Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Protocol for modelling the risk of alcohol-attributable mortality and hospital admission in Ireland

13 August 2025

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory body established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

Reporting to the Minister for Health and engaging with relevant government Ministers and departments, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.

- **Regulating social care services** — The Chief Inspector of Social Services within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.

- **Regulating health services** — Regulating medical exposure to ionising radiation.

- **Monitoring services** — Monitoring the safety and quality of permanent international protection accommodation service centres, health services and children's social services against the national standards. Where necessary, HIQA investigates serious concerns about the health and welfare of people who use health services and children's social services.

- **Health technology assessment** — Evaluating the clinical and cost effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.

- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.

- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health and social care services, with the Department of Health and the HSE.

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1 Background

Alcohol consumption is a leading risk factor for death and disability worldwide, with higher levels of alcohol consumption associated with a greater burden of disease.[1] In Ireland in 2024, 73% of people aged 15 years or older reported having drunk alcohol in the preceding 12 months. In order to make informed decisions,, these consumers should have access to accurate information on the associated risks.[2][3] Low-risk alcohol guidelines can provide this information, in addition to providing guidance on levels of alcohol consumption that are associated with lower levels of risk and when it is not safe to drink any alcohol. In providing this information, low-risk alcohol guidelines can be viewed as one tool in the portfolio of measures to reduce alcohol related harm.[3]

The current Irish low-risk alcohol guidelines were last revised in 2015. They recommend:

- consuming less than 11 standard drinks (one standard drink contains 10g or 12.5ml of pure alcohol) per week for women, and less than 17 standard drinks per week for men
- spreading drinks out over the week
- having two to three alcohol-free days per week
- drinking no more than six standard drinks on any one occasion.

Guidance is also provided on when it is not safe to drink any alcohol, such as:

- if you are pregnant or thinking about becoming pregnant
- if you are on certain medicines or have a condition made worse by drinking
- before you operate machinery
- before or while driving
- before doing anything risky or that requires skill
- before or during swimming.

Since these guidelines were last updated, new evidence has emerged and international practice has advanced in terms of the methods used to inform low-risk alcohol guidelines. Historically, expert groups reviewed and summarised epidemiological evidence on the health outcomes associated with drinking different amounts of alcohol. Defining ‘low risk’, and formulating guidelines, required informed but ultimately subjective decisions on methodological and technical factors that influence the outcome. In practice, determining what constituted a low risk level of drinking was a matter of expert opinion.[4]

It has been suggested that low-risk alcohol guidelines require a scientific basis that extends beyond individual or group judgements of risk.[5] Indeed, it has become

increasingly common to use mathematical modelling to estimate the risks of death and hospitalisation from various causes that are associated with specific levels of alcohol consumption, using defined risk thresholds to inform what constitutes a low risk level of drinking.[6-9] While expert judgment is still required with this approach, not least in defining these risk thresholds, the quantitative analysis provides valuable information and transparency to inform and justify these judgments.

Following a request from the Department of Health, HIQA agreed to model the risk of alcohol-attributable mortality and admission to hospital in Ireland to inform an update of the Irish low-risk alcohol guidelines. This protocol describes the approach that will be used to provide quantified risk estimates for mortality and hospital admission associated with different levels and patterns of alcohol consumption (that is, how much and how often alcohol is consumed) in Ireland.

2 Methods

2.1 Aim

This project will estimate the risk of mortality (that is, death, premature death and potential years of life lost (PYLL)) and hospitalisation (that is, admission to hospital) attributable to different levels and patterns of alcohol consumption in Ireland. This will subsequently inform the Department of Health's update of the 2015 Low Risk Drinking Guidelines.[10] Premature death is considered to be a death in those aged 74 years or younger,[11] and PYLL is determined by the number of potential years of life remaining at the age of death, up to 75 years of age. The level of alcohol consumption that corresponds to one or more risk thresholds (that is, the levels of alcohol consumption that are associated with pre-defined levels of risk of mortality and hospitalisation) will also be identified. Drawing on similar modelling work that informed updates of the Low Risk Drinking Guidelines in Australia, Canada, France and the UK,[6-9] three steps, further detailed throughout this section, will be followed:

- relevant data will be identified and sourced
- relative risk functions for alcohol-related health conditions will be identified or estimated
- risk curves representing the average risk of alcohol-attributable mortality and hospitalisation across included health conditions will be estimated.

2.2 Quality assurance process

The work will be undertaken in accordance with HIQA's Quality Assurance Framework and led by experienced members of staff. The report will be reviewed by two senior members of the team to ensure processes are followed and quality maintained.

An Expert Advisory Group comprising representation from the Department of Health, patient representatives, and individuals with relevant expertise in alcohol epidemiology, public health, public health policy, addiction, primary care and dietetics will be convened. The Expert Advisory Group will review this protocol, the final and draft report and attend two virtual meetings to inform the planned approach and interpretation of the evidence and development of the advice to the Department of Health.

2.3 Data sources

The key data inputs into the mathematical model are:

- health conditions that are causally linked to alcohol

- mortality and hospitalisation rates in Ireland for the identified health conditions that are causally linked to alcohol
- population demographics
- baseline levels and patterns of alcohol consumption in Ireland.

The data required and potential sources are further detailed in the following sections (2.3.1 to 2.3.4).

2.3.1 Alcohol-related health conditions

Previous approaches in Australia, Canada, France and the UK assessed various health conditions in estimating alcohol-attributable deaths and disability, ranging from a total of 30 to 43 ICD-10 subcategories of the International Classification of Diseases, 10th Revision (ICD-10).[6-9] In total, 62 health conditions were assessed across the four reports, and 25 were included in each of the four reports. In the current analysis, as in the Canadian update, the inclusion of relevant health conditions will be based on three criteria:

- The health condition must be causally related to alcohol use. Recent relevant reports and reviews will be identified to determine causality. Potential sources include the Institute for Health Metrics and Evaluation,[12] the World Health Organization[13] or the International Agency for Research on Cancer.[14] Additionally, specific health conditions included in the Low Risk Drinking Guidelines for Australia, Canada, France and the UK will be assessed.[6-9]
- A continuous dose-response risk function for the relationship between alcohol consumption and the health condition must be provided. Alternatively, if a continuous dose-response function is not available, the systematic review should provide relative risk (RR), odds ratio (OR), and or hazard ratio (HR) for at least three levels of alcohol consumption categories. The measurement unit used for the dose-response must be specified and convertible into grams per day of alcohol consumed.
- Either mortality or morbidity must be measured specifically.

2.3.2 Mortality and hospitalisation data

Mortality and hospitalisation data for relevant health conditions will be sourced for the years 2022 to 2024.

Mortality data will be sourced from the General Mortality Register via the Central Statistics Office.[15] This register provides the total number of deaths registered in Ireland, along with date of occurrence and associated causes (categorised using ICD-10 codes), by sex and age groups. Data will be analysed by year of occurrence (as opposed to year of registration).

Healthcare utilisation (for example, primary care visits, hospitalisations etc.) is typically used as a proxy for morbidity. However, as relevant Irish data on many components of healthcare utilisation in the general population are not available (for example, primary care and emergency department attendance), data specifically on hospitalisations from the Hospital In-Patient Enquiry (HIPE) database will be used.[16] The HIPE system collects information on inpatient and day-case patients discharged from Irish acute public hospitals. A HIPE discharge record is created when a patient is discharged from or dies in hospital. Each record contains administrative, demographic and clinical information for a discrete episode of care. In the absence of a unique patient identifier, it is not possible to link hospital episodes to individual patients. HIPE is held and maintained by the Healthcare Pricing Office, HSE.

The average annual number of deaths and hospitalisations between 2022 and 2024 will be calculated to facilitate the inclusion of conditions with low prevalence rates and to account for short-term variability between years.

2.3.3 Population demographics

Data on the age and sex breakdown of the Irish population for the years 2014 to 2022 will be sourced from the Central Statistics Office.[17]

2.3.4 Alcohol consumption

Annual alcohol sales figures for 2024 will be obtained from the Office of the Revenue Commissioners to estimate per capita alcohol consumption.[18] Revenue provides annual alcohol sales figures for beer, spirits, wine, and cider. These figures represent the volume of alcoholic beverages released from bonded warehousing and where excise duty has been paid. Beer and spirits volumes are provided in litres of pure alcohol. Wine and cider volumes are provided in litres of beverage and will be converted to pure alcohol based on an alcohol by volume (ABV) of 12.5% and 4.5%, respectively.[19] Litres of pure alcohol will be converted to grams based on a density of 789 grams per litre of pure alcohol.[20]

Data on levels and patterns of alcohol consumption in Ireland will be sourced from the 2024 Healthy Ireland Survey.[2] These data will be used to estimate the proportion of individuals aged 15 years and older considered as current drinkers (that is, people who report having consumed alcohol in the past 12 months), ex-drinkers (that is, people who report not having consumed alcohol in the past 12 months) and lifetime abstainers (that is, people who report having never consumed alcohol or having only consumed a few sips of alcohol in their lifetime). Similarly, proportions of the population by average alcohol consumption per week and per drinking day and peak daily consumption will be estimated.

2.4 Sources for relative risk estimates for alcohol-related health conditions

Relative risk functions for the health conditions identified as causally related to alcohol consumption are required to provide quantified estimates for the risk of morbidity and mortality attributable to different mean daily volume levels and or patterns of alcohol consumption in Ireland. The alcohol-related health conditions that will be examined can be classified as detailed in Table 1.

Table 1. Types of alcohol-related health conditions

	Partially-attributable conditions	**Wholly-attributable conditions**
Chronic conditions	These are conditions that can occur without alcohol consumption but for which the risk of occurrence changes with chronic exposure to alcohol (for example, liver cancer).	These are conditions that cannot occur in the absence of alcohol consumption and for which the risk of occurrence depends on chronic exposure to alcohol (for example, alcohol-related liver disease).
Acute conditions	These are conditions that can occur without alcohol consumption but for which the risk of occurrence changes with acute exposure to alcohol (for example, falls).	These are conditions that cannot occur in the absence of alcohol consumption and for which the risk of occurrence depends on acute exposure to alcohol (for example, alcohol poisoning).

The sources for relative risk estimates for each condition will depend on whether a given condition is acute or chronic and wholly or partially attributable to alcohol. Further details are provided in sections 2.4.1 to 2.4.3.

2.4.1 Relative risk estimates for partially-attributable chronic conditions

A systematic review of systematic reviews and meta-analyses will be performed to identify the most recent and highest quality risk estimates for a range of chronic health outcomes that are partially attributable to alcohol. Priority will be given to the highest quality reviews and, in the case where the same number of quality criteria are met, the review with the most recent search date will be retained. The risk estimates are required to derive alcohol attributable fractions (AAFs) for these health conditions (see Section 2.5.3).

This systematic review will update the systematic review conducted in 2022 by the Canadian Centre on Substance Use and Addiction (CCSA) entitled *Update of Canada's Low-Risk Alcohol Drinking Guidelines: Evidence Review Technical Report*.[21] The quality of this review was assessed using AMSTAR 2 and no major issues were identified (see Appendix 1). Two research questions from the CCSA

report will also be addressed in the current review. A third research question addressed in the CCSA review, on pregnancy and child development risks and benefits, will not be assessed as the risk of alcohol-attributable mortality and hospitalisation curves do not consider alcohol consumption while pregnant. In order to consider this third question, data on alcohol consumption patterns and levels during pregnancy would be required, and these data are not readily available in Ireland. Additionally, many primary outcomes that would be of interest, such as foetal alcohol spectrum disorder, fall into the category of harm-to-others rather than conditions that are experienced by the drinkers themselves, which is the focus of the current work. Using the PECO (Population, Exposure/Comparison, Outcome) criteria (see Table 2), these questions specify 1) the target populations for the exposure; 2) the exposures and comparators being considered; and 3) the outcomes that are most relevant to assess:

1. What are the short-term risks and benefits (physical and mental health) associated with varying levels of alcohol consumption (including no alcohol use) associated with a single episode of drinking in the general population?
2. What are the long-term risks and benefits (physical and mental health) associated with varying levels and patterns of alcohol consumption (including no alcohol consumption) in the general population?

Table 2. PECO for the two research questions

Population	*Acute and chronic* The general population. If evidence is identified, the following specific subpopulations will be considered: 1. Sex 2. Age groups
Exposure/comparator	*Acute* Varying levels of alcohol consumption (including no alcohol consumption), in different contexts, associated with a single episode of drinking. *Chronic* Varying levels of alcohol consumption (including no alcohol consumption).
Outcomes	*Both research questions* Physical and mental health **Physical health** *Acute* 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) *Chronic* 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 (for example, neuropathy) Gastro-oesophageal reflux Hormonal disorders Physical disability Alterations in brain structure, functions and connectivity Eczema Changes in appetite Weight loss **Mental health** *Acute* Acute exacerbation of a mental illness Neuropsychiatric conditions *Chronic* 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

Note: PECO adapted from CCSA report[22]

Identification of systematic reviews

Electronic searches will be conducted in six databases: PubMed, Embase via OVID, PsycInfo via EBSCO, The Cochrane Database of Systematic Reviews, INAHTA Database and Epistimonikos. The search strategy for Embase is presented in Appendix 2. The search will be limited to systematic reviews and meta-analyses published from 17 February 2021 onwards (that is, from the end date of the CCSA review search). A comprehensive search of the grey literature will also be undertaken on 16 websites (see Appendix 3). Retrieved citations will be exported and de-duplicated in Endnote.

Screening of systematic reviews

Retrieved titles and abstracts will be screened independently by two reviewers, using Covidence software. Disagreements will be resolved by discussion or a third reviewer, if necessary.

Full texts of potentially eligible studies, in addition to the full texts of reviews included in the CCSA report,[21] will be screened independently by two reviewers and disagreements will be resolved by discussion or a third reviewer, if necessary. Full-text screening will be done in three steps (detailed below).

Step 1. PECO and study design criteria

Selected full text systematic reviews will be assessed against the PECO (see Table 2) and study design criteria. To be considered for inclusion, a systematic review must:

- Be published in either English or French, or a translation software can provide an adequate translation
- Have alcohol use as the main exposure of interest
- Include cohort, case-control or case-crossover studies. Where other types of studies are included in the systematic review, such as cross-sectional studies, the results from the cohort, case-control or case-crossover studies must be reported separately for the review to be considered eligible
- Have an outcome that is considered causally related to alcohol use, for example those listed by the Institute for Health Metrics and Evaluation,[12] the World Health Organization[13] or the International Agency for Research on Cancer[14]
- Have an outcome that is associated with an International Classification of Disease, version 10 (ICD-10) code, or a group of ICD-10 codes

- Have at least three varying levels of alcohol use assessed in a dose-response or dose-stratified meta-analysis, and pooled relative risks (RRs), odds ratios (ORs) or hazards ratios (HRs) are provided.

Systematic reviews that focused only on one type of alcoholic beverage such as wine or beer will be excluded as, in these studies, people who do not consume alcohol from a specific beverage may consume other types of alcoholic beverages. Populations deemed not relevant to the context of people living in Ireland (for example, studies that focus on specific ethnic minorities) will also be excluded.

Step 2. Methodological quality criteria

Following Step 1, the remaining systematic reviews will be assessed against four methodological quality criteria:

- Comprehensive literature search: The systematic reviews must have searched two or more databases, specified which ones, provided the timeframe when the search was conducted, and the search strategy that was used (key words and MESH terms). Reference lists of the included primary studies also need to have be screened.
- Characteristics of included studies in systematic reviews: The systematic reviews must have reported the age and sex of the participants and any confounding variables included in the primary studies. They also must have stated and described the exposure, comparator, and study design of the included primary studies.
- Quality assessment of included studies in systematic reviews: The systematic reviews must have used a pre-determined quality assessment tool to review the quality of every primary study included in the review.
- Inclusion and exclusion criteria: The systematic reviews must have reported their inclusion and exclusion criteria along with specific descriptions and rationales for the criteria. This includes the rationales for the population, exposure and outcome.

A systematic review is required to meet at least two of the four criteria described above to be considered for inclusion. These criteria ensure that the included systematic reviews meet the threshold for minimum methodological quality, and are reflective of quality criteria outlined in both the Australian and Canadian reviews.

Step 3. Methods of analysis criteria

Following Step 2, the remaining systematic reviews also need to provide a clear description and justification of the methodology used to analyse the individual studies to be further considered for inclusion. Analytical methods have to be sufficient to allow for reliable extraction and interpretation of the results. The use of

inappropriate analytical methods will lead to the exclusion of a systematic review (for example, where associations between alcohol consumption and a health condition included in the meta-analysis are not adjusted for potential confounders).

Systematic reviews that meet all the above selection criteria will then be carried forward for use in mathematical modelling to estimate the health impact of alcohol consumption on an individual. However, as only one systematic review will be included in the mathematical modelling for each outcome, if there is more than one systematic review for the same outcome, the review that meets the most methodological quality criteria will be retained. In the case where the same number of criteria are met, the study with the most recent search date will be retained.

All the remaining systematic reviews will be included in the mathematical modelling for the updated Low Risk Drinking Guidelines.

Appraisal of systematic reviews

All included systematic reviews will be assessed by two reviewers independently using A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2), and the Grading of Recommendations, Assessment, Development and Evaluations system (GRADE).[23, 24] Disagreements will be resolved by discussion or a third reviewer, if necessary.

AMSTAR 2 comprises 16 items covering domains that can affect the validity of a systematic review, such as the risk of bias from individual studies included in the review, the impact of publication bias, the literature search strategy and the appropriateness of meta-analytical methods. Each item is coded as ‘yes’, ‘partial yes’, or ‘no’.

The GRADE system allows a judgment to be made on the certainty of evidence of the included systematic reviews. The certainty of evidence can be categorised as high, moderate, low or very low. As the current project is building upon the work previously done by the CCSA, GRADE assessments will only be conducted for newly-included systematic reviews. The assessments of studies previously selected by the CCSA will be included in the current report.

Data extraction

Two reviewers will extract data independently. Disagreements will be resolved by discussion or a third reviewer, if necessary. A standardised data extraction template will be developed and piloted before undertaking data extraction. Where available, separate risk estimates for males and females and mortality and morbidity will be extracted. If separate risk estimates are not identified, the same risk estimates will be used for both sexes and outcomes. Additional data on study characteristics,

design and populations, exposure, outcomes, and results will be extracted (see Appendix 4).

Results presentation

The purpose of this review is to identify risk estimates for a range of health outcomes partially attributable to alcohol consumption. These will be inputted into a mathematical model to provide quantified risk estimates for the mortality and hospitalisation associated with different levels and patterns of alcohol consumption among the population in Ireland. These risk estimates will be used to model the number of deaths, premature deaths, potential years of life lost (PYLL) and hospitalisations due to alcohol in order to identify acceptable risk thresholds of alcohol consumption. Therefore, a full synthesis of identified reviews will not be performed. A narrative summary of the search and screen process, appraisal of included systematic reviews and meta-analyses, and key findings will be presented.

2.4.2 Relative risk estimates for partially-attributable acute conditions

The risk of partially-attributable acute conditions relies on levels of acute alcohol consumption, rather than average weekly or annual consumption. Risk estimates for injuries are typically not available in the published literature and so an alternative method is required for deriving risk functions. Specifically, AAFs which in this instance would describe the proportion of injuries that would be avoided if the population did not consume any alcohol, will be extracted from a report published in 2021 by the Health Research Board (HRB).[19] These AAFs, calculated by Sheffield University, used alcohol prevalence data from the 2016 Healthy Ireland Survey[25] along with mortality and hospitalisation data from the National Drug Related Deaths Index[26] and the HIPE[16] databases, respectively. These AAFs, and population prevalence of acute alcohol consumption levels, will be used in the current mathematical modelling, to derive risk functions for partially-attributable acute conditions such as road traffic or fall injuries (see Section 2.5.3). The population prevalence for each level of acute alcohol consumption will be sourced from the Healthy Ireland Survey and based on the highest number of drinks consumed on a single occasion in the previous 12 months.

Two assumptions must be made to estimate the risk function from an AAF. Firstly, an assumption must be made on the functional form of the risk function (for example, linear or log-linear). There is no clear consensus on the most appropriate functional form to be assumed, with the Canadian modelling report assuming a log-linear functional form,[27] while the Australian and UK models assumed a linear functional form.[28, 29] Secondly, an assumption must be made on the consumption threshold below which the risk of consuming alcohol is equal to the risk of

abstaining. This threshold was assumed to be 'no alcohol' in the Australian and UK models,[28, 29] and 0.08 grams per deciliter (g/dL) for blood alcohol content in the Canadian model.[27]

2.4.3 Absolute risk for wholly-attributable chronic and acute conditions

Unlike for health conditions that are partially attributable to alcohol, it is not possible to derive relative risk functions for wholly alcohol-attributable health conditions (acute and chronic). By definition, people who do not consume alcohol have no risk of developing health conditions that are wholly attributable to alcohol. Nonetheless, how risk among drinkers varies based on the amount of alcohol consumed remains important. Therefore, absolute risk functions will be estimated based on the mortality or hospitalisation rate of the condition and daily peak (for acute conditions) and mean weekly (for chronic conditions) alcohol consumption for particular sex and age groups (see Section 2.5.2). Similar to the relative risk functions for partially-attributable acute conditions, assumptions must be made on the functional form of the risk function and the threshold below which the risk of consuming alcohol is equal to the risk of abstaining. The absolute risk function calibrated to the observed incidence of each condition will be derived as described by Churchill et al.[30] This approach relies on calculation of a cumulative distributive fraction based on disease incidence and population prevalence at each level of alcohol consumption, thereby providing an estimate of the disease distribution across alcohol consumption levels.

2.4.4 Latency period for mortality and hospitalisation attributable to alcohol use

The effect of alcohol on the risk of developing some health conditions is understood to be the result of long-term exposure. Estimates are available for the latency period between alcohol consumption and the resultant onset of some conditions, such as several cancers, alcoholic polyneuropathy and degeneration of the nervous system due to alcohol.[31-33] For example, a review noted latency periods of 11–12 years for breast, colorectal, oral cavity and pharynx, and oesophagus cancers and of 8–9 years for larynx and liver cancers across 15 high-quality cohort studies.[31] If appropriate historical alcohol consumption data are available, a latency period will be incorporated into the mathematical model.

2.5 Mathematical modelling

The mathematical modelling will estimate the lifetime risk of mortality (that is, death, premature death and PYLL) and risk of hospitalisation attributable to different levels and patterns of alcohol consumption (that is, how much and how often alcohol is consumed) in Ireland. This will be completed by adapting the modelling approach detailed in the CCSA report entitled *Lifetime Risk of Alcohol-Attributable Death and*

Disability.[34] The methodological approach will be adapted to include consideration of the hospitalisation burden associated with alcohol consumption. Due to the challenges of modelling the full hospitalisation history of individuals across their lifetime, hospitalisations will be modelled using a relative risk approach and lifetime risk of hospitalisation will not be modelled. The outputs of the modelling will be 'the risk of hospitalisation' and 'the lifetime risk of mortality'. Additionally, the impact of drinking patterns (that is, the number of days drinking per week) will be considered. This approach can be divided into four steps, which are detailed in the subsequent sections:

1. Deriving relative risk estimates
2. Estimating alcohol consumption behaviours
3. Estimating mortality and hospitalisation levels associated with alcohol consumption
4. Assessing lifetime risk of mortality and risk of hospitalisation.

Primary outcomes assessed as part of Step 4 will be:

- Lifetime risk of death, premature death, and PYLL associated with acute and chronic alcohol consumption, by sex
- Lifetime risk of death, premature death, and PYLL associated with chronic alcohol consumption, by sex and number of days per week over which consumption is spread
- Risk of hospitalisation associated with acute and chronic alcohol consumption, by sex
- Risk of hospitalisation associated with alcohol consumption, by sex and number of days per week over which consumption is spread

2.5.1 Step 1. Deriving relative risk estimates for each health condition

In the first step, risk estimates for chronic and acute health conditions that are partially or wholly attributable to alcohol will be identified or estimated. Where data permit, separate risk estimates will be derived for men and women and mortality and hospitalisation. This process is detailed in Section 2.4.1. Briefly, for partially-attributable chronic conditions, a systematic review of systematic reviews and meta-analyses will be performed to identify relevant relative risk estimates. For partially-attributable acute conditions, AAFs will be extracted from a 2021 report from the HRB.[19] For wholly-attributable chronic and acute conditions, absolute risk functions based on the mortality rate or hospitalisation prevalence of the condition and daily

peak (for acute conditions) and mean weekly (for chronic conditions) alcohol consumption will be estimated.

2.5.2 Step 2. Estimating alcohol consumption behaviours

In the second step, three sets of risk estimates will be derived separately for males and females. These will describe three consumption metrics and their relationship with acute and or chronic conditions:

1. Mean weekly consumption and risk of chronic alcohol-related conditions
2. Peak daily consumption of the last 12 months and risk of acute alcohol-related conditions
3. Mean weekly consumption distributed evenly over one to seven days and risk of all alcohol-related health conditions.

Alcohol consumption levels and patterns in the population will be assessed using:

- Weekly average consumption, based on the estimated alcohol intake over a specific period by considering both the typical number of standard drinks consumed per week and the number of days drinking.
- Heavy episodic drinking, based on the highest number of drinks consumed on a single occasion within a specific period.

This approach takes into account both regular and episodic consumption (the latter posing higher risks of acute effects such as alcohol poisoning) of alcohol by the population.

Mean weekly alcohol consumption by age group and sex will be estimated by combining estimates of individual-level alcohol consumption and reported per capita alcohol sales (see Section 2.3.4). Age- and sex-specific prevalence of current drinkers and abstainers and mean weekly grams of pure alcohol consumed will be derived from the Healthy Ireland Survey data.[2] These survey estimates will be scaled so that they sum to 80% of the population-level consumption as estimated by Revenue sales data. This 80% level has been suggested so as to account for i) alcohol that is sold but not consumed and ii) the underreporting of alcohol consumption in the observational studies from which risk estimates used in this work will be obtained.[35]

Finally, a validated gamma distribution method will be used to estimate the population distribution of mean weekly alcohol consumption among current drinkers.[34, 36, 37] This approach relies on three main assumptions: (1) the proportions of lifetime abstainers and former drinkers reported in the Healthy Ireland Survey reflect current consumption patterns; (2) the discrepancy between survey coverage and per capita alcohol sales is evenly distributed across sex and age

groups;[38] and (3) the standard deviation of the gamma distribution can be empirically derived from the mean weekly alcohol consumption.[36, 39]

2.5.3 Step 3. Estimating mortality and hospitalisation levels associated with alcohol consumption

In the third step, the risk of death and hospitalisation attributable to alcohol consumption will be estimated for each health condition included in the model. For partially-attributable chronic conditions, AAFs will be calculated by combining relative risk estimates (from Step 1) with population-level alcohol consumption data (from Step 2), stratified by age, sex, and consumption level. For partially-attributable acute conditions, published AAFs from existing sources will be applied directly, as detailed in Section 2.4.2.[19] For wholly-attributable conditions, the absolute risk of death or hospitalisation will be estimated directly, as these conditions do not occur among non-drinkers and therefore have an AAF of one.

These cause-specific risk estimates will be used to derive the risk of death and hospitalisation for current drinkers at varying levels of average weekly and peak daily consumption. Outcomes will be stratified by age and sex. These risks serve as intermediate inputs to estimate overall burden in Step 4.

2.5.4 Step 4. Assessing total risk and potential years of life lost

In the fourth step, the cause-specific risks derived in Step 3 will be summed for each age, sex, and alcohol consumption level to estimate the overall risk of death and hospitalisation attributable to alcohol. These aggregate risks will then be used to calculate the:

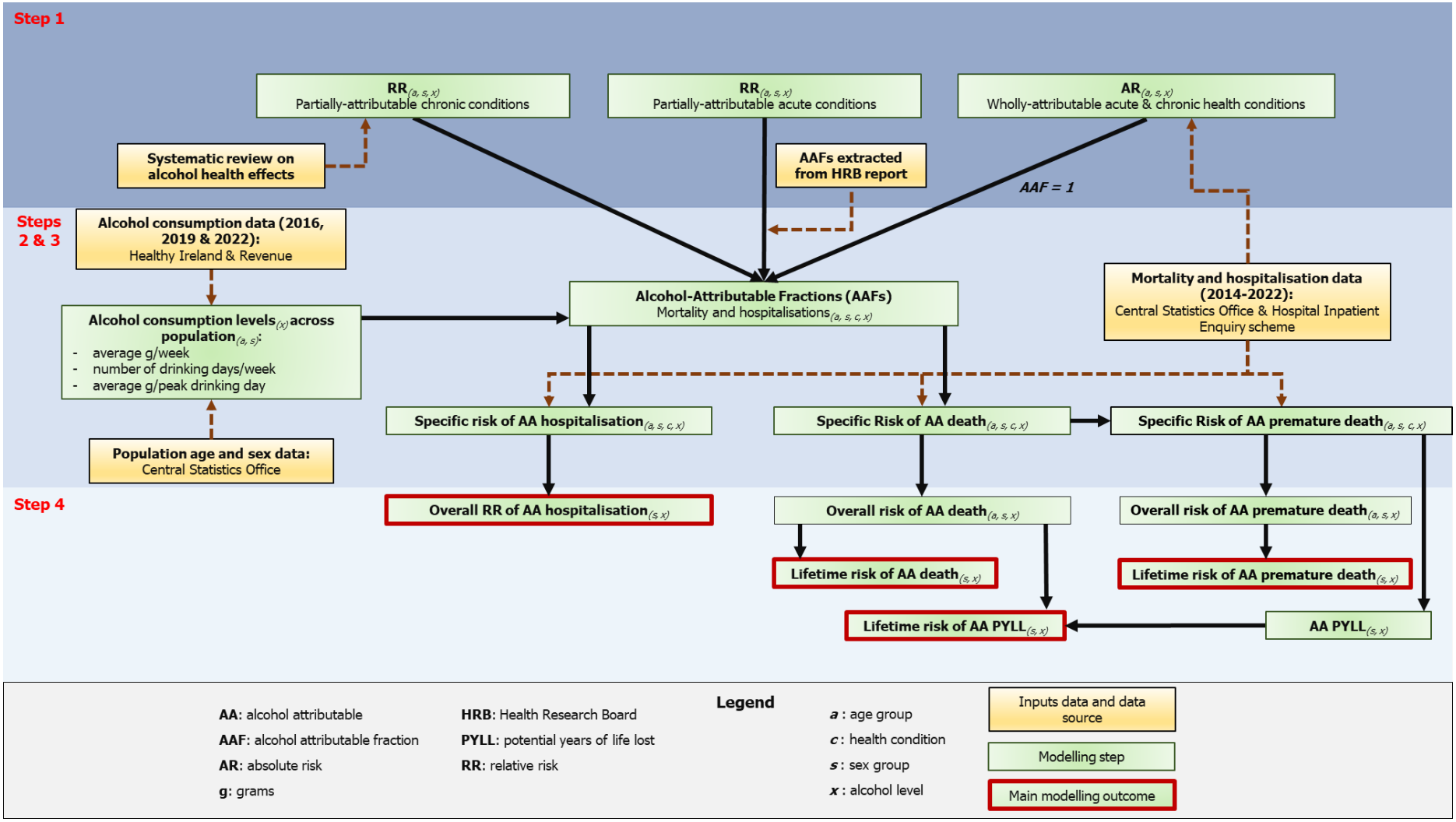
- relative risk of hospitalisation compared with lifetime abstainers
- lifetime risk of death and premature death per capita
- lifetime PYLL associated with alcohol consumption per capita.

An overview of the above steps is provided in Figure 1.

2.5.5 Sensitivity and uncertainty analyses

Sensitivity and or uncertainty analyses will be undertaken to explore the robustness of model outputs to key assumptions and input values. These analyses will assess the extent to which variation in input parameters or assumptions may influence the model outputs. The approach will be guided by prior international modelling studies.

Figure 1. Graphical overview of the proposed mathematical modelling approach



3 Report presentation

The final report will present findings from the systematic review (Section 2.4.1) and the mathematical modelling (Section 2.5). Primary outcomes from the modelling that will be presented are:

- Lifetime risk of death, premature death, and PYLL associated with acute and chronic alcohol consumption, by sex
- Lifetime risk of death, premature death, and PYLL associated with alcohol consumption, by sex and number of days over which consumption is spread
- Risk of hospitalisation associated with acute and chronic alcohol consumption, by sex
- Risk of hospitalisation associated with alcohol consumption, by sex and number of days over which consumption is spread.

The levels of alcohol consumption that correspond to specific levels of risk will be highlighted (for example, for lifetime risk of an alcohol-attributable death, this could be the level of alcohol consumption that is associated with 0.1% (1 in 1,000) or 1.0% (1 in 100) of deaths attributable to alcohol).

Additionally, the final report will include a high-level discussion on other effects of alcohol that are not considered in the mathematical modelling (such as the risks of harm to others due to an individual's drinking and the impact of alcohol consumption on quality of life and wellbeing), as well as considerations for using the modelling to inform the updated low-risk alcohol guidelines.

4 Anticipated timeline

It is estimated that the final report will be submitted to the Department of Health and published on the HIQA website by Q2 2026.

References

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number of deaths attributable to alcohol consumption in the European Union in 2004. BMC medical research methodology. 2013;13:1-9.

Appendix 1. AMSTAR 2 assessment of the Canadian Centre on Substance Use and Addiction systematic review.

AMSTAR 2 Question		Answer	Reference
1.	Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	Defining Research Questions (page 8): "With the view to guiding the identification of systematic reviews, facilitating interpretation of the findings and informing the formulation of recommendations, three more specific research questions were developed. Using the PECO (Population, Exposure/Comparison, Outcome) criteria, these questions specify 1) the target populations for the exposure; 2) the exposures and comparators being considered; and 3) the outcomes that are most relevant to assess (for more information, see Canadian Centre on Substance Use and Addiction, 2021a)."
2.	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	No	
3.	Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	Step 1: PECO and Study Design Criteria (page 11): "Systematic reviews had to include cohort, case-control or case-crossover studies to be eligible for inclusion. Where other types of studies were included in the systematic review, such as cross-sectional studies, the results from the cohort, case-control or case-crossover studies had to be reported separately for the review to be considered."
4.	Did the review authors use a comprehensive literature search strategy?	Yes	Identification of Systematic Reviews (page 9): "Nine databases were searched: PubMed, PsycNET, Embase, Cochrane Library's Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, International

			Health Technology Assessment Database, Joanna Briggs Institute, Database of Abstracts of Reviews of Effects, and Epistemonikos. The search was limited to systematic reviews and meta-analyses published from January 6, 2017, to February 17, 2021. Variations of search terms related to alcohol were used to encompass the full range of possible systematic review in this field. The detailed search strategy is presented in Table 1. A comprehensive search of the grey literature was also undertaken on sixteen websites (see Table 2)."
5.	Did the review authors perform study selection in duplicate?	Yes	Identification of Systematic Reviews (page 9): "Once the search was complete, an Information Specialist removed duplicates and articles that, based on titles and abstracts, were clearly outside of the scope of the project." Screening of Systematic Reviews (page 11): "Two independent investigators from the ERWG went through the titles and abstracts of the remaining studies from the updated search to identify which systematic reviews should be assessed in full text, along with the studies already selected by the AAWC. