed no lower risk threshold (Bagnardi et al., 2015; Sun et al., 2020; Vieira et al., 2017; World Cancer Research Fund International, 2018).
- The risk relationship between alcohol use and hypertensive heart disease has been observed to have no lower risk threshold (Liu et al., 2020).
- Risks for hemorrhagic stroke have been investigated further, with the risk functions for intracerebral hemorrhage showing protective effects at lower levels of alcohol use but for subarachnoid hemorrhage, detrimental effects at lower levels of alcohol use (Larsson et al., 2016).
- Alcohol's protective impact on ischemic heart disease at lower levels of alcohol use is more uncertain than previously estimated. The risk is modified by binge drinking (Roerecke & Rehm, 2010; Sundell et al., 2008) and genetics (Chikritzhs et al., 2015; Larsson et al., 2020).

Data Sources

Several data sources were used to make the necessary calculations:

- Data on death and disability for 2017 to 2019 were obtained from Statistics Canada and the Institute for Health Metrics and Evaluation's Global Burden of Disease study (2018).
- 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 (2021) and the World Health Organization's Global Information System on Alcohol and Health (2021).

• Relative risk estimates for diseases and injuries were obtained following the evidence review (see previous section) that enabled us to identify the highest quality meta-analyses.

The calculations for this project are 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).

2.2.2 Results and Implications

The relative risk estimates by cause of disease and average weekly alcohol consumption are outlined in Table 1 for females and Table 2 for males. The absolute risk estimates (measured in YLLs) by cause of disease and average weekly alcohol consumption are outlined in Table 3 for females and Table 4 for males. For most diseases and injuries, alcohol had a net negative impact on health at all levels of alcohol use, with net impacts being defined by confidence intervals not crossing a zero effect. For diabetes mellitus (females only), ischemic stroke and pancreatitis (females only), alcohol was associated with a protective effect at lower levels of alcohol use. However, for ischemic heart disease and intracerebral hemorrhage, alcohol was neither associated with a negative nor protective net effect at lower alcohol use amounts. (Confidence intervals associated with increased risk of diseases and injuries are presented in Appendix 2.)

Table 1. Increased risk of diseases and injuries for females based on average weekly alcohol use (standard drinks per week)

Disease or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	3.7%	7.5%	11.4%	15.5%	19.7%	24.1%	26.3%	62.4%	105.2%	233.3%
Lower respiratory infections	1.0%	1.9%	2.9%	3.9%	4.9%	5.9%	6.4%	13.7%	21.0%	37.6%
Oral cavity and pharynx cancer	5.1%	10.3%	15.8%	21.6%	27.6%	33.8%	37.0%	89.4%	152.3%	338.4%
Oesophagus cancer	2.7%	5.4%	8.2%	11.1%	14.1%	17.2%	18.7%	42.7%	69.1%	139.3%
Colorectal cancer	1.4%	2.7%	4.1%	5.6%	7.0%	8.5%	9.2%	20.0%	31.1%	57.4%
Liver cancer	0.8%	1.6%	2.4%	3.2%	4.0%	4.8%	5.2%	11.2%	17.0%	30.1%
Breast cancer	1.8%	3.7%	5.6%	7.6%	9.5%	11.6%	12.6%	27.9%	44.0%	84.2%
Larynx cancer	3.0%	6.0%	9.1%	12.3%	15.5%	18.8%	20.5%	46.3%	73.8%	143.5%
Pancreatitis	-5.3%	-10.3%	-15.0%	-19.2%	-22.7%	-25.5%	-26.7%	-20.8%	14.8%	173.9%
Diabetes Mellitus	-15.2%	-19.9%	-23.0%	-25.2%	-26.9%	-28.3%	-28.9%	-33.5%	-34.6%	-32.7%
Liver cirrhosis	61.5%	94.3%	124.3%	153.3%	182.1%	211.0%	225.5%	444.7%	685.5%	1337.2%
Atrial fibrillation and flutter	1.3%	2.6%	3.9%	5.3%	6.6%	8.0%	8.7%	18.9%	29.2%	53.7%
Hypertension	1.2%	2.4%	3.6%	4.8%	6.0%	7.1%	7.7%	16.1%	24.8%	45.2%
Ischemic heart disease	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	4.0%	4.0%	15.0%
Ischemic stroke	-10.0%	-10.0%	-10.0%	-10.0%	-10.0%	-8.0%	-8.0%	8.0%	8.0%	14.0%
Intracerebral hemorrhage	-8.0%	-8.0%	-8.0%	-8.0%	-8.0%	-1.0%	-1.0%	25.0%	25.0%	67.0%
Subarachnoid haemorrhage	21.0%	21.0%	21.0%	21.0%	21.0%	11.0%	11.0%	39.0%	39.0%	82.0%
Epilepsy	3.1%	5.7%	8.3%	11.0%	13.8%	16.6%	18.0%	40.2%	64.5%	129.2%
Road injuries	1.9%	3.9%	5.9%	8.0%	10.1%	12.2%	13.3%	29.6%	46.8%	90.2%
Other unintentional injuries	1.6%	3.2%	4.8%	6.4%	8.1%	9.8%	10.6%	23.3%	36.5%	68.3%
Intentional injuries	5.1%	10.5%	16.1%	22.1%	28.3%	34.9%	38.3%	96.1%	171.2%	431.9%

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

Table 2. Increased risk of diseases and injuries for males based on average weekly alcohol use (standard drinks per week)

Disease or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	3.7%	7.5%	11.4%	15.5%	19.7%	24.1%	26.3%	62.4%	105.2%	233.3%
Lower respiratory infections	1.0%	1.9%	2.9%	3.9%	4.9%	5.9%	6.4%	13.7%	21.0%	37.6%
Oral cavity and pharynx cancer	5.1%	10.3%	15.8%	21.6%	27.6%	33.8%	37.0%	89.4%	152.3%	338.4%
Oesophagus cancer	2.7%	5.4%	8.2%	11.1%	14.1%	17.2%	18.7%	42.7%	69.1%	139.3%
Colorectal cancer	1.4%	2.7%	4.1%	5.6%	7.0%	8.5%	9.2%	20.0%	31.1%	57.4%
Liver cancer	0.8%	1.6%	2.4%	3.2%	4.0%	4.8%	5.2%	11.2%	17.0%	30.1%
Breast cancer	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Larynx cancer	3.0%	6.0%	9.1%	12.3%	15.5%	18.8%	20.5%	46.3%	73.8%	143.5%
Pancreatitis	3.5%	7.2%	11.0%	14.9%	18.9%	23.1%	25.3%	59.7%	100.1%	219.7%
Diabetes Mellitus	0.0%	0.0%	0.1%	0.1%	0.2%	0.2%	0.3%	1.1%	2.4%	5.9%
Liver cirrhosis	6.2%	12.4%	18.8%	25.6%	32.9%	40.5%	44.5%	113.6%	207.1%	553.0%
Atrial fibrillation and flutter	1.3%	2.6%	3.9%	5.3%	6.6%	8.0%	8.7%	18.9%	29.2%	53.7%
Hypertension	2.8%	5.7%	8.7%	11.8%	15.0%	16.6%	17.4%	29.3%	35.9%	47.2%
Ischemic heart disease	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	-5.0%	4.0%	4.0%	15.0%
Ischemic stroke	-8.0%	-8.0%	-8.0%	-8.0%	-8.0%	-8.0%	-8.0%	8.0%	8.0%	14.0%
Intracerebral hemorrhage	-8.0%	-8.0%	-8.0%	-8.0%	-8.0%	-1.0%	-1.0%	25.0%	25.0%	67.0%
Subarachnoid haemorrhage	21.0%	21.0%	21.0%	21.0%	21.0%	11.0%	11.0%	39.0%	39.0%	82.0%
Epilepsy	3.1%	5.7%	8.3%	11.0%	13.8%	16.6%	18.0%	40.2%	64.5%	129.2%
Road injuries	3.0%	6.1%	9.2%	12.5%	15.9%	19.3%	21.1%	48.8%	80.2%	168.0%
Other unintentional injuries	1.6%	3.2%	4.8%	6.4%	8.1%	9.8%	10.6%	23.3%	36.5%	68.3%
Intentional injuries	5.1%	10.5%	16.1%	22.1%	28.3%	34.9%	38.3%	96.1%	171.2%	431.9%

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

Table 3. Cause-specific lifetime number of years of life lost (YLLs) per 1,000 females based on average weekly alcohol use (standard drinks per week)

Disease or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	0.1	0.2	0.3	0.4	0.5	0.6	0.7	1.4	2.4	5.1
Lower respiratory infections	2.3	4.6	6.9	9.3	11.6	13.9	16.3	31.4	48.1	79.4
Oral cavity and pharynx cancer	1.1	2.3	3.5	4.7	6.0	7.4	8.8	19.3	33.6	71.6
Oesophagus cancer	0.9	1.8	2.7	3.6	4.6	5.5	6.6	13.6	22.5	43.5
Colorectal cancer	3.8	7.6	11.4	15.3	19.2	23.2	27.2	54.0	85.0	149.3
Liver cancer	0.5	1.1	1.6	2.2	2.7	3.3	3.9	7.6	11.7	19.8
Breast cancer	7.6	15.3	23.2	31.1	39.3	47.5	55.9	113.3	182.2	335.5
Larynx cancer	0.1	0.2	0.4	0.5	0.6	0.8	0.9	1.9	3.1	5.7
Pancreatitis	-0.8	-1.5	-2.2	-2.8	-3.3	-3.7	-3.9	-2.9	2.6	24.3
Diabetes Mellitus	-30.3	-39.5	-45.5	-49.8	-53.2	-55.9	-58.0	-64.9	-66.0	-59.3
Liver cirrhosis	24.1	37.0	48.8	60.1	71.3	82.6	93.9	172.7	272.0	515.3
Atrial fibrillation and flutter	1.3	2.6	3.9	5.2	6.5	7.8	9.1	17.7	27.4	45.6
Hypertension	1.4	2.8	4.2	5.7	7.1	8.4	9.7	18.4	28.3	47.6
Ischemic heart disease	-39.4	-39.3	-39.3	-39.2	-39.1	-39.0	-38.9	30.3	29.7	104.8
Ischemic stroke	-7.7	-7.7	-7.7	-7.7	-7.7	-6.1	-6.1	5.9	5.8	9.5
Intracerebral hemorrhage	-8.5	-8.5	-8.5	-8.5	-8.4	-1.1	-1.1	25.8	25.3	64.6
Subarachnoid haemorrhage	7.6	7.6	7.6	7.6	7.6	4.0	4.0	14.0	13.9	28.4
Epilepsy	0.3	0.6	0.9	1.1	1.4	1.7	2.0	4.1	6.8	13.1
Road injuries	1.3	2.7	4.1	5.5	6.9	8.3	9.8	20.1	32.7	61.8
Other unintentional injuries	3.9	7.8	11.8	15.8	19.8	23.9	28.1	55.4	87.2	151.5
Intentional injuries	6.2	12.8	19.7	26.9	34.5	42.5	50.8	116.7	215.7	536.0

Table 4. Cause-specific lifetime number of years of life lost (YLLs) per 1,000 males based on average weekly alcohol use (standard drinks per week)

Disease or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	0.1	0.2	0.3	0.4	0.5	0.7	0.8	1.7	2.9	6.0
Lower respiratory infections	2.1	4.1	6.1	8.1	10.2	12.2	14.3	27.6	42.3	69.6
Oral cavity and pharynx cancer	1.8	3.7	5.6	7.7	9.8	12.0	14.3	31.2	54.5	115.2
Oesophagus cancer	2.4	4.8	7.3	9.9	12.5	15.1	17.9	37.2	61.3	117.6
Colorectal cancer	3.6	7.2	10.8	14.5	18.3	22.0	25.9	51.3	80.7	140.8
Liver cancer	1.0	2.0	2.9	3.9	4.9	5.9	6.9	13.5	20.9	35.2
Breast cancer	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Larynx cancer	0.5	1.0	1.5	2.0	2.6	3.1	3.6	7.5	12.1	22.2
Pancreatitis	0.5	0.9	1.4	1.9	2.4	2.9	3.5	7.5	12.8	26.8
Diabetes Mellitus	0.0	0.1	0.1	0.2	0.4	0.5	0.7	2.5	5.4	12.6
Liver cirrhosis	4.1	8.1	12.4	16.8	21.6	26.5	31.8	73.7	138.7	356.6
Atrial fibrillation and flutter	0.8	1.7	2.5	3.4	4.2	5.1	6.0	11.6	17.9	29.8
Hypertension	2.6	5.3	8.1	10.9	13.8	15.2	16.7	26.2	31.9	39.4
Ischemic heart disease	-64.4	-64.3	-64.1	-64.0	-63.9	-63.8	-63.7	49.9	49.0	174.0
Ischemic stroke	-5.8	-5.8	-5.8	-5.8	-5.7	-5.7	-5.7	5.6	5.5	9.0
Intracerebral hemorrhage	-7.7	-7.7	-7.6	-7.6	-7.6	-1.0	-0.9	23.2	22.8	57.8
Subarachnoid haemorrhage	4.4	4.4	4.4	4.4	4.4	2.3	2.3	8.1	8.0	16.4
Epilepsy	0.3	0.5	0.8	1.1	1.3	1.6	1.9	3.8	6.3	12.2
Road injuries	3.2	6.4	9.8	13.3	16.8	20.5	24.3	51.5	87.1	178.8
Other unintentional injuries	4.5	9.1	13.7	18.3	23.1	27.8	32.7	65.0	102.9	181.5
Intentional injuries	10.8	22.1	34.0	46.5	59.7	73.5	88.0	201.7	372.4	921.4

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

YLLs were used to model the alcohol-attributable burden of disease as it accounts for the age at which a death occurs. The acceptable risk threshold for a lifetime death can also be stated based on the average YLLs per death, which is 17.5 YLLs (Institute for Health Metrics and Evaluation, 2021). Figure 3 presents lifetime risk of a YLL because of alcohol use, for both males and females, for average levels of alcohol intake varying from one to 35 standard drinks per week. All models of alcohol-attributable harms used grams of alcohol per day. In Canada, where a standard drink is 13.45 grams of pure alcohol, this corresponds to consuming zero to three (2.97) standard drinks per day in an average week.

The modelling reveals that the number of YLLs increases as alcohol use increases among both males and females. Among males and females, a protective association was observed for those consuming one drink per week when compared to people who engaged in lifetime abstention. In all cases, the 95% uncertainty intervals (UIs) crossed the null hypothesis threshold, which means there is not enough evidence to confirm the protective effect.

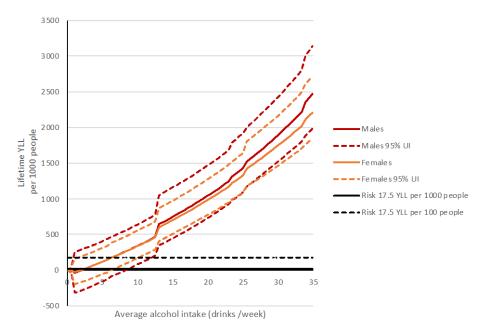
The risk threshold based on one in 1,000 deaths (17.5 YLLs in 1,000 lifetimes) would be:

- 2 (95% UI: <1, 6) standard drinks/week for females
- 2 (95% UI: <1, 8) standard drinks/week for males

The risk threshold based on one in 100 deaths (17.5 YLLs in 100 lifetimes) would be:

- 6 (95% UI: <1, 10) standard drinks/week for females
- 6 (95% UI: <1, 11) standard drinks/week for males

Figure 3. Lifetime risk of a year of life lost (YLL) attributable to alcohol use at varying levels of average alcohol intake



Based on the systematic review of the published literature on the risk relationships between alcohol use and disease and injury occurrence, this study estimated that for people in Canada, the lifetime risk of death and disability attributable to alcohol use increases as the amount of alcohol use increases. The selected model did not demonstrate a significant negative nor protective net effect at lower levels of alcohol use; that is, we did not observe a J-shape curve. This is likely due to more recent and higher quality meta-analyses on the association between average alcohol use, ischemic stroke and ischemic heart disease. (See box entitled "What Evidence Has Changed Since the Release of the 2011 LRDGs?" for more details.) Therefore, alcohol should not be promoted or used as a product to improve health.

