

Update of Canada's Low-Risk Alcohol Drinking Guidelines: Development of Research Questions

Background

This report was produced by the Evidence Review Working Group of the Canadian Centre on Substance Use and Addiction (CCSA) for the project to update Canada's Low-Risk Alcohol Drinking Guidelines (LRDGs).^{*} The report presents the process used to develop the research questions for the project. It is intended for members of the LRDG Scientific Expert Panels and those interested in understanding in detail the process followed in developing the new guidelines.

To develop evidence-based guidelines, research questions to inform a systematic search for evidence are required. Clear and well-framed questions guide the conduct of systematic reviews, facilitate interpretation of the findings, and inform the formulation of recommendations (Guyatt et al., 2011). To update the Canadian LRDGs, CCSA's Evidence Review Working Group used the GRADE-ADOLPMENT framework (Schünemann et al., 2017), which provides a method for generating research questions and recommends a standard framework such as PICO or PECO to formulate them. These standard frameworks require explicit descriptions of the populations (P) to whom the guidelines are meant to apply, the interventions (I) or exposures (E), depending on the guidelines, the comparators (C) and the outcomes (O). This report presents the method for generating PECO research questions to support the update of the LRDGs, a draft of the questions and an outline of how the questions align with the PECO framework.

Method for Generating Research Questions

CCSA's Evidence Review Working Group developed the PECO research questions by evaluating the research questions used in developing other LRDGs, including the previous Canadian LRDGs (Butt, Beirness, Gliksman, Paradis, & Stockwell, 2011), and the most recent LRDGs from the United Kingdom (U.K. Chief Medical Officers, 2016) and Australia (National Health and Medical Research Council, 2020). The Working Group also consulted with two panels for the LRDG update project, the Physical Health Expert Panel and the Mental Health and Social Impact Expert Panel. These steps are described in the next two subsections.

^{*} This document was prepared Hanie Edalati, Ph.D., and Christine Levesque, Ph.D., both of whom are research and policy analysts at CCSA. They are members of the Evidence Review Working Group that was established by CCSA to perform some of the tasks required to update the LRDGs. This document was reviewed by members of the LRDGs Scientific Expert Panels.



Reviewing LRDGs from Other Alcohol Guideline Development Groups

Research questions from the original Canadian LRDGs and the most recent guidelines from the U.K. and Australia are presented in Table 1. These guidelines were evaluated using the Appraisal of Guidelines for REsearch & Evaluation II (AGREE II; Brouwers et al., 2010) instrument. Details of the evaluations are provided in *Update of Canada's Low Risk Alcohol Drinking Guidelines: Evaluation of Selected Guidelines* (Canadian Centre on Substance Use and Addiction, 2021).

One item in the AGREE II instrument evaluates the health questions covered by the guidelines and whether guideline developers provided a detailed description of the original research questions related to the guidelines' key recommendations. Although health questions do not need to be phrased as questions, they should provide enough information for others to initiate the development of a guideline on this topic and to understand the populations and contexts profiled in the guidelines. Both the Australian and U.K. guidelines included questions or terms of reference related to their guidelines. The Australians followed the PECO framework to formulate their research questions. The U.K. guidelines include more detailed terms of reference, but no standard framework was followed and the language lacks clarity. The Canadian guidelines did not provide descriptions of the health questions covered by them.

Table 1. Research questions included in the original Canadian, U.K. and Australian Low-Risk Alcohol Drinking Guidelines

Canada 2011	U.K. 2016	Australia 2020
<p>The first aim of this document is to provide concise summaries of the evidence on how different levels of drinking are likely to impact on different aspects of health and safety.</p> <p>(No specific research questions were provided.)</p>	<ol style="list-style-type: none"> 1. What are the health consequences arising from regular consumption of alcohol? <ol style="list-style-type: none"> a. How do the risks of alcohol change with different levels consumption? Is it possible to assign different degrees of risk (e.g., lower risk, higher risk) to particular levels of alcohol consumption? b. What are the impacts, if any, of having alcohol free days (zero consumption) within a pattern of regular alcohol consumption? 2. What are the health consequences arising from heavy or episodic 'binge' drinking of alcohol? 3. What are the beneficial effects, if any, of low to moderate consumption of alcohol? 4. What are the effects, both beneficial and harmful, of alcohol consumption on social and individual well-being? 5. Are there any changes in the direction, form or strength of the evidence for health and social impacts of alcohol consumption since the 1995 guidelines? 6. Are there any changes in the direction, form or strength of the evidence on alcohol and pregnancy since the 2008 NICE review? 	<ol style="list-style-type: none"> 1. What are the short term health risks and benefits of varying levels and/or patterns of alcohol consumption (including no alcohol consumption) associated with any single episode of drinking in the general population? 2. What are the long term health risks and benefits associated with varying levels and/or patterns of alcohol consumption (including no alcohol consumption) in the general population? 3. What are the health risks and benefits of varying levels and/or patterns of alcohol consumption (including no alcohol consumption) for pregnant women and their fetuses, including longer term effects on babies and children exposed in utero? 4. What are the health risks and benefits of varying levels and/or patterns of alcohol consumption (including no alcohol consumption) for breastfeeding women and their babies?



	7. Are there any changes in the direction, form or strength of the evidence on young people and alcohol since the 2009 CMO for England's guidance?	
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Meetings with the Physical Health Expert Panel and the Mental Health and Social Impact Expert Panel

The Physical Health Expert Panel and the Mental Health and Social Impact Expert Panel met to discuss developing research questions using PECO criteria to inform the update of the LRDGs. During the meetings, the expert panels made the following recommendations.

Population: The updated LRDGs should target all Canadians. A component of the project will study risk reduction among individuals who use alcohol. Vulnerabilities within specific populations should not be ignored. The updated LRDGs could include information targeting different subpopulations, such as youth under the legal drinking age or women who are pregnant or breastfeeding, if the scientific evidence shows there are substantive differences in these groups.

Exposure/Comparator: With regards to exposure, it is key to include ethanol rather than the type of alcoholic product (beer, wine, spirit) in search criteria and the formulation of recommendations. Types of alcoholic product are not relevant to the search criteria and including them in recommendations would distract from the main purposes of LRDGs. It was also discussed that various levels and patterns of use should be considered, whenever possible.

Outcomes: Because alcohol use has numerous effects, for individuals who drink and others, the recommendations will focus on multiple outcomes of various kinds (physical health, mental health and social harm). The quality of evidence associating different levels and patterns of alcohol consumption with various outcomes is likely to vary greatly. It was acknowledged, particularly by the Mental Health and Social Impact Expert Panel, that the relationship between alcohol consumption and outcomes can be conveyed in different ways, from specific and numerical to general and qualitative, such as:

- The evaluation of whether any level of alcohol use is safe.
- Risk curves with thresholds for a person's exposure to alcohol and the associated risk of harms to physical and mental health, and social harm.
- Systematic literature reviews of both short- and long-term risks and benefits[†] of various levels and patterns of alcohol consumption to physical and mental health, and social harm.
- Prevalence rates of alcohol consumption and alcohol-related harms in the general population.

PECO Research Questions

Having a clearly defined systematic approach such as PECO enables researchers to formulate questions to guide the identification of the scientific evidence to be analyzed. This approach helps to identify the proper search terms, define inclusion and exclusion criteria for selecting the evidence, and evaluate outcomes including the assessment of short- and long-term risks and benefits.

[†] Risks refer to the probability of harm associated with various levels and patterns of alcohol use, while benefits refer to a valued or desired outcome, or an advantage associated with alcohol use.



Based on the review of the Canadian, U.K. and Australian LRDGs, and discussions with the expert panel members, the project to update the LRDGs will address three PECO research questions, which are detailed in the tables below. All outcomes listed in the tables, while non-exhaustive, are examples of alcohol-related risks and benefits (physical, mental and social) experienced at the individual level that have been suggested by expert panel members or identified in key documents such as the *Australian Guidelines to Reduce Health Risks from Drinking Alcohol* (National Health and Medical Research Council, 2020), *Canadian Substance Use Costs and Harms 2015–2017* (Canadian Substance Use Costs and Harms Scientific Working Group, 2020), the World Health Organization's *Global Status Report on Alcohol and Health* (2018) and Laslett, Room, Waleewong, Stanesby, & Callinan, (2019). Short-term risks and benefits are defined as effects that are immediate and affect a person right away. Long-term risks and benefits are defined as effects that accumulate over time and may have long-term consequences.

One evidence search will be carried out for all three research questions. This method will ensure that all studies, regardless of the population, the pattern or level of alcohol use and the outcomes, will be identified by the search. As explained by the Australian guideline development group, outcomes should not be included as search terms because they are often poorly indexed using controlled vocabulary terms in medical databases, which would result in relevant references being missed (NHMRC Clinical Trials Centre, 2020).



PECO Research Question 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 use), in different contexts, associated with a single episode of drinking in the general population?

Population	General population If evidence is identified, the following specific subpopulations will be considered: <ul style="list-style-type: none">• Sex differences• Age differences• People with existing mental and physical illnesses• People with a strong family history of alcohol dependence• People on medicines or other drugs (prescribed and illicit), including interactions
Exposure/Comparator	Varying levels of alcohol consumption (including no alcohol consumption), in different contexts, associated with a single episode of drinking
Outcomes	Short-term risks and benefits Physical health: Injury to self, including motor vehicle crashes, falls, burns, occupational accidents, drowning, overdose and poisoning Self-injury and suicide Acute cardiovascular events Hangover Headaches Sexually transmitted infection Harmful alcohol-drug interactions Sexual malfunction Acute gastrointestinal events (gastritis, reflux) Mental health: Acute exacerbation of a mental illness Neuropsychiatric conditions Social harm: Intimate partner violence (physical, psychological and sexual) Child neglect and abuse Elder neglect and abuse Other violence (physical, psychological and sexual) Risky sexual behaviour and unwanted pregnancies Harm to co-workers (increased workload to co-workers due to absenteeism, reduced work productivity) Loss of productivity in the workplace (absenteeism, poor work performance) Poor educational performance Conflict with family members Conflict at school Peer victimization Involvement with deviant peers Crime and public disorder, criminal justice involvement



PECO Research Question 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?

<p>Population</p>	<p>General population</p> <p>If evidence is identified, the following specific subpopulations will be considered:</p> <ul style="list-style-type: none"> • Sex differences • Age differences • People with existing mental and physical illnesses • People with a strong family history of alcohol dependence • People on medicines or other drugs (prescribed and illicit), including interactions
<p>Exposure/Comparator</p>	<p>Varying levels of alcohol consumption (including no alcohol consumption)</p>
<p>Outcomes</p>	<p>Long-term risks and benefits</p> <p>Physical health: All-cause mortality and morbidity Cancer Cardiovascular conditions Digestive conditions Endocrine conditions Respiratory conditions HIV Obesity, overweight Sleep disorders Central neurological disorders Cognitive impairment, dementia, including Korsakoff's syndrome Seizures (as a co-morbidity) Fertility Osteoporosis (+/- fracture, bone healing) Gout Thiamine deficiency Peripheral neurological disorders (e.g., neuropathy) Gastro-oesophageal reflux Hormonal disorders Physical disability Alterations in brain structure, functions and connectivity Eczema Changes in appetite Weight loss</p> <p>Mental health: Mental health disorders, including depression, anxiety and alcohol-related psychosis Low self-esteem Alcohol use disorders, dependence and withdrawal syndrome Quality of life Financial burden</p> <p>Social harm: Insecure attachment relationships Losing child custody rights Unstable or loss of family relationships Unstable employment or unemployment School dropout Involvement in youth protection services</p>



PECO Research Question 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) by women who are pregnant or breastfeeding, for fetal, infant and child development?

Population	Pregnant women and fetuses, infants and children with prenatal alcohol exposure Women who are breastfeeding and their infants
Exposure/Comparator	Varying levels of alcohol consumption (including no alcohol consumption)
Outcomes	<p>The outcomes are in addition to outcomes listed for short- and long-term risks and benefits in questions 1 and 2.</p> <p>Physical health: Outcomes for fetuses and children prenatally exposed to alcohol Fetal alcohol spectrum disorders (FASD) Low birth weight Small for gestational age Developmental delay Birth defects Stillbirth Neonatal alcohol withdrawal Premature birth Spontaneous abortion and miscarriage</p> <p>Outcomes for infants exposed to alcohol through breast milk Cognitive impairment Sudden infant death syndrome (SIDS) Sedation</p> <p>Mental health: Behavioural problems in child Exacerbation of postpartum depression and anxiety in mothers</p> <p>Social harm: Lack of mother-child bonding Child neglect Failure to thrive</p>



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