As the lifetime risk of mortality and morbidity is similar for males and females, one guideline for alcohol consumption can be used for Canada. According to established definitions of acceptable risks and based on the risk thresholds of 17.5 YLLs attributable to alcohol per 1,000 and 100 lifetimes, risk thresholds for alcohol use should be set at either two or six standard drinks per week respectively, for both females and males in Canada.

Canada's 2011 LRDGs Pose Higher Risks in Light of Current Evidence

To reduce the risk of long-term harm, Canada's 2011 LRDGs recommended consuming no more than 15 drinks a week among males (~29 grams/day) and 10 drinks a week for females (~19 grams/day). Based on today's data sources and the life course approach to estimate the risk of an alcohol-attributable death, the 2011 recommendations would be associated with the following risk thresholds:

- Consumption by males of 29 grams/day would result in 757 YLLs per 1,000 lifetimes
- Consumption by females of 19 grams/day would result in 336 YLLs per 1,000 lifetimes

Put differently, the 2011 LRDGs would be associated with a risk for males that is between 76 and 757 higher than established definitions of acceptable risk, and with a risk for females that would be between 34 and 336 higher than those definitions.

2.3 Alcohol Use Per Occasion

The risks from alcohol use for most health outcomes (e.g., death, certain cancers, heart disease, injuries) are usually based on how much alcohol is consumed on average or the total amount consumed over the past week or month (see tables 1 and 2). That is why the mathematical modelling led to results expressed in an average number of standard drinks per week, that is, 2 or less, between 3 and 6, or more than 6 standard drinks per week, depending on which level of risk is considered.

However, most people do not drink their average amount every day. On days they use alcohol there is considerable variability in how much they use on different drinking "occasions." For this reason, many people who drink relatively low weekly or monthly amounts of alcohol may in fact drink large quantities on a single occasion, which may put them at risk for harm (Naimi et al., 2003). In the context of personal well-being, the experts discussed the latest evidence on alcohol use per drinking occasion to be able to advise people in Canada on this issue.

With alcohol use during any drinking occasion, each drink increases one's blood alcohol concentration (BAC). An increased BAC is what leads to alcohol impairment (a reduced ability to think clearly or perform certain activities) and intoxication (which is the appearance or sensation of being drunk). The

risk begins to increase with any use of alcohol, and with more than two standard drinks, most individuals will have a demonstrably increased risk of "acute" problems. For example, compared to no alcohol use, studies of injuries in emergency departments show increasing risk for each drink consumed for both men and women (Cherpitel et al., 2015; Vinson et al., 2003) Similarly, studies of motor vehicle crash fatalities demonstrate increasing risk above a BAC of 0.02% (Blomberg et al., 2009; Compton & Berning, 2015; Voas et al., 2012), which corresponds to about one drink. After about two standard drinks consumed within an hour, one's BACs may be approximately 0.05% (the level will differ on the basis of body mass and other factors). Above this level, risk gets progressively and substantially higher the more one drinks on any occasion and the higher one's BAC. It is important to recognize that people typically exhibit behaviour changes or become impaired starting at BAC levels below those at which they feel "drunk" or appear intoxicated (Midanik, 1999).

Binge drinking, usually defined as consuming five standard drinks or more for men or four standard drinks or more for women in one setting (National Institute of Alcohol Abuse & Alcoholism, 2004; Wechsler & Austin, 1998) is a common yet dangerous pattern of consumption that results in legal impairment (i.e., a BAC > 0.08%) for most persons, and is significantly associated with a range of alcohol-related health and social problems (Centers for Disease Control and Prevention; Fillmore & Jude, 2011). Specifically, binge drinking and resulting BAC levels are well-established risk factors for death from any cause, including unintentional injuries (road crashes, drownings, falls), physical and sexual violence, cardiovascular disease (hypertension, myocardial infarction, stroke), inflammation of the gastrointestinal system (gastritis, acute pancreatitis), and the development of an alcohol use disorder (Alpert et al., 2022; Brewer & Swahn, 2005; Dawson et al., 2005; Devries et al., 2014; Dietary Guidelines Advisory Committee, 2020; Mukamal et al., 2005; Roerecke & Rehm, 2014).

Many of the complications arising from acute impairment and binge drinking involve second-hand effects that affect someone other than the person who drinks (e.g., domestic violence, child abuse and neglect). Because binge drinking is common and involves large volumes of alcohol consumption, binge drinking occasions account for a substantial proportion of all alcohol consumed in the population. Binge drinking is also an important contributor to long-term health problems like liver disease and certain cancers (Llerena et al., 2015). For example, binge drinking increases risks of breast cancer and proliferative benign breast disease, as increased blood alcohol levels exceed the capacity to metabolize and eliminate alcohol. Not only are alcohol and its metabolites carcinogenic, but consuming multiple drinks in one setting can increase inflammatory toxins, sex hormone levels and mutagenic DNA, and induce the activity of additional enzymes that can result in the formation of cancer cells (White et al., 2017). The mechanism may be especially risky for young females since breast tissue is most susceptible to neoplastic transformation between menarche and first pregnancy (Liu et al., 2015).

Fortunately, effective alcohol control policies can reduce rates of binge drinking and related problems (Naimi et al., 2014; Wagenaar et al., 2009; Wagenaar et al., 2010). Although most persons who engage in binge drinking do not meet criteria for an alcohol use disorder, virtually all persons with an alcohol use disorder engage in binge drinking.

In sum, the evidence is clear and consistent: in terms of health, fewer standard drinks per drinking occasion means less risk of harm to the person consuming the alcohol and reduced risk of second-hand effects to those other than that person. Although some risk begins at one drink and increases more

⁴Some scientists have questioned this criteria and suggested that a lowered standard defining impairment should be used for women (Canadian Centre on Substance Abuse, 2014; Thomas et al., 2014).

substantially with more than two standard drinks, risks are higher and increase very rapidly at or above binge drinking levels (five or more standard drinks for men, four or more standard drinks for women).

2.4 Rapid Reviews

At the beginning of this project, a public consultation was held to hear what alcohol, health and well-being issues mattered most and were most useful to people living in Canada. (We will return to this topic in section 2.6.) A key finding from the consultation was that from a list of eight topics, the one respondent asked to be prioritized in the updated guidelines was the impact of drinking alcohol on mental health. It was followed by the impact of drinking alcohol on physical health and how alcohol can impact people's lives via, for example, violence and sexual assaults.

Unfortunately, the updated evidence review on the effects of alcohol on health did not identify high quality-evidence systematic reviews on alcohol use and mental health nor on alcohol use and social harms. Not a single review met all the selection criteria. (See section 2.1 and <u>Update of Canada's Low-Risk Alcohol Drinking Guidelines: Evidence Review Technical Report</u>.) This means that the modelling presented in the previous section ignores the impact that alcohol may have on mental health and violence and, therefore, on people's overall risk of death and disability. To overcome this blind spot, the experts agreed to commission two rapid reviews, one on the effects of alcohol on violence and another one on the effects of alcohol on mental health.

2.4.1 Association Between Alcohol Use, Aggression and Violence

In the absence of recent high-quality systematic reviews or meta-analyses on alcohol and violence and to inform experts opinion, an overview of recent reviews of the literature on alcohol and aggression and violence (A/V) was commissioned.

Alcohol is associated with many health and social harms, including various forms of aggression and violence. There are multiple factors affecting the relationship of alcohol and A/V, including the effects of alcohol experienced by people who consume alcohol; their personalities, beliefs, attitudes and other characteristics; the immediate drinking situation; and the culture within which the drinking occurs (Choenni et al., 2017; Exum, 2006; Graham et al., 1997; Graham et al., 1998; Parrott & Eckhardt, 2018).

Three common forms of A/V that have shown high rates of alcohol involvement and that experts agreed to consider to update Canada's 2011 LRDGs are intimate partner A/V (IPV), male-to-female sexual A/V (SV), and non-intimate and non-sexual A/V between adults or general A/V (GV). The role of alcohol in both A/V perpetration (being aggressive or violent toward another adult) and victimization (having an act of aggression or violence done toward them) was considered.⁵ Relevant details about findings related to sex/gender differences are reported where available.⁶

The full report, <u>Update of Canada's Low-Risk Alcohol Drinking Guidelines: Overview of Reviews of the Association Between Alcohol Use and Aggression and Violence</u>, including references, is available on CCSA's LRDG 2022 webpage. A summary of the report is presented in here.

⁵ In the context of this overview, "perpetrator" refers to the person who was aggressive or violent toward another person or persons. "Perpetration" refers to the act of carrying out A/V. "Victim" refers to the person or persons to whom the aggressive or violent act was done (commonly referred to in the literature as the victim, target or survivor); that is, the person who was victimized by the perpetrator. "Victimization" refers to the process of being victimized. These terms are not meant to label those who experience violence. Use of terms "victim" or "victimization" is by no means intended to assign blame, imply weakness or guilt, or otherwise stigmatize those who experience A/V, nor is it meant to imply any particular response or impact of the A/V on the person.

⁶ We use the term "sex/gender" in this overview because, while some studies restricted their analyses to sex (biological attributes), both alcohol consumption and A/V are inextricably linked to gender (socially constructed roles, norms, values and behaviours).

Method

A comprehensive search was performed of the literature published from the year 2000 to January 2022, including systematic reviews (i.e., meta-analyses and narrative literature reviews), using the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) and Excerpta Medica Database (Embase) using the OVID platform, and PubMed, PsychINFO, PsychNET, Web of Science, Criminal Justice Abstracts, Cochrane CENTRA and other reviews from our collection.

- The search resulted in 3,826 records.
- After removal of duplicates, 2,744 titles and abstracts were retrieved.
- After screening by two independent screeners, 54 reviews were included (30 IPV, 10 SV and 14 GV). Results are reported separately for IPV, SV and GV, and separately for perpetration and victimization.

Key Findings

Alcohol and Intimate Partner Violence (IPV) Perpetration

Event-level alcohol consumption (i.e., having consumed alcohol at the time or prior to the A/V incident) was associated with perpetration of IPV, but the strength of the relationship varied by sample and the sex/gender of the perpetrator (larger for male than for female perpetrators). In terms of usual drinking pattern (e.g., usual number of standard drinks consumed per occasion, frequency of consumption over a specific time period, a regular pattern of drinking to intoxication), heavy episodic drinking (or binge drinking) and drinking to intoxication were positively associated with IPV perpetration, with weaker associations found for drinking frequency. As with event-level drinking, the relationship between usual drinking pattern and IPV perpetration was stronger for men than for women. Drinking problems and alcohol use disorders were positively associated with IPV perpetration, with stronger relationships for male than for female perpetrators (although some inconsistent findings were also reported). Some evidence suggested that alcohol use was also associated with more severe IPV perpetration.

Alcohol and IPV Victimization

Event-level drinking was associated with greater risk of being the victim of IPV. Findings were inconsistent relating to drinking pattern of the victim, but generally suggested that IPV victimization was associated with a pattern of heavy episodic drinking and intoxication, as well as drinking problems and alcohol use disorders. However, estimates of associations were usually smaller than were found for drinking by perpetrators, and some estimates were non-significant.

Alcohol and Male-to-Female Sexual Violence (SV) Perpetration

Small-to-medium effect sizes were found for the relationship between event-level alcohol consumption and male-to-female SV perpetration, although some experimental paradigms did not produce a significant effect of alcohol on SV. As well, moderating factors such as personality and attitudes were noted in the relationship. Associations were found between perpetration of SV and both drinking patterns and drinking problems, particularly for heavy episodic drinking. However, not all studies found significant associations, especially when key variables such as past perpetration were controlled.

Alcohol and Male-to-Female SV Victimization

Consuming higher amounts of alcohol prior to SV was associated with greater severity of SV experienced by victims in some, but not all studies. This finding may relate to heavier drinking by the perpetrator because drinking by perpetrators and victims is highly correlated. Although there is relatively little research, some evidence suggested that women who engaged in a pattern of heavy episodic drinking, drinking to intoxication or problem drinking were more likely to be victims of SV.

Alcohol and General Violence (GV) Perpetration

Experimental, laboratory-based and other research indicates that alcohol increases aggressive behaviour (medium effect sizes), with variability related to how aggression was measured in the laboratory and sex/gender of aggressors. The research also identified important moderators of the association. Research suggests positive associations between GV perpetration by individuals and heavier drinking patterns as well as drinking problems. However, the evidence is less clear for usual quantity consumed per occasion (i.e., average number of drinks usually consumed) by individuals and frequency of drinking than for alcohol in the event (i.e., consumption during or prior to an A/V event), and the reviews in this area have methodological weaknesses.

Alcohol and GV Victimization

A large proportion of homicide victims tested positive for alcohol (larger for women than men), and many were defined as intoxicated (BAC > 0.08 or 0.10), although these studies found large variability in estimates. Homicide rate was found to be positively correlated with per capita consumption in some countries but not others. Emergency department studies indicated that patients with violence-related injuries were significantly more likely to have consumed alcohol than were patients with non-violence-related injuries, with some evidence suggesting the relationship was stronger for men than for women. There were insufficient data on drinking patterns of GV victims to draw conclusions about the relationship between alcohol consumption and being the victim of GV.

Discussion

Although the exact mechanisms by which alcohol is associated with A/V are unknown, there is overwhelming evidence that alcohol consumption, especially intoxication, is associated with perpetration of A/V, and some evidence indicates that alcohol may increase the severity of A/V. However, there are insufficient data to define the exact dose-response relationship. Thus, although existing research does not allow the calculation of a risk curve for alcohol and A/V, it is reasonable to infer that individuals can reduce their risk of perpetrating A/V by limiting their alcohol consumption. Based on consistent evidence, it is highly likely that avoiding drinking to intoxication will reduce individuals' risk of perpetrating alcohol-related violence. Therefore, efforts to reduce or eliminate alcohol-related A/V need to focus on reducing alcohol use, especially among those who may be likely to perpetrate A/V or get involved in violent incidents. Because A/V decreases with age and is perpetrated more by men than women, prevention efforts should focus on young adults, particularly young men. Overall, people should be encouraged to avoid drinking high levels of alcohol or avoid drinking altogether to reduce their risk of perpetrating violence. Persons who have a history of alcohol-related violence should avoid any consumption of alcohol.

The literature on the association between alcohol and A/V victimization is less clear. The findings suggest there is likely an association, but there are some mixed and null findings, and noteworthy limitations of this literature. Alcohol's role in victimization likely reflects many different mechanisms that may work in combination, such as alcohol intoxication reducing the ability to avoid or escape

danger, use of alcohol by victims due to trauma, increased exposure to risk in drinking settings, targeting by perpetrators of people who are intoxicated, and use of substances to control victims.

Attributing A/V victimization to alcohol contributes to beliefs that victims of A/V who had used alcohol are responsible or blameworthy for being victimized. Moreover, evidence suggests that interventions that place the burden to avoid risk of victimization on women and girls are ineffective. While alcohol might be a contributing factor in A/V victimization, we state unequivocally that drinking alcohol does not make a person responsible for A/V perpetrated on them. Thus, we conclude that lower risk drinking guidelines should focus on reducing alcohol use by potential perpetrators.

2.4.2 Association Between Alcohol Use and Mental Health

In 2016, when Australia's National Health and Medical Research Council was asked to revisit their 2009 alcohol guidelines, their systematic review on the health effects of alcohol consumption revealed there was actually very little synthesized evidence on how different levels of alcohol consumption influence mental health (National Health and Medical Research Council, 2020). Because this question was of interest for drafting updated alcohol guideline recommendations, the Adelaide Health Technology Assessment, University of Adelaide, was contracted to conduct a systematic literature review on the latest and best scientific evidence on the mental health risks and benefits of alcohol consumption (Newton et al., 2018). The Newton et al. systematic review, plus six new systematic reviews on the association between alcohol consumption and mental health and substance use disorders were evaluated for the current project (see <u>Update of Canada's Low-Risk Alcohol Drinking Guidelines: Evidence Review Technical Report</u>). None of the reviews met the criteria for inclusion.

Given the previously mentioned importance that people living in Canada associated with the relationship between alcohol and mental health, the experts decided to commission Cochrane Canada, McMaster University, to conduct a rapid update of a systematic review of the effect of alcohol consumption on the development of depression, anxiety and suicidal ideation. The full report, Effect of Alcohol Consumption on the Development of Depression, Anxiety and Suicidal Ideation: Update of a Systematic Review, is available on CCSA's LRDG 2022 webpage.

Limitations of the Rapid Update and Experts' Decision

With this rapid update, the intention was to be able to pool together results across studies using statistical analyses. Unfortunately, as with the 2018 review prepared by Newton et al., thresholds and definitions for alcohol quantity or frequency varied across studies and so a statistical analysis could not be performed. In addition, studies often failed to report odds ratios with standard errors or confidence intervals so results could not be easily pooled. The review also found that many studies did not report results that could be easily interpreted and even the most recently published studies provided little data that could be used to make healthcare decisions. Experts highlighted that just as was the case for many studies on the relationship between alcohol and physical health, many studies on alcohol and mental health misclassified abstainers. Specifically, to assess the impact of alcohol on mental health, the reference group against which those who use alcohol were compared were people who do not consume alcohol, including people who quit using alcohol because of health problems, such as mental health issues.

For these reasons, the experts agreed that further work would be required for mental health outcomes to be considered when making alcohol guidelines recommendations. The experts were unanimous in opting to make the rapid review publicly available but agreed that it would not inform their final discussions on formulating and presenting updated guidelines.

2.5 Women's Health and Alcohol

The mathematical modelling revealed identical risk thresholds for females and males at low levels of alcohol consumption. This was not unexpected. When the U.K. and Australia updated their alcohol guidelines, both made identical recommendations for men and women. Since 2017, France also recommends the same alcohol limits for both sexes and when Denmark released its new alcohol guidelines in spring 2022, they recommended the same alcohol limits for adult women and men alike, and no alcohol consumption for those under 18 years old.

The results obtained by our modelling align with the global trend to not differentiate between females and males when formulating alcohol guidelines. This conclusion is because at low levels of consumption the physiological differences between women and men have only a small impact on lifetime risk of death. However, above low risk, lifetime risk increases more steeply for women than for men.

The experts are mindful of the complexity of this reality and the necessity to describe it well. Proper understanding of sex-related and gender-related factors on women's health and reproductive issues is key to reach and inform audiences in a meaningful way. Updated alcohol guidelines need to be shared with the appropriate nuances. To this end, a comprehensive multi-part review of the recent literature on sex, gender, alcohol and health was commissioned.

The full report prepared by Galvanizing Equity, including references, is available here: <u>Sex, Gender and Alcohol: What Matters for Women in Low-Risk Drinking Guidelines?</u> and was recently published (Greaves et al., 2022). A short version is presented below. This section concludes with evidence-based key messages that health professionals and policy makers may want to consider in their programs, practices and communications about alcohol.

2.5.1 What Are Some Sex-Related Factors?

The four main categories of sex-related biological factors that are important to understanding how alcohol affects male and female bodies are hormones and enzymes, physiology and anatomy, genetics, and neurobiology. Within these categories, various sex-related differences, factors or processes exist. The absorption, distribution and metabolism of alcohol is affected by sex-related factors. For example, females absorb ethanol faster than males, and reach a higher BAC due to faster absorption and slower elimination. Significantly, females generally experience more risk of damage or disease, such as liver disease, at lower levels of alcohol consumption than do males. In general, males are more likely to develop alcohol use disorders, but females are more likely to develop organ and other bodily damage from drinking alcohol.

2.5.2 What Are Some Gender-Related Factors?

There are different impacts on women or men or gender and sexual minorities as a result of alcohol consumption. The four main aspects of gender that account for these impacts are gender roles and norms, gender relations, gender identity and institutionalized gender. Gender identity matters in that the strength of adherence to masculinities or femininities affects style and volume of drinking behaviour, with men and sexual and gender minorities often drinking larger quantities of alcohol and more often than women as a group. Gendered relations often mean that women are influenced by a partner's drinking and the impacts of alcohol reflect gender inequities such as vulnerability to sexual assault and violence. Gender roles lead to women using alcohol to cope with stresses of caregiving roles, trauma and IPV. Institutionalized gender differentially impacts women by applying increased stigma to women who drink, and barriers to treatment for women and mothers who use alcohol.

2.5.3 How Do Sex and Gender Interact and Intersect with Other Factors?

All these factors and processes are exacerbated by sex-gender interactions. For example, sex-related and gender-related factors coincide to create specific and heightened negative impacts of alcohol during pregnancy on both women's and fetal health. Pregnancy-related processes affect the pharmacokinetics of ingesting alcohol, while stigma and social policing are heightened during pregnancy. Vulnerability to sexual assault is enhanced by being young, female and intoxicated, amid pervasive gender-based violence. Intersections, such as those with poverty, racialization, past trauma, or sexual and gender minority status merge to create more harms.

2.5.4 How Does Alcohol Affect Reproduction?

Reproductive health is compromised by alcohol use, particularly during pregnancy and breastfeeding. Long-term damage to children can occur after being exposed to alcohol in the womb, and alcohol use during breastfeeding can reduce milk production. Furthermore, alcohol passes into breastmilk and therefore exposes the infant to alcohol. During pregnancy, increased water and blood volume, along with the impact of alcohol on glucose and insulin lipid metabolism, create complex effects on the body.

There is mixed evidence on the impact of alcohol on pregnancy and delivery outcomes, with possible increases in miscarriage and placental abnormalities. However, exposure to alcohol in the womb results in a well-established risk for learning, health and social effects with lifelong impacts on the fetus as well as brain injury, birth defects, behavioural problems, learning disabilities and other health problems typically referred to as fetal alcohol spectrum disorder (FASD). Recent reviews that considered **low** levels of exposure have also found some adverse effects, reinforcing the message that it is safest not to drink during pregnancy. Effects of alcohol consumption on breastfeeding include a decrease in milk production, early cessation of breastfeeding and effects on infant sleep patterns.

2.5.5 Discussion

Women are particularly susceptible to the negative effects of drinking alcohol. This is due to factors related to both sex (biological) and gender (social). The female body's response to alcohol results in faster intoxication and more damage from lesser amounts of alcohol, and in a shorter time. Gendered social and cultural factors about alcohol negatively affect girls and women via enhanced stigma, social pressures, exploitative marketing and increased vulnerability to sexual assault and IPV. Sex and gender, along with the determinants of health and intersecting factors, such as race, age, income and education, shape the overall impacts of alcohol, resulting in differential impacts on women, men and gender and sexual minorities. While all people living in Canada can benefit from nuanced information and messaging about alcohol use and safe drinking levels, it is especially important for women and girls.

Alcohol use also presents numerous sex- and gender-specific risks for reproductive processes such as fertility and conception, pregnancy, breastfeeding and childcare. Males and females experience differential alcohol-related reproductive risks and effects, at different life stages. Alcohol use during pregnancy is particularly unsafe, as it heightens the risk of FASD in offspring, often with lifelong disabilities and impacts. Gendered social attitudes about alcohol use and reproduction mean that those who use alcohol during pregnancy experience negative, punitive and stigmatizing attitudes. In some jurisdictions, these manifest as state sanctioned interventions, barriers to treatment or child apprehension.

2.5.6 What Are the Key Messages for Women?

The collective impact of sex, gender and interactive and intersectional factors on alcohol use has particular importance for girls and women. It is necessary to transmit this emerging and growing body of evidence to women, service providers, practitioners and policy makers to improve health literacy and inform more specific and tailored prevention, treatment and harm reduction efforts.

- Female bodies can be more damaged by drinking, compared to males.
- Sex-related (biological) factors enhance the impact of alcohol, causing more harm and faster intoxication in girls and women from lesser amounts.
- Gender-related (social) factors contribute to the negative impacts of alcohol in real life, increasing vulnerability to marketing exploitation, stigma, sexual assault and IPV.
- Sex, gender and factors such as trauma and poverty interact and make dependence on alcohol, treatment and recovery more difficult for women.
- Practitioners need to recognize both biological and social factors affecting alcohol use that create differential impacts on and require tailored responses for women, men and gender and sexual minorities.

2.6 Views, Preferences and Expectations About Guidelines of People Living in Canada

Throughout this project, there was a commitment to consider the views, preferences and expectations of people living in Canada about alcohol guidelines to improve the strength of updated recommendations. Therefore, as evidence was being gathered on alcohol and health, parallel activities were undertaken to better understand people's views about guidelines and to obtain insight on alcohol, health and issues of well-being that matter most and are most useful to people living in Canada.

Three different types of evidence were collected to inform experts' deliberations and final decisions for the updated guidelines: an update of a systematic review, a public consultation and interviews with stakeholders.

2.6.1 Summary of Evidence on Understanding and Response to Alcohol Guidelines

To learn about the acceptability and feasibility of the updated guidelines, the systematic review previously prepared for the behavioural evidence expert group for the U.K. guidelines (Jones & Bellis, 2013) was updated with a focus on understandings and responses to official public health guidelines. The update was prepared by Cochrane Canada. (See the full report: Understanding and Response to Alcohol Consumption Guidelines.) Some of the results have proven to be of great importance to the experts charged with making judgments about the acceptability and feasibility of recommendations.

There appears to be little understanding among the public about what a standard drink is, and
most times people overestimated the standard drink size. The public also overestimated the
number of daily and weekly standard drinks recommended in guidelines. Typically, people indicated
that those recommendations were unrealistic and did not want to count standard drinks.

- Views about the amount of alcohol consumption that was not sensible or that was harmful were
 often associated with excessive intake or "problem drinking," but people often noted that their
 own drinking was not a problem.
- Less than half the people who responded to surveys were aware of the harms of alcohol intake, and there was less awareness in people who drink at high- or very high-risk levels. While some people were aware of the harms, they still had a positive attitude toward alcohol use, especially in social situations.
- People suggested that guidelines should include strategies to help apply the low-risk drinking recommendations, such as refusing drinks when not really wanted or eating while drinking.
- The applicability to their own lives of guidelines generally and guidelines specifically for low-risk drinking was questioned by the public with many reasons given for why guidelines might not be applicable. For example, individual tolerance levels and physical reactions to alcohol can differ, and the effects of different types of alcohol on an individual can also differ.
- While participants in the studies indicated that a health agency should provide recommendations, they preferred advice rather than strict rules or patronizing messages.
- Overall, the experts considered these findings to indicate that regardless of the scientific quality
 of the guidelines, to be credible updated guidelines must meet people where they are at. They
 would have to bridge the gap between the way people consume alcohol and the evidence on the
 health impacts by providing them with actionable guidance.

2.6.2 Public Consultation on Alcohol Guidelines

In spring 2021, CCSA held an online public consultation in which 4,845 people living in Canada participated. (See the full report: <u>Update of Canada's Low-Risk Alcohol Drinking Guidelines:</u> <u>Summary of Findings from Public Consultation</u>.) The consultation focused on the experiences of people living in Canada with the current LRDGs and their needs and expectations for updated guidelines. The public consultation revealed alcohol-related topics of importance to people living in Canada that, in return, influenced the topics for which it was decided to conduct rapid reviews (see Section 2.4). The experts also retained two major lessons in terms of the type of information to be emphasized and prioritized in the development of resources to promote the new guidelines:

- Among contributors who said they had used the 2011 LRDGs in the past, the most often cited challenge with using the guidelines was "not wanting to follow the LRDGs."
- The contributors shared an interest in understanding their risk of experiencing alcohol-related harms and receiving information about long-term risks and benefits of alcohol use.

Both these results point to the importance of not only informing people about the existence of the guidelines, but also about the reasons for their existence. Without fully understanding the risks associated with alcohol use, people are unlikely to understand why they should follow the guidelines.

2.6.3 Interviews with Stakeholders

To explore the familiarity and understanding of the 2011 LRDGs, and to discuss specific knowledge mobilization recommendations including ideal messaging and communication strategies, Leger was contracted to assist in the completion of eight virtual focus groups. A total of 48 persons representing various health-related organizations were interviewed. The summary report, Commissioned Report: Update on Canada's Low-Risk Alcohol Drinking Guidelines: Summary of Stakeholder Focus Groups, is available on CCSA's LRDG webpage.

Overall, stakeholders were familiar with the LRDGs. They mentioned frequently referencing the guidelines, which they found to be particularly useful to start a conversation about alcohol use and drinking patterns. Still, they mentioned that encouraging people to follow alcohol guidelines was challenging because awareness of the dangers of alcohol was low and people living in Canada tended to normalize consuming alcohol.

Stakeholders mentioned that the goal of the updated guidelines should be to get people rethinking their alcohol consumption. They requested a focus on the adverse effects of alcohol on overall health and wellness, including information on alcohol being a known teratogen and carcinogen, and its association with mental health and social harms. Messaging for teens and young adults should focus on the immediate short-term impacts of drinking. Finally, many participants mentioned the importance for updated guidelines to challenge the alcohol-centred culture and to include messaging promoting a non-drinking culture. Participants also mentioned keeping the guidelines as simple as possible and providing standard drink measurements that are easy to follow as the ideal approach to conveying the guidelines.

In terms of resources, stakeholders said they wanted a variety of different types of information. They also viewed infographics as important for communicating the updated guidelines. The guidelines should be kept as simple as possible, and providing standard drink measurements that are easy to follow is viewed as the ideal approach to conveying them. In fact, the interviews further revealed a firm belief among stakeholders that the public should be provided with information about standard drink size, nutritional information and potential health risks related to consuming alcohol. Hence, they expressed support for the addition of mandatory enhanced alcohol container labels with a health message, drink guidelines, standard drink information and nutrition information.

Standard Drink Labelling: A Necessary Condition for the Adoption of the Guidance on Alcohol and Health by the Public

The concept of standard drink is central to understanding the Guidelines on Alcohol and Health. To adhere to the guidance and reduce the risk of negative consequences due to alcohol, consumers need consistent, easy-to-use information when serving alcohol to accurately track and monitor their drinking.

In Canada, a standard drink is 17.05 ml or 13.45 grams of pure alcohol, which is equivalent to:

- A bottle of beer (12 oz., 341 ml, 5% alcohol)
- A bottle of cider (12 oz., 341 ml, 5% alcohol)
- A glass of wine (5 oz., 142 ml, 12% alcohol)
- A shot glass of spirits (1.5 oz., 43 ml, 40% alcohol)

In practice, people in Canada have a limited understanding of a standard drink (Osiowy et al., 2015; Public Health Ontario, 2017b). According to this project's public consultation (*Update of Canada's Low-Risk Alcohol Drinking Guidelines: Summary of Findings from Public Consultation*), 38% of contributors said they had previously heard of the 2011 LRDGs. Among those who reported using the guidelines, less than half (43%) said they were extremely familiar with the concept of standard drink. When asked about challenges associated with using the 2011 LRDGs, two of the three most popular answers were that it was not clear to them "what a standard drink is" and that the standard drinks in the guidelines did not represent the types of alcoholic beverages they typically drink. These results echo those of other studies showing that a lack of

knowledge about standard drinks can preclude people from adhering to guidelines, even if they are aware of them and motivated to monitor and regulate their alcohol consumption (de Visser & Birch, 2012; Dowling et al., 2006; Hawks, 1999).

Percent alcohol by volume (%ABV) information is mandated on alcohol beverage containers in Canada. However, communicating alcohol content on beverage containers using %ABV information is problematic because alcohol drinking guidelines are expressed in terms of standard drinks. The inconsistency in messaging causes consumer confusion and creates barriers for consumers to adhere to alcohol guidance. Standard drink labelling (SDL) can help consumers to accurately monitor their alcohol use in terms of standard drinks (Osiowy et al., 2015; Wettlaufer, 2018). According to a 2022 systematic review of the impacts of alcohol container labels on consumer outcomes, the evidence consistently suggests that compared to %ABV labels, exposure to SDL results in more accurate estimates of the amount of alcohol in a standard drink, the number of standard drinks in an alcohol container, and the number of standard drinks to reach drink limit guidelines (Hobin et al., 2022). Evidence also indicates that by providing information at the point of pour, SDL better supports accurately pouring one standard drink of alcohol relative to %ABV labels (Brunk et al., 2020; Wettlaufer, 2018). In the only real-world experimental study testing alcohol container labels, results suggest when consumers are exposed to SDL, they are more likely to use the labels to drink within guidelines and accurately estimate the number of standard drinks in their preferred drink (Schoueri-Mychasiw et al., 2021).

Considering that:

- The concept of standard drink is central to understanding and following Canada's Guidance on Alcohol and Health;
- SDL can help consumers follow alcohol guidelines by monitoring their personal alcohol use;
- A fundamental idea underlying this project is that people living in Canada have a right to clear information about alcohol;

A corollary of this project is highlighting that a particular effective policy change could be the mandatory labelling of all alcoholic beverages to indicate the number of standard drinks in a container.

2.6.4 Focused Discussions with Indigenous People

Throughout the project, focused discussions were held with Indigenous people serving on the LRDG executive committee or scientific expert panels. These experts included Dr. Carol Hopkins, Lenape Nation, Chief Executive Officer, Thunderbird Partnership Foundation; the late Harold Johnson, Nehiyaw lawyer and author; and Dr. Christopher Mushquash, Anishinabek Professor, Lakehead University, and Canada Research Chair in Indigenous Mental Health and Addiction.

The discussions began very broadly with regards to Indigenous peoples' historical relationship with alcohol (Johnson, 2016). The participants reflected on how alcohol has been used as a tool or weapon of colonization from its first introduction during the fur trade. They recalled that the negative impacts were so severe that the numbered treaties included a clause to ban alcohol from Indigenous territory and communities. This prohibition led to the criminalization of alcohol sales, transportation and consumption that in turn contributed to high levels of incarceration of Indigenous people, negative stereotyping, racism and stigma. In the frontier context, binge drinking and related harms like violence, injuries and accidents became pervasive (Ehrlander, 2010). Drinking alcohol became a

coping mechanism for dealing with trauma and grief resulting from the losses of self-government, cultural practices, ceremonies, language and a viable economy, as well as the apprehension, isolation and abuse of children in the Indian Residential Schools. Indigenous people's situation illustrates that the effects of alcohol are not the same for all people and communities.

In this larger context it is important to recognize the bi-modal drinking pattern amongst Indigenous people. Compared to other adults in Canada, there are proportionately more First Nations adults who do not use alcohol (42.6%) or engage in binge drinking (50.5%) (First Nations Information Governance Centre, 2018). Using alcohol without binge drinking is uncommon (6.9%) and generally confined to those who are urban and have more education and greater career responsibilities. In most communities, tribal councils and Indigenous organizations, the emphasis has been on abstinence-based treatment programs with a strong cultural content. The latter serves to reinforce Indigenous identity with the exploration of hope, belonging, meaning and purpose (Assembly of First Nations et al., 2011; Thunderbird Partnership Foundation, 2015). Nevertheless, pragmatic harm reduction strategies have also been embraced by Indigenous communities.

Because of the above considerations, the Indigenous experts questioned the relevance of the LRDGs for Indigenous people, in terms of the enormity of the challenges with alcohol, the inequity in resources to address alcohol at the community level, and the cultural and historical contexts surrounding alcohol. They emphasized that in most Indigenous communities wellness is more oriented toward abstinence than low-risk alcohol use (Thunderbird Partnership Foundation, 2015). They further expressed concern that an Indigenous commentary or takeaway, without the correct context, would simply reinforce systemic racism, negative stereotyping and stigma. Instead, it was suggested that broad social determinants of health need to be recognized and linked to policies, like addressing epistemic racism through poverty reduction, income security, accessible employment, colonialism diminishment, and ensuring Indigenous culture is the foundation of policy (Czyzewski, 2011).

On a smaller scale, Indigenous experts agreed that Indigenous peoples should be involved in developing knowledge mobilization practices for their people and the following initiatives should be prioritized for development:

- A risk-based approach to increase alcohol literacy, aligned with the culturally congruent focus on wellness;
- A harm reduction initiative to promote substance use health among those who choose to use alcohol, focused on how to reduce the harms of alcohol consumption to self, families and Indigenous communities; and
- Community-based alcohol interventions, framed as community-based alcohol strategies, with appropriate guidance, knowledge mobilization and resources.

A narrative approach identifying risk factors, resiliency and the success of different communities was encouraged. Evaluation resources should accompany the development of these initiatives to ensure they meet their intended goals. Each objective should be funded to ensure that alcohol issues are explored and addressed in the appropriate historical and cultural context, guided by an evidence-based, culturally relevant approach, and using enhanced community-based resources.

Part 3: Experts' Recommendations

Canada's LRDGs were originally published in November 2011 and the evidence since then on the association between drinking alcohol and physical, mental and social harms has continuously evolved. An update of the guidelines was required to take into account these advancements in what we know about the risks and benefits associated with alcohol. In July 2020, with the support of Health Canada, CCSA was mandated to update Canada's LRDGs. The project has been guided by a public health perspective and its stated focus has been to provide people living in Canada with the latest evidence-based advice on alcohol to support them in making informed decisions about its use, and reduce the risk of harms from alcohol.

When the update of Canada's LRDGs was initiated, it was anticipated that the new guidelines would set lower limits for alcohol use. This was, in part, due to several trends that have emerged since the guidelines were released in 2011: that alcohol use was a risk factor for an increasing number of diseases; an important proportion of alcohol-attributable deaths in Canada were among people adhering to the 2011 guidelines; and alcohol guidelines coming from other countries in recent years had all recommended limits below the 2011 Canadian guidelines. What was not anticipated was that the evidence review would reveal the extent to which even very small amounts of alcohol can be harmful to people's health and well-being. In this context, the experts have agreed to replace Canada's LRDGs with Canada's Guidance on Alcohol and Health.

Canada's Guidance on Alcohol and Health

To reduce the risk of harm from alcohol, it is recommended that people in Canada consider reducing their alcohol use.

The reasons to do so derive from the following facts:

- a. There is a continuum of risk associated with weekly alcohol consumption where the risk of harm from alcohol is:
 - Low for individuals who consume 2 standard drinks or less per week;
 - Moderate for those who consume between 3 and 6 standard drinks per week; and
 - Increasingly high for those who consume 7 standard drinks or more per week.
- b. Consuming more than **2** standard drinks per drinking occasion is associated with an increased risk of harms to self and others, including injuries and violence.
- c. When pregnant or trying to get pregnant, there is no known safe amount of alcohol use.
- d. When breastfeeding, not drinking alcohol is safest.

Sex and Gender

Above the upper limit of the moderate risk zone for alcohol consumption, the health risks increase more steeply for females than males.

Far more injuries, violence and deaths result from men's alcohol use, especially in the case of per occasion drinking.

3.1 Canada's Guidance on Alcohol and Health

Throughout the life course, there are established thresholds of mortality risk that people are willing to accept (BMJ Best Practice, n.d.; Starr, 1969). For voluntary activities like unprotected sexual practices or smoking cigarettes, that level is a 1 in 1,000 mortality risk (i.e., people are willing to accept a 1 in 1,000 risk of premature death when participating in these activities). For alcohol, people appear willing to accept a higher risk of death associated with consumption as compared with other voluntary activities. It is not uncommon for countries to base their guideline recommendations on a 1 in 100 mortality risk limit (e.g., Australia, France, U.K.). This project revealed that in Canada, the limit associated with a 1 in 1,000 chance of premature death related to an alcohol condition is two standard drinks per week, while the 1 in 100 risk limit is six standard drinks per week.

There is a continuum of risk whereby the risk for those who consume two standard drinks or less per week is low; it is moderate for those who consume between three and six standard drinks per week; and it is increasingly high for those who consume more than six standard drinks per week, with increasing risk conferred by every additional drink.⁷

In light of results obtained through this project's knowledge mobilization activities and with a view to meet people where they are at, the experts agreed that instead of providing people with strict rules and recommendations, people in Canada should be presented with a continuum of risk associated with various levels of alcohol use. The experts anticipate that a continuum of risk will allow people to situate themselves where they are on that continuum and understand in which risk zone their alcohol use places them. It is hoped that this will lead people to develop intentions to adopt healthier and safer behaviours — that is, to move toward a less risky drinking zone along that continuum.

Presenting people in Canada with a continuum is also a direct response to stakeholders' wishes for the new guidance to be broadly relatable to all segments of the population, reflecting the different ways people in Canada use alcohol and the unique health and social outcomes associated with those patterns of use.

The weekly number of standard drinks that delineate the continuum's risk zones align with weekly recommendations in the U.K. (8.3 standard drinks), Australia, Denmark, France (7.4 standard drinks) and the Netherlands (5.2 standard drinks). In Canada, among persons aged 15 and older, about a fifth of females (23%) and males (21%) do not drink alcohol, 27% of females and 16% of males usually consume two standard drinks or less per week; 19% of females and 15% of males consume three to six standard drinks per week on average and a third of females (32%) and half of males (49%) usually consume more than six standard drinks per week. These proportions are based on data sources from the World Health Organization (2021) and Statistics Canada (2021).

Among people living in Canada aged 15 and older, one fifth (20%) do not drink alcohol, another fifth (21%) consume two standard drinks or less per week on average, 17% consume three to six standard drinks per week and 40% consume more than six standard drinks per week.

The continuum of risk is based on average quantities of alcohol people consume per week and the impact it has on their physical health. The experts looked at other types of evidence to support people in Canada who may wonder about the consequences of occasional drinking or the immediate effects that could fall outside the realm of physical health. This line of inquiry uncovers a second

⁷ Guidelines from BMJ on how to talk about risk were followed to qualify the risk zones (BMJ Best Practice, n.d.).

reason behind the recommendation to consider reducing alcohol use: consuming more than two standard drinks per drinking occasion is associated with an increased risk of harms to self and others, including injuries and violence.

The experts on this project are aware that the new Guidance on Alcohol and Health with its continuum of risk will be surprising and unsettling to large segments of the population, including members of the media, policy makers and those in the alcohol industry. However, the project is based on the principles of pragmatism and autonomy in harm reduction (Hawk et al., 2017) and the fundamental idea behind these principles is that people have the right to know. Alcohol is a carcinogen related to at least seven types of cancer, including common ones like colon and breast cancer (Canadian Cancer Society, 2022). It is a main cause of liver diseases, which are on the rise in Canada (Frolkis et al., 2022; Shaheen et al., 2022). Furthermore, in contrast to common perceptions, current evidence shows that drinking a little alcohol neither decreases nor increases the risk of ischemic heart disease. In fact, alcohol consumption is a risk factor for most types of cardiovascular diseases (Arora et al., 2022) and lower respiratory infections (Morojele et al., 2021), as well as injuries resulting from violence (see Update of Canada's Low-Risk Alcohol Drinking Guidelines: Overview of Reviews of the Association Between Alcohol Use and Aggression and Violence) and road crashes (Lyon et al., 2019). It is clear that people should not start to use alcohol or increase their alcohol use for health benefits. Hence, this project has confirmed that when it comes to drinking alcohol, less consumption means less risk of harm from alcohol and from this fact, it is necessary to promote the message that it is okay not to drink alcohol.

An encouraging fact associated with this new evidence is that every standard drink counts and any reduction in alcohol use is beneficial. Research demonstrates that many harms related to chronic disease caused by alcohol are reversible. People who decrease their alcohol consumption experience improvements in liver function, insulin resistance, weight, blood pressure and cancer-related growth factors (Mehta et al., 2018; Thomes et al., 2021). Reductions in alcohol consumption also decrease hypertension (Roerecke et al., 2017), and reduce the risk of cancer, atrial fibrillation, stroke, diabetes, pancreatitis and liver cirrhosis (Heckley et al., 2011; Lee et al., 2021; Nikkola et al., 2013; Verrill et al., 2009; Voskoboinik et al., 2020; Wu et al., 2021). In addition, the risk of infectious diseases, epilepsy and injuries are affected by the acute effects of alcohol and reductions in alcohol consumption will immediately decrease the risk of these outcomes (Imtiaz et al., 2017; Samokhvalov et al., 2010a; Samokhvalov et al., 2010b; Taylor et al., 2010).

The fact that any reduction in alcohol consumption is beneficial is all the more encouraging because it also applies to those who are unable or unwilling to reduce their risk to low or moderate levels. In fact, those consuming high levels of alcohol have even more to gain by reducing their consumption by as much they are able. It should also be noted that those who, regardless of their level of alcohol use, wish to reduce consumption but are unable to, may want to speak with a primary care provider about the various evidence-based approaches, including medications and treatment options, that are available to help reduce alcohol consumption (Regier & Jensen, 2021).

The project's work on the differences between women and men revealed some surprising results, namely that at low levels of consumption, the physiological differences between females and males as they affect the lifetime risk of death due to alcohol are minimal. However, the experts are unequivocal in stating that this should not distract from the evidence that **above the upper limit of the moderate risk zone for alcohol consumption, the lifetime risk of harm increases more steeply for women than for men.** On the one hand, biological factors enhance the impact of alcohol, causing more harm and faster intoxication on lesser amounts in females. For example, females sustain more liver damage on lesser amounts of alcohol compared to males. On the other hand, girls and women

suffer disproportionately from social factors that contribute to the negative impacts of alcohol in real life, such as increasing vulnerability to marketing exploitation, stigma, sexual assault and IPV.

On this note, the experts find it imperative to highlight that men's vulnerability to alcohol should not be overlooked. The work completed in this project has shown that men are more likely than women to experience and cause alcohol-related harms. Men drink more alcohol than women do (80% vs. 77%) and are more likely to drink in excess (28% vs 20%) (Government of Canada, 2022). As a consequence, they are over-represented among drivers involved in alcohol-related serious injury crashes (75% vs 22%) (Brown et al., 2021). They are also more likely to be treated in hospitals and hospitalized for alcohol-related medical emergencies and health problems (355 vs 165 hospitalizations per 100,000) (Canadian Institute for Health Information, 2022), to be diagnosed with an alcohol use disorder (4.7% vs 1.7%) (Pearson et al., 2013), and to die from alcohol-related causes (7.7% vs 2.6%) (World Health Organization, 2022). Alcohol is also more strongly associated with perpetration of violence for men then for women. Far more injuries, violence and deaths result from men's drinking, especially in the case of per occasion drinking.

Furthermore, reproductive health is compromised by alcohol use. People in Canada need to be aware that alcohol is a teratogen or agent that can cause malformation of the fetus. It can lead to learning, health and social effects with lifelong impact as well as brain injury, birth defects, behavioural problems, learning disabilities and other health problems typically referred to as FASD. These adverse effects are observed at relatively low levels of exposure or short-term exposure to high levels of consumption. For this reason, when pregnant or trying to get pregnant, there is no known safe amount of alcohol use.

Alcohol consumption can also negatively impact breastfeeding by causing a decrease in milk production, early cessation of breastfeeding and effects on infant sleep patterns. Alcohol enters breast milk through passive diffusion within 30 to 60 minutes following ingestion, so breastfeeding infants can be exposed to alcohol through breastmilk. However, infants are less able to metabolize alcohol. Therefore, when breastfeeding, no alcohol use is safest for the baby.

Finally, it should be pointed out that there are circumstances, other than those related to reproductive health, where the guidance's main recommendation does not apply and where no alcohol is safest. That is when driving a motor vehicle, using machinery and tools, taking medicine or other drugs that interact with alcohol, doing any kind of dangerous physical activity, being responsible for the safety of others or making important decisions.

3.2 Limitations

This project represents a synthesis of the best available evidence about the relationship between alcohol use and health outcomes. However, the current evidence base has limitations that are important to acknowledge. Specifically, there have been no randomized trials of alcohol consumption for any morbidity or mortality outcome. As noted in section 2.1.3, the observational studies that comprise the bulk of the evidence incorporated in this report are subject to a variety of threats to validity, mainly not controlling for confounding variables, only adjusting to age and sex. However, this is not to imply that observational studies are not helpful or valid when there is growing explicit acknowledgement in epidemiology that observational studies can also aim to estimate causal effects (Boon et al., 2022; Hernán, 2018).

Genetic (Mendelian) randomization studies were not included in our evidence base because they do not generally provide risk estimates in small enough increments of consumption to be useful for guidelines, and because there are few meta-analyses of genetic randomization studies. However, genetic studies do not find protective effects from low volume alcohol consumption for coronary

heart disease or ischemic strokes, contradicting findings from observational studies, including when the two analytic methods are compared side-by-side using the same data (Au Yeung et al., 2013; Chen et al., 2008; Cho et al., 2015; Holmes et al., 2014; Lawlor et al., 2013). On this basis, because coronary heart disease and ischemic stroke are important contributors to total mortality, it is possible that we are underestimating the impact of alcohol on the risk of premature death compared to not drinking, particularly at lower levels of consumption.

Most studies included in the meta-analyses used for this project assessed alcohol-outcomes based on weekly average levels of alcohol use and failed to account for the effects of drinking patterns (e.g., binge drinking or spacing out drinking over time) within those average levels. Hence, we were unable to directly model how binge drinking affects the risk of disease and injury. However, binge drinking is indirectly accounted for in our models as weekly alcohol consumption is correlated with the probability of binge drinking (Stahre et al., 2006).

Our report focuses mainly on health conditions that result in death. Existing literature was not adequate to characterize the relationship between alcohol use and important non-lethal conditions. These conditions would include those related to mental health but also several outcomes within the social realm. While this project reviewed the association between alcohol, aggression and violence, future alcohol guidelines should aim to incorporate other social issues such as neglect, crime, and job or school performance. Our report also does not cover the intangible effects of alcohol use, including suffering related to adverse outcomes or social enjoyment from alcohol consumption.

This project and its conclusions are based largely on population averages, and do not necessarily apply to any individual and their unique socio-behavioural, genetic and medical circumstances, nor do they account for risk and protective factors at the community, familial or individual levels. As mentioned below, these issues should be addressed in the next phase of this project, which will focus on the guidance's dissemination, appropriation and use. Individualizing risk should be an important goal of this project's knowledge mobilization activities.

Finally, the parameters of the project did not allow for a detailed analysis of the relationship between alcohol use and harm among youth, especially those under the legal drinking age, an area that should be pursued. It is well established that alcohol is the most common psychoactive substance used by youth and that it is a leading behavioural risk factor for death and social problems in this age group (American College Health Association, 2016; Health Canada, 2015, 2021; Pearson et al., 2013). A high proportion of alcohol consumed by youth is consumed through binge drinking with its attendant risks of alterations to brain development and cognitive function (Carson, 2015; Crews et al., 2016; Spear, 2018). Binge drinking also increase the risk of injury, aggression, violence and other age-related consequences such as dating violence and worsening academic performance (American College Health Association, 2016; Health Canada, 2015, 2021), Even for the same number of drinks consumed per drinking occasion, the risk of adverse outcomes from alcohol consumption is greater for youth than for adults. This may be due to several factors, including greater impulsivity and less emotional maturity among youth, lower body mass on average, less experience doing complex tasks that are made more dangerous by alcohol, and faster drinking speeds (Crews et al., 2016). For these reasons, the prudent advice to youth is to delay alcohol use for as long as possible.

3.3 Moving Forward

In light of the new Guidance on Alcohol and Health and the fact that alcohol literacy in the population is low (Canadian Centre on Substance Use and Addiction, 2021), substantial and sustained efforts will be required to develop messaging that speaks directly to the unique concerns of people with

diverse backgrounds and personal experiences who ultimately will make their own choices. For example, work developed in parallel with this project has shown that alcohol consumers aged 18 to 30 may be more receptive to health messaging about the effects of their alcohol use on life expectancy, than to messages that simply present a guideline (Stockwell et al., 2022). Others may want to direct their prevention efforts toward young adults, particularly boys and young men among whom drinking to intoxication is normalized. For example, there is a need to address the belief among men that alcohol serves as an excuse for risky and aggressive behaviours. The message needs to be sent to men that that they should take extra care when they drink alcohol so that they and others are not injured or hurt because of their alcohol use. Other recommendations and suggestions, particularly in relation to sex and gender, have been prepared in connection with this project and are available to those who would like to build a campaign around them (see Appendix 3).

Furthermore, the individualization of risk should be an important goal of this project's knowledge mobilization. Health professionals, family doctors and nurses, who are crucial allies with credibility in explaining the continuum of risks associated with alcohol to patients and the general public, will need to be involved. They could make a valuable contribution to health care by reducing direct alcohol-related costs; we will return to this issue below.

People in Canada should "Learn the facts. Parse the fictions. Act accordingly." To do so, they will need more than plain and clear information, no matter how effective newly developed target campaigns may be. Alcohol, like tobacco or processed foods, has been termed a "sinful good," meaning that when people use it they get the pleasure now and suffer the consequences later. To make wise decisions about such goods, people need encouragement (Thaler & Sunstein, 2008). People in Canada who want to move toward the lower end of the continuum of alcohol-related risks need an environment that supports healthier and safer decisions. There needs to be a cultural shift away from an *alcogenic culture* (Johnston, 2014). Therefore, a corollary to the current project is for governments to design a healthier environment to make it easier for people to make difficult decisions about alcohol.

First and foremost, evidence shows that, to adhere to the Guidance on Alcohol and Health, consumers will need consistent, easy-to-use information on alcohol containers to accurately track and monitor their alcohol use in terms of standard drinks. While beer remains the alcoholic beverage of choice for people in Canada, the growing craft movement is producing beer with a variety of alcohol content levels and in a variety of sizes of cans and bottles for consumption at home. Now, more than ever, to count how many standard drinks they consume, people need information at the point of pour. While Canada is a world leader in mandating enhanced labels on tobacco and cannabis packages, alcohol containers are exempt from these requirements. Enhanced alcohol container labels are an increasingly popular strategy for providing information to consumers, and a key recommendation by national and international health organizations (Jané-Llopis et al., 2020; Vallance et al., 2021; World Health Organization, 2022). A direct consequence of the current project is the recognition that an especially effective policy change could be the mandatory labelling of all alcoholic beverages with the number of standard drinks in a container.

Many studies have shown that people are most likely to follow guidance if they know the reasons why they should (Pettigrew et al., 2021; Wakefield et al., 2018). Our public consultation revealed that without understanding the risks and benefits associated with alcohol use, people are unlikely to understand why they should follow the guidelines. Therefore, mandatory labelling of all alcoholic beverages with health warnings and Canada's Guidance on Alcohol and Health would also be adequate and effective. Labelling can be an important intervention in a more comprehensive alcohol

⁸These words are used by Alec Bruce in an op-ed published in *The Globe and Mail* on Nov. 12, 2021 (Bruce, 2021, Nov. 12).

strategy (Kokole et al., 2021). Evidence has shown that adding health warnings to alcohol labels can increase public awareness of the causal link with cancer and reduce per capita alcohol consumption. Health warning labels can also strengthen public support for policies that are often unpopular but known to reduce population-level alcohol-caused harms (Weerasinghe et al., 2020).

To support people living in Canada who want to move toward the less risky end of the continuum, governments will need to be involved on other policy fronts. Cost-effective policies and feasible interventions that reduce the overall level of alcohol consumption are well documented at the global, national and provincial levels (Vallance et al., 2021; World Health Organization, 2022). For example, work conducted by the Canadian Alcohol Policy Evaluation committee and the National Alcohol Strategy Advisory Committee has highlighted that measures such as strengthened regulations of alcohol advertising and marketing, restrictions on the physical availability of alcohol, and the adoption of a minimum price for alcohol sold are all beneficial to public health. If the new Guidance on Alcohol and Health were to facilitate policy discussions and initiatives, the effects could be considerable and extend beyond the public health sphere to include economic benefits.

Alcohol is a leading preventable cause of death, disability injuries, accidents and social problems. In 2017, it caused 18,000 deaths in Canada, and the year before, there were about 77,000 hospitalizations due to conditions entirely caused by alcohol, an average of 212 a day (Canadian Institute for Health Information, 2022). According to the Canadian Substance Use Costs and Harms study (Canadian Substance Use Costs and Harms Scientific Working Group, 2020), the annual direct costs of alcohol are \$16.7 billion, with \$5,4 billion of that sum being spent on health care. This is far more than the direct costs associated with tobacco (\$12.3 billion), opioids (\$5.9 billion) or cannabis (\$3.2 billion), and far exceeding the value of the revenue produced by alcohol sales and taxation, which was last estimated to be \$13.5 billion (Statistics Canada, 2021). Hence, by adopting policies to support healthier and safer decisions around alcohol use, government may save money and reduce per-person costs attributable to alcohol use in Canada, most recently estimated at \$455 per year (Canadian Substance Use Costs and Harms Scientific Working Group, 2020).

3.4 Future Update of Canada's Guidance on Alcohol and Health

We recommend that the Guidance on Alcohol and Health be regularly reviewed as the field of alcohol epidemiology develops. More specifically, an update should be requested when:

- Emerging or improved methods are available to address the previously mentioned limitations;
- The availability of evidence changes. For example, when high-quality studies on alcohol-caused conditions like mental health become available, or when evidence identifies new alcohol-caused conditions that are currently unappreciated or wholly recognized. This could be the case for conditions such as melanoma and prostate, pancreatic, gastric and stomach cancers, for which evidence is accumulating that alcohol consumption could be a risk factor.
- The prevalence of alcohol consumption changes within the population, new segments of the
 population become particularly at risk or new consumption patterns such as polysubstance use
 emerge.

3.5 Conclusion

Canada's Guidance on Alcohol and Health reflects the conclusions drawn from global evidence reviews, mathematical modelling, consultations with the public and experts, and discussion among

the experts on the project. It is hoped that this work will be useful to people in Canada who are health conscious and want to know more about the effects of alcohol consumption on their well-being. The Guidance on Alcohol and Health was developed to help them make informed decisions about their alcohol use.

The Guidance on Alcohol and Health requires a cultural shift that, by and large, can only be orchestrated by governments through policies and collaboration with employers, healthcare providers and community stakeholders to make people aware of and better at managing their risks. The evidence reviewed and presented here should influence provincial and federal governments to implement alcohol policies focused on reducing alcohol-related harms and promoting health and wellness. Information and advice are useful and necessary for people in Canada, but an environment supporting healthier and more informed-behaviour choices around alcohol is an absolute pre-requisite for a healthy society.

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Appendix 1: Lifetime Risk of Alcohol-Attributable Death and Disability: Shadow Analysis

Purpose

To inform decisions regarding the formation of Canadian drinking guidelines, a primary analysis was performed whose results were a collection of risk relationships that estimated the risk of death and disability as a function of average daily alcohol use by those who live in Canada.

Toward ensuring accuracy of the primary analysis, this shadow analysis process was designed and undertaken. The general objective of a shadow analysis is for the main and shadow analysts to come together and share the desired project input and broad methodology. The two analyses are conducted independently, in parallel, and results are compared to ensure accuracy of the primary collection of results.

Method

The primary and shadow researchers met several times to discuss strategy and determine raw input that would be shared by both analyses. Shared inputs were as follows:

- Relative risk function definitions: Each alcohol-attributable condition considered was assigned a
 dose-response relative risk function, and the source and definition of these risk functions was
 shared. Relative risk functions were prepared by the primary researcher.
- Prevalence and consumption data: Raw survey data for Canada was transformed into total and relative population alcohol consumption, where relevant population strata were sex and age.
 Prevalence and consumption data were prepared by the primary researcher.
- Deaths, years lived with disability, and incidence in the population, by condition: Raw data were
 aggregated and summarized into alcohol-attributable condition categories for each outcome
 category. Death data was prepared by the primary researcher and also the shadow researcher.
 Years lived with disability and incidence were prepared by the primary researcher.

The two analysts discussed the broad methodologies. The implementation of the lifetime risk methodology was then performed in R in both the primary and shadow analyses. Researchers wrote their scripts and/or packages independently. Primary and shadow analysis results were compared with an eye toward whether differences would have an impact on the quantitative guidelines endeavour.

Summary of the Comparison of Findings

The shadow analysis is a very near-match with the primary analysis, with differences accounted for by expected, random differentials in the model-building exercise, the random draws employed throughout the process and slight differences in methodological choices between analysts. Small differences between the shadow analyses and the primary analysis **are not expected to lead to differences in interpretations of results for the quantitative guidelines endeavour.**

Figures 1 and 2 compare the results of the primary and shadow analyses. Figure 1 displays lifetime deaths per 1,000 people at each level of consumption up to an average of 100 g ethanol/day. Figure 2 displays the same statistic on the range of up to an average of 40 g ethanol/day. In each figure, the results of the primary analysis (and associated 95% confidence intervals [CIs]) are shown

in red and the shadow analyses in blue. In Figure 2, it is clear that the shadow analysis produced results that would not lead to substantive differences in interpretation when designing alcohol use guidelines for people who live in Canada. A high similarity between the shadow and primary analysis is observed for all levels of average daily alcohol use, and in particular the match is near-perfect at levels of average daily alcohol use below 50 g ethanol/ day. This behaviour is consistent throughout the remainder of the shadow results, distributed separately.

Figure 1: Visual comparison between primary results and shadow results in the category of male death, range of average consumption of from 1 to 100 g ethanol/day

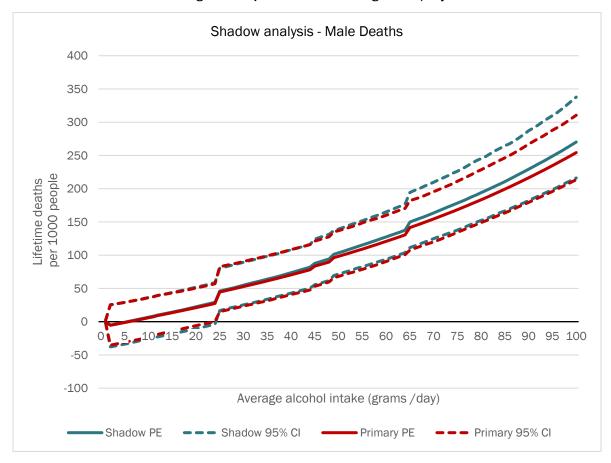
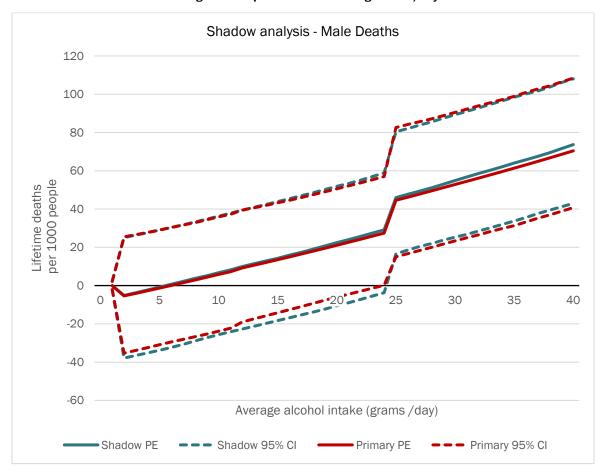


Figure 2: Visual comparison between primary results and shadow results in the category of male death, range of average consumption of from 1 to 40 g ethanol/day



Appendix 2: Confidence Intervals for Risk of Disease and Injury

Table 1. Increased risk of diseases and injuries, with 95% confidence intervals, for females, based on average daily alcohol use

Condition or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	1.04	1.07	1.11	1.15	1.20	1.24	1.26	1.62	2.05	3.33
	(1.01, 1.07)	(1.01, 1.14)	(1.02, 1.21)	(1.03, 1.29)	(1.03, 1.38)	(1.04, 1.47)	(1.04, 1.52)	(1.09, 2.38)	(1.14, 3.61)	(1.25, 8.60)
Lower respiratory infections	1.01	1.02	1.03	1.04	1.05	1.06	1.06	1.14	1.21	1.38
	(1.00, 1.02)	(1.00, 1.03)	(1.01, 1.05)	(1.01, 1.07)	(1.01, 1.09)	(1.01, 1.10)	(1.01, 1.11)	(1.03, 1.25)	(1.04, 1.39)	(1.07, 1.74)
Oral cavity and pharynx cancer	1.05	1.10	1.16	1.22	1.28	1.34	1.37	1.89	2.52	4.38
	(1.04, 1.06)	(1.09, 1.12)	(1.13, 1.18)	(1.18, 1.25)	(1.23, 1.31)	(1.28, 1.39)	(1.31, 1.42)	(1.74, 2.04)	(2.24, 2.80)	(3.68, 5.15)
Oesophagus cancer	1.03	1.05	1.08	1.11	1.14	1.17	1.19	1.43	1.69	2.39
	(1.03, 1.03)	(1.05, 1.06)	(1.08, 1.09)	(1.11, 1.12)	(1.13, 1.15)	(1.16, 1.18)	(1.18, 1.20)	(1.40, 1.45)	(1.64, 1.74)	(2.28, 2.50)
Colorectal cancer	1.01	1.03	1.04	1.06	1.07	1.08	1.09	1.20	1.31	1.57
	(1.01, 1.02)	(1.02, 1.04)	(1.03, 1.05)	(1.04, 1.07)	(1.05, 1.09)	(1.06, 1.11)	(1.06, 1.12)	(1.14, 1.26)	(1.21, 1.42)	(1.38, 1.79)
Liver cancer	1.01	1.02	1.02	1.03	1.04	1.05	1.05	1.11	1.17	1.30
	(1.00, 1.01)	(1.01, 1.02)	(1.01, 1.04)	(1.02, 1.05)	(1.02, 1.06)	(1.02, 1.07)	(1.03, 1.08)	(1.05, 1.17)	(1.08, 1.26)	(1.14, 1.48)
Breast cancer	1.02	1.04	1.06	1.08	1.10	1.12	1.13	1.28	1.44	1.84
	(1.01, 1.02)	(1.03, 1.05)	(1.04, 1.07)	(1.06, 1.09)	(1.07, 1.12)	(1.09, 1.15)	(1.09, 1.16)	(1.21, 1.36)	(1.32, 1.57)	(1.60, 2.14)
Larynx cancer	1.03	1.06	1.09	1.12	1.16	1.19	1.21	1.46	1.74	2.43
	(1.02, 1.04)	(1.04, 1.07)	(1.07, 1.11)	(1.09, 1.15)	(1.11, 1.19)	(1.14, 1.24)	(1.15, 1.26)	(1.34, 1.59)	(1.54, 1.95)	(2.02, 2.91)
Pancreatitis	0.95	0.90	0.85	0.81	0.77	0.74	0.73	0.79	1.15	2.74
	(0.91, 0.99)	(0.82, 0.98)	(0.74, 0.98)	(0.68, 0.97)	(0.62, 0.97)	(0.58, 0.97)	(0.56, 0.97)	(0.53, 1.21)	(0.69, 1.94)	(1.05, 7.47)
Diabetes Mellitus	0.85	0.80	0.77	0.75	0.73	0.72	0.71	0.66	0.65	0.67
	(0.80, 0.89)	(0.75, 0.86)	(0.71, 0.84)	(0.68, 0.83)	(0.65, 0.82)	(0.63, 0.81)	(0.63, 0.80)	(0.56, 0.78)	(0.53, 0.80)	(0.52, 0.86)
Liver cirrhosis	1.61	1.94	2.24	2.53	2.82	3.11	3.25	5.45	7.85	14.37
	(1.51, 1.72)	(1.77, 2.12)	(2.00, 2.50)	(2.23, 2.87)	(2.44, 3.24)	(2.66, 3.61)	(2.76, 3.81)	(4.30, 6.82)	(5.90, 10.32)	(9.92, 20.47)
Atrial fibrillation and flutter	1.01	1.03	1.04	1.05	1.07	1.08	1.09	1.19	1.29	1.54
	(1.01, 1.02)	(1.02, 1.03)	(1.03, 1.05)	(1.04, 1.07)	(1.05, 1.08)	(1.06, 1.10)	(1.07, 1.11)	(1.14, 1.24)	(1.22, 1.38)	(1.39, 1.71)
Hypertension	1.01	1.02	1.04	1.05	1.06	1.07	1.08	1.16	1.25	1.45
	(1.00, 1.02)	(1.00, 1.04)	(1.01, 1.06)	(1.01, 1.09)	(1.01, 1.11)	(1.02, 1.12)	(1.03, 1.13)	(1.06, 1.26)	(1.12, 1.39)	(1.20, 1.74)
Ischemic heart disease	0.95	0.95	0.95	0.95	0.95	0.95	0.95	1.04	1.04	1.15
	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.81, 1.34)	(0.81, 1.34)	([0.86, 1.52)

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Ischemic stroke	0.90	0.90	0.90	0.90	0.90	0.92	0.92	1.08	1.08	1.14
	(0.85, 0.95)	(0.85, 0.95)	(0.85, 0.95)	(0.85, 0.95)	(0.85, 0.95)	(0.87, 0.97)	(0.87, 0.97)	(1.01, 1.16)	(1.01, 1.16)	(1.01, 1.28)
Intracerebral	0.92	0.92	0.92	0.92	0.92	0.99	0.99	1.25	1.25	1.67
hemorrhage	(0.77, 1.10)	(0.77, 1.10)	(0.77, 1.10)	(0.77, 1.10)	(0.77, 1.10)	(0.83, 1.19)	(0.83, 1.19)	(0.92, 1.69)	(0.92, 1.69)	(1.26, 2.25)
Subarachnoid	1.21	1.21	1.21	1.21	1.21	1.11	1.11	1.39	1.39	1.82
haemorrhage	(0.48, 3.06)	(0.48, 3.06)	(0.48, 3.06)	(0.48, 3.06)	(0.48, 3.06)	(0.33, 3.90)	(0.33, 3.90)	(0.32, 5.94)	(0.32, 5.94)	(0.38, 10.12)
Epilepsy	1.03	1.06	1.08	1.11	1.14	1.17	1.18	1.40	1.64	2.29
	(1.02, 1.04)	(1.04, 1.07)	(1.06, 1.10)	(1.08, 1.14)	(1.10, 1.17)	(1.13, 1.21)	(1.14, 1.23)	(1.30, 1.51)	(1.46, 1.84)	(1.89, 2.76)
Road injuries	1.02	1.04	1.06	1.08	1.10	1.12	1.13	1.30	1.47	1.90
	(1.01, 1.03)	(1.02, 1.06)	(1.03, 1.09)	(1.04, 1.13)	(1.04, 1.16)	(1.05, 1.20)	(1.06, 1.21)	(1.12, 1.50)	(1.19, 1.82)	(1.34, 2.73)
Other unintentional injuries	1.02	1.03	1.05	1.06	1.08	1.10	1.11	1.23	1.36	1.68
	(1.01, 1.02)	(1.02, 1.04)	(1.03, 1.06)	(1.05, 1.08)	(1.06, 1.10)	(1.07, 1.13)	(1.07, 1.14)	(1.16, 1.31)	(1.25, 1.49)	(1.45, 1.95)
Intentional injuries	1.05	1.10	1.16	1.22	1.28	1.35	1.38	1.96	2.71	5.32
	(1.04, 1.06)	(1.08, 1.13)	(1.12, 1.20)	(1.17, 1.28)	(1.21, 1.36)	(1.26, 1.44)	(1.29, 1.49)	(1.69, 2.28)	(2.17, 3.39)	(3.66, 7.73)



Table 2. Increased risk of diseases and injuries, with 95% confidence intervals, for males, based on average daily alcohol use

Condition or injury	1	2	3	4	5	6	7	14	21	35
Tuberculosis	1.04	1.07	1.11	1.15	1.20	1.24	1.26	1.62	2.05	3.33
	(1.01, 1.07)	(1.02, 1.14)	(1.02, 1.21)	(1.03, 1.30)	(1.04, 1.38)	(1.05, 1.48)	(1.05, 1.52)	(1.11, 2.40)	(1.17, 3.66)	(1.30, 8.77)
Lower respiratory infections	1.01	1.02	1.03	1.04	1.05	1.06	1.06	1.14	1.21	1.38
	(1.00, 1.02)	(1.00, 1.04)	(1.01, 1.05)	(1.01, 1.07)	(1.01, 1.09)	(1.01, 1.11)	(1.01, 1.12)	(1.03, 1.27)	(1.04, 1.42)	(1.07, 1.80)
Oral cavity and pharynx cancer	1.05	1.10	1.16	1.22	1.28	1.34	1.37	1.89	2.52	4.38
	(1.04, 1.06)	(1.09, 1.12)	(1.14, 1.18)	(1.19, 1.25)	(1.24, 1.32)	(1.29, 1.39)	(1.32, 1.43)	(1.75, 2.06)	(2.25, 2.83)	(3.69, 5.19)
Oesophagus cancer	1.03	1.05	1.08	1.11	1.14	1.17	1.19	1.43	1.69	2.39
	(1.03, 1.03)	(1.05, 1.06)	(1.08, 1.09)	(1.10, 1.12)	(1.13, 1.15)	(1.16, 1.18)	(1.18, 1.20)	(1.40, 1.46)	(1.64, 1.74)	(2.28, 2.51)
Colorectal cancer	1.01	1.03	1.04	1.06	1.07	1.08	1.09	1.20	1.31	1.57
	(1.01, 1.02)	(1.02, 1.04)	(1.03, 1.05)	(1.04, 1.07)	(1.05, 1.09)	(1.06, 1.11)	(1.07, 1.12)	(1.15, 1.26)	(1.22, 1.41)	(1.40, 1.79)
Liver cancer	1.01	1.02	1.02	1.03	1.04	1.05	1.05	1.11	1.17	1.30
	(1.00, 1.01)	(1.01, 1.02)	(1.01, 1.04)	(1.02, 1.05)	(1.02, 1.06)	(1.02, 1.07)	(1.03, 1.08)	(1.06, 1.17)	(1.08, 1.26)	(1.14, 1.48)
Breast cancer	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)
Larynx cancer	1.03	1.06	1.09	1.12	1.16	1.19	1.21	1.46	1.74	2.43
	(1.02, 1.04)	(1.04, 1.07)	(1.07, 1.11)	(1.09, 1.15)	(1.11, 1.20)	(1.14, 1.24)	(1.15, 1.26)	(1.33, 1.59)	(1.53, 1.97)	(2.03, 2.94)
Pancreatitis	1.04	1.07	1.11	1.15	1.19	1.23	1.25	1.60	2.00	3.20
	(1.02, 1.05)	(1.04, 1.10)	(1.06, 1.16)	(1.08, 1.22)	(1.10, 1.28)	(1.12, 1.34)	(1.13, 1.38)	(1.30, 1.94)	(1.47, 2.67)	(1.91, 5.17)
Diabetes Mellitus	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.01	1.02	1.06
	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.00)	(1.00, 1.01)	(1.00, 1.01)	(0.99, 1.01)	(0.99, 1.01)	(0.98, 1.05)	(0.97, 1.09)	(1.01, 1.11)
Liver cirrhosis	1.06	1.12	1.19	1.26	1.33	1.40	1.44	2.14	3.07	6.53
	(1.05, 1.07)	(1.11, 1.14)	(1.16, 1.22)	(1.22, 1.30)	(1.28, 1.38)	(1.34, 1.47)	(1.38, 1.52)	(1.94, 2.37)	(2.66, 3.57)	(5.13, 8.41)
Atrial fibrillation and flutter	1.01	1.03	1.04	1.05	1.07	1.08	1.09	1.19	1.29	1.54
	(1.01, 1.02)	(1.02, 1.03)	(1.03, 1.05)	(1.04, 1.06)	(1.05, 1.08)	(1.06, 1.10)	(1.07, 1.11)	(1.14, 1.24)	(1.21, 1.37)	(1.38, 1.69)
Hypertension	1.03	1.06	1.09	1.12	1.15	1.17	1.17	1.29	1.36	1.47
	(1.02, 1.04)	(1.03, 1.08)	(1.05, 1.13)	(1.07, 1.17)	(1.09, 1.22)	(1.10, 1.24)	(1.11, 1.25)	(1.21, 1.40)	(1.27, 1.48)	(1.37, 1.60)
Ischemic heart disease	0.95	0.95	0.95	0.95	0.95	0.95	0.95	1.04	1.04	1.15
	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.75, 1.21)	(0.81, 1.34)	(0.81, 1.34)	([0.86, 1.52)
Ischemic stroke	0.92	0.92	0.92	0.92	0.92	0.92	0.92	1.08	1.08	1.14
	(0.87, 0.97)	(0.87, 0.97)	(0.87, 0.97)	(0.87, 0.97)	(0.87, 0.97)	(0.87, 0.97)	(0.87, 0.97)	(1.02, 1.15)	(1.02, 1.15)	(1.01, 1.27)
Intracerebral hemorrhage	0.92	0.92	0.92	0.92	0.92	0.99	0.99	1.25	1.25	1.67
	(0.78, 1.11)	(0.78, 1.11)	(0.78, 1.11)	(0.78, 1.11)	(0.78, 1.11)	(0.82, 1.19)	(0.82, 1.19)	(0.93, 1.68)	(0.93, 1.68)	(1.24, 2.22)

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Condition or injury	1	2	3	4	5	6	7	14	21	35
Subarachnoid haemorrhage	1.21	1.21	1.21	1.21	1.21	1.11	1.11	1.39	1.39	1.82
	(0.51, 2.81)	(0.51, 2.81)	(0.51, 2.81)	(0.51, 2.81)	(0.51, 2.81)	(0.32, 4.00)	(0.32, 4.00)	(0.25, 6.42)	(0.25, 6.42)	(0.32, 10.36)
Epilepsy	1.03	1.06	1.08	1.11	1.14	1.17	1.18	1.40	1.64	2.29
	(1.02, 1.04)	(1.04, 1.07)	(1.07, 1.10)	(1.09, 1.14)	(1.11, 1.17)	(1.13, 1.21)	(1.14, 1.23)	(1.31, 1.52)	(1.48, 1.85)	(1.93, 2.78)
Road injuries	1.03	1.06	1.09	1.12	1.16	1.19	1.21	1.49	1.80	2.68
	(1.02, 1.04)	(1.05, 1.07)	(1.07, 1.11)	(1.10, 1.15)	(1.12, 1.20)	(1.15, 1.24)	(1.16, 1.26)	(1.37, 1.62)	(1.60, 2.04)	(2.19, 3.30)
Other unintentional injuries	1.02	1.03	1.05	1.06	1.08	1.10	1.11	1.23	1.36	1.68
	(1.01, 1.02)	(1.02, 1.04)	(1.03, 1.06)	(1.05, 1.08)	(1.06, 1.10)	(1.07, 1.13)	(1.08, 1.14)	(1.16, 1.31)	(1.25, 1.49)	(1.45, 1.95)
Intentional injuries	1.05	1.10	1.16	1.22	1.28	1.35	1.38	1.96	2.71	5.32
	(1.04, 1.06)	(1.08, 1.13)	(1.12, 1.20)	(1.17, 1.28)	(1.21, 1.36)	(1.26, 1.44)	(1.28, 1.48)	(1.68, 2.27)	(2.16, 3.38)	(3.63, 7.67)

Appendix 3: Specific Messages for Girls and Women to Supplement the Guidance on Alcohol and Health

It is important for girls and women to know:

- There are risks of alcohol use for both men and women, but it is not a level playing field, as alcohol affects women's bodies more negatively
- Alcohol is processed by women's bodies differently, causing more negative health effects, earlier, after lesser amounts of alcohol
- Women become intoxicated faster after drinking less than men due to smaller bodies and organs, less body water, hormonal effects, and different enzyme actions that break down alcohol
- Alcohol has more serious health effects on females than males, due to body size, body fat/water ratio, hormonal effects and differing actions of enzymes that break down alcohol
- Alcohol consumption increases risk of breast cancer, a very common cancer in Canadian women
- Women experience more liver injuries on lower levels of alcohol, compared to men

It is also important for girls and women to know:

- Perpetrators of sexual assault often target someone who has been drinking alcohol or is intoxicated
- Women often use alcohol to cope with the stress of trauma, intimate partner violence and caregiving, which can lead to poorer, not better health
- Girls and women with histories of childhood abuse progress more quickly from starting to drink to becoming alcohol dependent

And some ideas for the pregnancy-related messages:

- Alcohol use in pregnancy negatively affects both women's and fetal health
- There is no safe level of alcohol use in pregnancy, so it is safest not to drink at all while pregnant
- The more alcohol consumed, the greater the risk of harm for women's and fetal health
- Alcohol use in pregnancy especially when combined with poor nutrition and tobacco use can result in infant death, birth defects, and lifelong behavioural and cognitive problems
- Alcohol use in pregnancy can increase the risk of miscarriage.

Appendix 4: Update of Canada's Low-Risk Alcohol Drinking Guidelines: Open Consultation

A total of 886 completed submissions for the open consultation on the update of Canada's Low-Risk Alcohol Drinking Guidelines were received. Respondents were mostly individuals who are concerned about the effects of alcohol use on themselves, their family or their friends (75.3%). Others identified themselves as professionals who use alcohol guidelines in their work (15%) or as representatives of an organization (4.7%). Five percent of the respondents preferred not to disclose this information. Among respondents, 746 indicated they would like to answer questions related to the public summary, 377 indicated they would like to answer questions related to the technical summary and 307 mentioned they would like to answer questions related to the technical report.

Public Summary

Please indicate how strongly you agree with the following statement: The **Public Summary** is clear, simple, and easy to understand.

Level of agreement	Frequency	Percent
Strongly agree	276	37.0
Agree	311	41.7
Neither agree nor disagree	63	8.4
Disagree	55	7.4
Strongly disagree	31	4.2
Prefer not to answer	10	1.3
Total	746	100.0

Technical Summary

Please indicate how strongly you agree with the following statement: The **Technical Summary** is clear, simple, and easy to understand.

Level of agreement	Frequency	Percent
Strongly agree	111	29.4
Agree	171	45.4
Neither agree nor disagree	51	13.5
Disagree	20	5.3
Strongly disagree	15	4.0
Prefer not to answer	9	2.4
Total	377	100.0

Please indicate how strongly you agree with the following statement: The information presented in the **Technical Summary** is likely to make people reconsider their alcohol drinking habits.

Level of agreement	Frequency	Percent
Strongly agree	73	19.4
Agree	146	38.7
Neither agree nor disagree	88	23.3
Disagree	35	9.3
Strongly disagree	22	5.8
Prefer not to answer	13	3.4
Total	377	100.0

Please indicate how strongly you agree with the **Technical Summary's** Policy Implications.

Level of agreement	Frequency	Percent
Strongly agree	140	37.1
Agree	117	31.0
Neither agree nor disagree	44	11.7
Disagree	32	8.5
Strongly disagree	30	8.0
Prefer not to answer	14	3.7
Total	377	100.0

Technical Report

Takeaway 1: All levels of alcohol consumption are associated with some risk, so drinking less is better for everyone.

Please indicate how strongly you agree with takeaway 1.

Level of agreement	Frequency	Percent
Strongly agree	166	54.1
Agree	77	25.1
Neither agree nor disagree	21	6.8
Disagree	16	5.2
Strongly disagree	21	6.8
Prefer not to answer	6	2.0
Total	307	100.0

Takeaway 2: There is a continuum of risk whereby the risk for those who consume 2 standard drinks or less per week is negligible to low; it is moderate for those who consume between 3 and 6 standard drinks per week; and it is high for those who consume more than 6 standard drinks per week, with increasingly higher levels of risk with every additional drink.

Please indicate how strongly you agree with takeaway 2.

Level of agreement	Frequency	Percent
Strongly agree	129	42.0
Agree	83	27.0
Neither agree nor disagree	34	11.1
Disagree	30	9.8
Strongly disagree	25	8.1
Prefer not to answer	6	2.0
Total	307	100.0

Takeaway 3: On any occasion, any level of consumption has risks, and with more than two standard drinks, most individuals will have an increased risk of injuries or other problems.

Please indicate how strongly you agree with takeaway 3.

Level of agreement	Frequency	Percent
Strongly agree	126	41.0
Agree	85	27.7
Neither agree nor disagree	39	12.7
Disagree	29	9.4
Strongly disagree	23	7.5
Prefer not to answer	5	1.6
Total	307	100.0

Takeaway 4: Disproportionately more injuries, violence and deaths result from men's drinking. Please indicate how strongly you agree with takeaway 4.

Level of agreement	Frequency	Percent
Strongly agree	151	49.2
Agree	88	28.7
Neither agree nor disagree	27	8.8
Disagree	14	4.6
Strongly disagree	18	5.9
Prefer not to answer	9	2.9
Total	307	100.0

Takeaway 5: Above low levels of alcohol consumption, the health risks increase more steeply for women than for men.

Please indicate how strongly you agree with takeaway 5.

Level of agreement	Frequency	Percent
Strongly agree	122	39.7
Agree	83	27.0
Neither agree nor disagree	55	17.9
Disagree	18	5.9
Strongly disagree	19	6.2
Prefer not to answer	10	3.3
Total	307	100.0

Takeaway 6: It is safest to not drink while pregnant and during the preconception period.

Please indicate how strongly you agree with takeaway 6.

Level of agreement	Frequency	Percent
Strongly agree	219	71.3
Agree	57	18.6
Neither agree nor disagree	16	5.2
Disagree	3	1.0
Strongly disagree	5	1.6
Prefer not to answer	7	2.3
Total	307	100.0

Takeaway 7: For women who are breastfeeding, it is safest not to use alcohol.

Please indicate how strongly you agree with takeaway 7.

Level of agreement	Frequency	Percent
Strongly agree	188	61.2
Agree	78	25.4
Neither agree nor disagree	20	6.5
Disagree	7	2.3
Strongly disagree	5	1.6
Prefer not to answer	9	2.9
Total	307	100.0

Public Consultation: Summary of Key Actions Taken

The responses received from the open consultation were analyzed and categorized. The table below presents the main categories of comments as well as the actions taken by the LRDG-Scientific Expert Panel (LRDG-SEP) to address comments which fell within the scope of this project's mandate.

There were several suggestions made for knowledge mobilization activities, including knowledge synthesis, dissemination, transfer and exchange. These suggestions have been recorded but are not listed here as they could not be considered for action (i.e., could not lead to edits and revisions of the final report).

Consultation comment or suggestion	Action taken
Public Summary	
Provide more information about specific cancers.	There are already many consequences of different types presented in the public summary, the suggested consequences were not added. However, the public summary was edited to link the average amount of weekly use with examples consequences.
In general, some respondents want to see more statistics.	The objective of the document is to communicate information without statistics that would need contextual information and more explanations to be easily understood. No statistics were added.
Explain and provide a graphic about the effect of alcohol on the body.	Adding this information would require including information that would be too detailed for a public summary.
Mention that alcohol is an addictive substance.	The focus of the public summary is on low- and moderaterisk alcohol drinking.
In general, some respondents want to see different social harms mentioned going beyond one own's health.	Mention of social harms added in the public summary. Mention of consequences for others added as well.
Clearly show the cumulative and long-term effects.	Rephrasing done to show the cumulative effects of the consequences. Information about long-term small amounts not included for lack of space.
Mention the consequences of binge drinking vs having drinks across the week.	No mention on binge drinking but a highlighted statement added stating do not drink more than two drinks on one occasion.
Mention the social aspect of drinking.	Out of scope for this summary.
Emphasize sobriety and its benefits.	Information about the benefits of not drinking or reduced consumption has been added in the document.
More emphasis on specific consequences related to the number of drinks.	The consequences of drinking are now paired with the number of drinks in the graphic. Colours used to show the continuum will be emphasized to make this information even clearer.
Mention the risk of dying for a young person so young people feel concerned.	There is already a mention that alcohol can shorten one's life.
Present clearly what are safe amount.	The colours on the continuum are adjusted to avoid indicating that 1 to 2 drinks per week is not without risk. Specifically, a hint of yellow is added in the circled numbers under 1 and 2 drinks.

Consultation comment or suggestion	Action taken
Respondents mention wanting to see other consequences: State clearly that there is no protective effect to alcohol.	The public summary was comprehensively edited to link the average amount of weekly use with examples consequences.
Include more information about alcohol use and reproductive health.	It was decided to maintain the focus of the summary on pregnancy and to put more emphasis on zero alcohol during pregnancy.
Request for a gender-inclusive language.	The content was rephrased to be more gender inclusive.
Provide information about different types of alcoholic beverages, their specific effects and their ingredients.	No information about specific products was added.
People requested clarification on what is a standard drink.	The word "standard" was added whenever relevant.
Mention if lifestyle factors and predispositions influence the causality between alcohol use and consequences.	Information added in the content mentioning that lifestyle does not prevent alcohol caused consequences.
Many comments are about the guidelines in relation to various socio-demographic variables.	The content already mentions that the consequences are the same regardless of age, gender, sex or lifestyle.
Some respondents want more tips to reduce drinking.	A clear and highlighted statement about not drinking more than two drinks per occasion will be included in the public summary. Tips will remain in the summary.
Add a tool or a link to help cut down drinking.	It is not possible to include a tracking tool in the public summary.
There were mixed feelings about the main title.	The main title was revised.
Some respondents criticized the use of "we."	When relevant, the pronoun "we" was removed.
Some respondents would like more white space.	The text was reduced and the graphic and the "Consequences" section were combined, which reduces visual overload.
Some respondent expressed concerns about the way the drinks, the various levels of risks and the consequences were presented.	The image and colours depicting the continuum of risk have been modified.
Respondents made different comments about the layout and made suggestions about highlighting specific information.	Layout was reorganized to combine the graphic and the "Consequences" section.
Some respondents mentioned that the font was a bit too small, and the resolution was poor.	This will not be an issue when the document is in a poster size.
Technical Summary	
Some submissions requested additional information and specifications.	The technical summary was entirely revised with additional statistics, information and sections.
Some submissions noted some contradictions between key messages.	The key messages have been revised.
Some submissions requested greater clarity about the thresholds.	The section on the risks associated with weekly levels of alcohol use has been clarified.
Takeaway 1: All levels of alcohol consumption are associate	d with some risk, so drinking less is better for everyone.
Several submissions queried clarity and nuances.	This takeaway has been modified into a more nuanced message that better reflects the complexity of the issue.

Consultation comment or suggestion	Action taken	
Takeaway 2: There is a continuum of risk whereby the risk for those who consume 2 standard drinks or less per week is negligible to low; it is moderate for those who consume between 3 and 6 standard drinks per week; and it is high for those who consume more than 6 standard drinks per week, with increasingly higher levels of risk with every additional drink.		
Some submissions mentioned that the terms used in the continuum of risk were misleading.	The takeaway has been revised and the term "negligible" has been removed.	
Some requested a clearer figure to accompany the takeaway.	The format, the design and the colours of the figure presented in the public summary and the technical summary have been modified.	
Make this statement more clear, concise and to the point.	The takeaway and the accompanying text have been revised to provide more clarity.	
Some requested more details about the evidence behind this takeaway.	No action required. The evidence and details about the methodology used to develop this takeaway are available in the technical report and the background report available here: Lifetime Risk of Alcohol-Attributable Death and Disability https://ccsa.ca/lifetime-risk-alcohol-attributable-death-and-disability-report	
Takeaway 3: On any occasion, any level of consumption has risks, and with more than two standard drinks, most individuals will have an increased risk of injuries or other problems.		
Requires simplifying and specifying.	Takeaway has been revised with greater emphasis on per occasion alcohol use and the fact that the risk for harm is to oneself and others.	
Takeaway 4: Disproportionately more injuries, violence and	deaths result from men's drinking.	
Takeaway 4: Disproportionately more injuries, violence and Some statistics comparing men and women's alcohol-related outcomes requested.	deaths result from men's drinking. Statistics were added throughout.	
Some statistics comparing men and women's alcohol-		
Some statistics comparing men and women's alcohol- related outcomes requested.	Statistics were added throughout. This takeaway has been moved into a sex and gender box that specifies that it is especially in the case of per occasion drinking that far more harms result from men's	
Some statistics comparing men and women's alcohol- related outcomes requested. Requires clarifying the pattern of alcohol use. Some submissions queried Information about factors that can influence alcohol use and its impact such as motives for drinking, context, personality traits, socialization, the	Statistics were added throughout. This takeaway has been moved into a sex and gender box that specifies that it is especially in the case of per occasion drinking that far more harms result from men's alcohol use.	
Some statistics comparing men and women's alcohol- related outcomes requested. Requires clarifying the pattern of alcohol use. Some submissions queried Information about factors that can influence alcohol use and its impact such as motives for drinking, context, personality traits, socialization, the pandemic, etc. Other gender-related harms from alcohol could be considered and noted (e.g., sexual violence, domestic and	Statistics were added throughout. This takeaway has been moved into a sex and gender box that specifies that it is especially in the case of per occasion drinking that far more harms result from men's alcohol use. No action required. This is out of scope for the mandate. No action required. The report includes a section on the	
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Some statistics comparing men and women's alcohol- related outcomes requested. Requires clarifying the pattern of alcohol use. Some submissions queried Information about factors that can influence alcohol use and its impact such as motives for drinking, context, personality traits, socialization, the pandemic, etc. Other gender-related harms from alcohol could be considered and noted (e.g., sexual violence, domestic and gender-based violence). For the "Association Between Alcohol Use, Aggression and Violence," it should be noted that alcohol is not the unique cause of violence. A submission raised concerns about creating a victim	Statistics were added throughout. This takeaway has been moved into a sex and gender box that specifies that it is especially in the case of per occasion drinking that far more harms result from men's alcohol use. No action required. This is out of scope for the mandate. No action required. The report includes a section on the association between alcohol use, aggression and violence. A paragraph acknowledging aggravating factor has been added to the section of the report on the association between alcohol use, aggression and violence. This section of the report was reviewed by two of the LRDG-SEP members with expertise in this area. Special attention will be given to this concern when knowledge mobilization activities are developed.	

Consultation comment or suggestion	Action taken	
Men and women should not be compared and the term "everyone" should be used instead.	No action required. This request does not reflect current scientific knowledge as alcohol use has sex- and gender specific risks.	
Requires clarifying low levels and the type of risks.	This statement has been moved into a sex and gender box that specifies that it is above the upper limit of the moderate risk zone for alcohol consumption that the health risks increase more steeply more women.	
Takeaway 6: It is safest to not drink while pregnant and duri	ng the preconception period	
This statement is not inclusive and needs to speak to other genders (i.e., people who are pregnant).	The report has been revised to avoid sex or gender specific statements.	
One submission suggested the promotion of early pregnancy awareness.	No action required. Out of scope.	
The term "preconception period" needs to be defined.	The term has been replaced with "planning to be pregnant."	
The wording of this statement should be strengthened and simplified.	The statement now specifies that there is no known safe amount of alcohol use.	
FASD should be mentioned.	The fact that FASD can be a consequence of alcohol use when pregnant is now clearly stated.	
The conclusion ignores the benefits of alcohol consumption on women who are pregnant (e.g., stress reduction, decreased blood pressure).	The research questions that guided this project were formulated to encompass all effects, so that studies focusing on both positive and negative effects could be identified. The recommendations do not include the benefits because overall results of systematic reviews did not show a significant beneficial effect even at low levels of alcohol use.	
Takeaway should address the impact of alcohol use on male reproductive capacity.	No action required. No high-quality systematic review has been found to support this claim.	
Clarify what studies were used to come up with this statement.	A detailed account and description of studies that form the basis of this statement are available here: Sex, Gender and Alcohol: What Matters for Women in Low-Risk Drinking Guidelines? https://ccsa.ca/sites/default/files/2022-08/CCSA-LRDG-Sex-Gender-and-Alcohol-what-matters-for-Women-in-LRDGs-en.pdf	
Information on how to minimize the risk if women choose to drink should be provided.	This report aims to review evidence to update the LRDGs. Harm reduction tips will be the focus of eventual knowledge mobilization activities.	
Takeaway 7: For women who are breastfeeding, it is safest not to use alcohol		
Sentence should be adjusted to reflect that babies do metabolize alcohol.	The report now accurately states that babies are "less able" instead of "unable" to metabolize alcohol.	
The benefits of alcohol consumption are missing.	The research questions that guided this project were formulated to encompass all effects, so that studies focusing on both positive and negative effects could be identified. The recommendations do not include the benefits because overall, results of systematic reviews did not show a significant beneficial effect even at low levels of alcohol use.	

Consultation comment or suggestion	Action taken
The message should be improved by adding information about how long alcohol stays in the breastmilk.	The message has been revised with additional information regarding the time it takes for alcohol to leave the body and breastmilk.
Overall Comments for the entire report	
Some submissions requested more details about the increased risk according to the number of standard drinks.	All tables and statistics throughout the report were revised to present risk according to standard drinks.
Submissions queried more information about absolute risk and years of life lost per specific cause of death.	To aid readers to better understand risk, tables with cause-specific risk of death have been added (see tables 3 and 4).
One submission queried why the J shaped curve is obsolete.	A specification was added to the technical report.
A comparison of the health risks between people who consume alcohol to those who do not should be added.	No action required. The information is presented in the technical report (tables 1 and 2), which describes the increased percentage risk of diseases and injuries of people who use alcohol compared to lifetime abstainers (i.e., those who have never consumed alcohol).
There should be a "zero limit" section.	The report now includes a section listing circumstances when no alcohol use is the safest.
One submission asked for more information about which specific risk curves were retrieved from meta-analyses and how they were used.	We have added a footnote to Table 1 of the document "Lifetime Risk of Alcohol-Attributable Death and Disability" to indicate source of this relative risk function.
Some submissions queried risk curves based on the frequency of drinking.	A sentence was added to the document "Lifetime Risk of Alcohol-Attributable Death and Disability" noting the absence of reliable evidence on how abstinence days increase or decrease people's risk of alcohol-attributable disease.
The quality of the evidence (i.e., GRADE) should be reported.	A paragraph about the quality of the evidence was added to the technical report.
Submissions found it difficult to understand where the threshold of 17.5 years of life comes from when the rest of the text speaks of 1 in 100 or 1,000.	An explanation was added noting how the risk thresholds of 17.5 YLLs in 100 and 1,000 lifetimes were derived.
Some submissions questioned how the risk zones were named.	A reference has been added.
One submission requested clarification on how the CCMTA data were reworked to create the risk curves.	A reference on the process of creating relative risk curves from CCMAT BAC data was added to the document "Lifetime Risk of Alcohol-Attributable Death and Disability."
Some submissions requested clarification about the non-protective effects of alcohol use on heart disease.	Throughout the report, text has been edited to better reflect the nuances of the results on this topic.
One submission requested a clarification as to why two specific studies used to revise the Australian alcohol guidelines (Patra et al, 2010; Yang et al, 2016) were not used here.	No action required. Patra et al. (2010) was replaced by Larsson et al. (2016), which is of equal quality (as assessed by GRADE) and more recent. Yang et al. (2016) was replaced by Zhao et al. (2017), which is of higher quality (as assessed by GRADE) and more recent.
One submission requested references on the mathematical modelling methods.	All models are based on peer-reviewed methodology and are cited in the document "Lifetime Risk of Alcohol-Attributable Death and Disability."

Consultation comment or suggestion	Action taken
A submission questioned the quality of the data on death, disability and alcohol exposure that were used in the modelling.	No action required. Only original public data files were used for both the original modelling analyses and the shadow analyses.
The use of controlled correlational prospective studies does not allow to eliminate several alternative explanations and limitations (e.g., publication bias and the fact that studies focus little on the beneficial effects of alcohol).	Causality for all diseases included and excluded from the analyses were determined based on recent animal, mechanistic and epidemiological evidence, which taken together allow elimination of alternative explanations. Moreover, all relative risks were assessed for bias through the GRADE criteria.
One submission questioned methodological decision (inflation of self-reported alcohol use, restrictive selection of risk curves for certain diseases), which may have contributed to an overestimation of the risk associated with low levels of alcohol use.	First, correction of population survey for under-reporting was done based on peer-reviewed studies cited in the report. Second, the relative risks obtained from systematic reviews were not adjusted for misestimation of alcohol use. Although there is hypothesized to be a slight underestimation of alcohol use in medical epidemiology studies, the direction of alcohol use measurement bias in cohort studies is unknown. We have added a note to the technical report acknowledging this limitation.
The methodological limitations and uncertainties need to be reported.	A limitation section has been added to the final report.
Provide an explanation as to why only systematic reviews were included.	As per GRADE guidelines.
Some submissions noted that the recommendations were too general and should consider other individual factors and special populations.	This report aims to provide general recommendations to the general population. This consideration will be taken into the knowledge mobilization phase of this project, when resources will be dedicated to the development of messaging that speaks directly to the unique concerns of people with diverse backgrounds and personal experiences.
There should be a clear numerical recommendation.	Key takeaways have been revised for clarity. However, considering the results obtained through this project, the experts have agreed that instead of providing people with strict rules and recommendations, people should be presented with a continuum of risk.
Some requested that the information in the report should be presented by age group.	The experts agreed to adopt a lifetime approach to alcohol use, which is much more in alignment with the way people consume alcohol throughout the lifetime. For example, people do not start to drink at 45 or 65 years old. We have added a sentence to the document "Lifetime Risk of Alcohol-Attributable Death and Disability" justifying the use of the lifetime approach based on empirical studies of life course alcohol use.
Provide an explanation as to why the binge-drinking amounts have not changed.	Revisiting the definition of binge-drinking is out of scope of the mandate. Moreover, the definition remains relevant in other contexts and for other types of interventions.
The recommendation should address the benefits of alcohol consumption.	The research questions that guided this project were formulated to encompass all effects, so that studies focusing on both positive and negative effects could be identified. The recommendations do not include the benefits because overall, our model did not show a significant beneficial effect even at low levels of alcohol use.

Consultation comment or suggestion	Action taken
Some submissions requested stronger message that no drinking is the only safe option, others queried messaging that alcohol is as important as abstinence, while others requested less abstinence-oriented messages.	The language was revised throughout the report to be more nuanced.
While there is acknowledgment that sex and gender are different, women/females and men/males seem to be used interchangeably in some contexts that are referring to physiological risks. If the statement refers to sex assigned at birth use the terms "males" and "females."	Throughout the report, text has been reviewed to clarify the biological (sex) and social concepts (gender). A note on terminology was added to the report.
The report is gender-biased and needs to be more inclusive of other genders.	Throughout this project, there has been a commitment to integrate sex-, gender- and diversity-based analysis (SGBA+). However, sex and gender science is nascent, the literature incomplete, and many effects and impacts of sex and gender on alcohol use, especially among subpopulations such as Indigenous Peoples, older people, sexual minorities and gender minorities, remain underresearched or unknown. The experts recognize that it will be important for people with various sex and gender identities to find themselves in the Guidance. As such, it will be crucial for the knowledge mobilization phase of this project to create resources that speak to gender or sexually diverse populations.
Request to remove the policy implications section.	The policy implications are evidence-based. They are included in the report as they suggest a path forward to increase awareness and support people who may want to follow the Guidance on Alcohol and Health.
A more specific definition of a standard drink should be reported in the beginning of the report.	A definition of a standard drink was added at the beginning of the report and an image was added to the technical summary.
Some submissions queried the impacts of alcohol use among youth.	This is a limitation that is now mentioned in the concluding part of the report. The message that youth under the legal drinking age should delay drinking as much as possible has also been added.
Provide more statistics on how many people die from alcohol-related diseases and experience health issues due to alcohol consumption, as well as the cost to the health care system.	More references and statistics were added throughout the report.
A discussion around the changes in outcomes if reducing alcohol consumption should be added.	A paragraph in the technical report devoted to this issue has been enhanced.
A discussion around mental health (e.g., depression suicide) and social (e.g., loneliness, isolation) risks is needed.	The experts commissioned a review on this topic. Effect of Alcohol Consumption on the Development of Depression, Anxiety and Suicidal Ideation: Update of a Systematic Review is available here: https://ccsa.ca/effect-alcohol-consumption-development-depression-anxiety-and-suicidal-ideation-update-systematic . The final report provides a summary and presents the limitations and implications of the review.
Some submissions requested a greater focus on harm reduction.	This project was based on the principle of autonomy in harm reduction, and this has now been made clearer. The public summary highlights safer drinking tips.

Consultation comment or suggestion	Action taken
Request for a mention of evidence-based treatment available for alcohol use disorder and that people should see their doctor for more information on treatment options	A note was added in the report.
Some submissions queried the impact of alcohol on the brain.	The project's focus has been on the risk relationships between alcohol use and the occurrence of and mortality from all disease or injury categories causally related to alcohol consumption and for which high quality systematic reviews were available.
One submission requested more precision about province-specific data.	Details and precisions have been added throughout the report.
Some submissions requested more consultations and co- construction of messages with stakeholders.	The public was invited to provide input on two separate occasions. Representatives from different health-related organizations were invited to discuss ideal messaging and communication strategies. It is hoped that the conclusions of the update will be useful to experts and partners who should work together to create interventions and messaging that will speak directly to the unique concerns of people with diverse backgrounds and personal experiences.
Specify where to find the evidence from which the recommendations are derived.	A figure was revised. Links to all background reports are available in that figure and throughout the document.
A submission questioned the decision to include three documents in the final report.	Three documents were designed to meet the needs of as many people as possible. The three documents were designed with particular audiences in mind but are not restricted to the intended audiences.
One submission requested focus on responsible safer use rather than low-risk guidance.	The experts agreed that presenting a continuum of risk associated with various levels of alcohol use should allow people to situate themselves where they are on that continuum and understand in which risk zone their alcohol use places them. It is hoped that this will lead people to develop intentions to adopt healthier and safer behaviours.
General typographical or grammatical errors and formatting suggestions.	Numerous grammatical, formatting and typographical edits were made to improve the clarity of the report.

A total of 19 articles were submitted as evidence to be considered for mathematical modelling. None of the submitted evidence was retained; the reasons are presented in the table below.

Articles submitted to be included as evidence	Action taken
Bryazka, D., Reitsma, M. B., Griswold, M. G., Abate, K. H., Abbafati, C., Abbasi- Kangevari, M., & Diress, M. (2022). Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. The Lancet, 400(10,347), 185–235. https://doi.org/10.1016/S0140-6736(22)00847-9	This article was excluded at step 2 of the screening process as it failed to meet at least two of the methodological quality criteria. The characteristics of the included studies were not reported, and the quality of the included studies was not assessed.
Daviet, R., Aydogan, G., Jagannathan, K., Spilka, N., Koellinger, P.D., Kranzler, H.R., Nave, G., Wetherill, R.R. (2022). Associations between alcohol consumption and gray and white matter volumes in the UK Biobank. Nature Communications, 13(1), Article 1175. https://doi.org/10.1038/s41467-022-28735-5	Not a systematic review.

Articles submitted to be included as evidence	Action taken
Demoury, C., Karakiewicz, P., & Parent, M. E. (2016). Association between lifetime alcohol consumption and prostate cancer risk: A case-control study in Montreal, Canada. Cancer Epidemiology, 45, 11–17. https://doi.org/10.1016/j.canep.2016.09.004	Not a systematic review.
Leong, C., Bolton, J. M., Ekuma, O., Prior, H. J., Singal, D., Nepon, J., Konrad, G., Paille, M., Finlayson, G., & Nickel, N. (2022). Association of alcohol use disorder on alcohol-related cancers, diabetes, ischemic heart disease and death: A population-based, matched cohort study. Addiction, 117, 368–381. https://doi.org/10.1111/add.15646	Not a systematic review.
Ma, H., Li, X., Zhou, T., Sun, D., Shai, I., Heianza, Y., Rimm, E. B., Manson, J. E., & Qi, L. (2021). Alcohol consumption levels as compared with drinking habits in predicting all-cause mortality and cause-specific mortality in current drinkers. Mayo Clinic proceedings, 96(7), 1758–1769. https://doi.org/10.1016/j.mayocp.2021.02.011	Not a systematic review.
Marcus, G. M., Vittinghoff, E., Whitman, I. R., Joyce, S., Yang, V., Nah, G., Gerstenfeld, E. P., Moss, J. D., Lee, R. J., Lee, B. K., Tseng, Z. H., Vedantham, V., Olgin, J. E., Scheinman, M. M., Hsia, H., Gladstone, R., Fan, S., Lee, E., Fang, C., Hahn, J. A. (2021). Acute consumption of alcohol and discrete atrial fibrillation events. Annals of Internal Medicine, 174(11), 1503–1509. https://doi.org/10.7326/M21-0228	Not a systematic review.
McIntosh, J. (2017). Alcohol and Canadian health. Global Journal of Health Science, 9(5), 96-104. https://doi.org/10.5539/gjhs.v9n5p96	Not a systematic review.
McIntosh, J. (2019). The truth about alcohol and health. European Journal of Medical and Health Sciences, 1(2). https://doi.org/10.24018/ejmed.2019.1.2.35	Not a systematic review.
Mørch, L. S., Johansen, D., Thygesen, L. C., Tjønneland, A., Løkkegaard, E., Stahlberg, C., & Grønbaek, M. (2007). Alcohol drinking, consumption patterns and breast cancer among Danish nurses: A cohort study. European Journal of Public Health, 17(6), 624–629. https://doi.org/10.1093/eurpub/ckm036	Not a systematic review.
Patra, J., Taylor, B., Irving, H., Roerecke, M., Baliunas, D., Mohapatra, S., & Rehm, J. (2010). Alcohol consumption and the risk of morbidity and mortality for different stroke types—a systematic review and meta-analysis. BMC Public Health, 10, Article 258. https://doi.org/10.1186/1471-2458-10-258	The study on stroke by Larsson et al. (2016) was included instead of the Patra et al. (2010) study as it was more recent and of similar quality as assessed by GRADE.
Perreault, K., Bauman, A., Johnson, N., Britton, A., Rangul, V., & Stamatakis, E. (2017). Does physical activity moderate the association between alcohol drinking and all-cause, cancer and cardiovascular diseases mortality? A pooled analysis of eight British population cohorts. British Journal of Sports Medicine, 51(8), 651–657. https://doi.org/10.1136/bjsports-2016-096194	Not a systematic review.
Schaefer, S. M., Kaiser, A., Behrendt, I., Eichner, G., & Fasshauer, M. (2022). Association of alcohol types, coffee and tea intake with mortality: prospective cohort study of UK Biobank participants. British Journal of Nutrition, 1–11. Advance online publication. https://doi.org/10.1017/S000711452200040X	Not a systematic review.
Van Heertum, K., & Rossi, B. (2017). Alcohol and fertility: How much is too much?. Fertility Research and Practice, 3, 10. https://doi.org/10.1186/s40738-017-0037-x	Not a systematic review.

Articles submitted to be included as evidence	Action taken
Veldhuis, C. B., Hughes, T. L., Drabble, L., Wilsnack, S. C., Riggle, E., & Rostosky, S. S. (2019). Relationship status and drinking-related outcomes in a community sample of lesbian and bisexual women. Journal of Social and Personal Relationships, 36(1), 244–268. https://doi.org/10.1177/0265407517726183	Not a systematic review.
White, A. J., DeRoo, L. A., Weinberg, C. R., & Sandler, D. P. (2017). Lifetime alcohol intake, binge drinking behaviors, and breast cancer risk. American Journal of Epidemiology, 186(5), 541–549. https://doi.org/10.1093/aje/kwx118	Not a systematic review.
White, H. R., Fite, P., Pardini, D., Mun, EY., & Loeber, R. (2013). Moderators of the dynamic link between alcohol use and aggressive behavior among adolescent males. Journal of Abnormal Child Psychology, 41(2), 211–222. https://doi.org/10.1007/s10802-012-9673-0	Not a systematic review.
Willett, W. C., Stampfer, M. J., Colditz, G. A., Rosner, B. A., Hennekens, C. H., & Speizer, F. E. (1987). Moderate Alcohol Consumption and the Risk of Breast Cancer. New England Journal of Medicine, 316(19), 1174–1180. https://doi.org/10.1056/NEJM198705073161902	Not a systematic review.
Wood, A. M., Kaptoge, S., Butterworth, A. S., Willeit, P., Warnakula, S., Bolton, T., Paige, E., Paul, D. S., Sweeting, M., Burgess, S., Bell, S., Astle, W., Stevens, D., Koulman, A., Selmer, R. M., Verschuren, W. M. M., Sato, S., Njølstad, I., Woodward, M., Danesh, J. (2018). Risk thresholds for alcohol consumption: Combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. The Lancet, 391(10129), 1513–1523. https://doi.org/10.1016/S0140-6736(18)30134-X	This article was excluded at step 2 of the screening process as it failed to meet at least two of the methodological quality criteria. There was no comprehensive search of the literature, the characteristics for each of the included studies were not reported, and the quality of the included studies was not assessed.
Yang, Y., Liu, D. C., Wang, Q. M., Long, Q. Q., Zhao, S., Zhang, Z., Ma, Y., Wang, Z. M., Chen, L. L., & Wang, L. S. (2016). Alcohol consumption and risk of coronary artery disease: A dose-response meta-analysis of prospective studies. Nutrition, 32(6), 637–644. https://doi.org/10.1016/j.nut.2015.11.013	The more recent study on ischaemic heart disease by Zhao et al. (2017) was included instead of the Yang et al. (2016) study as it was of higher quality as assessed by GRADE.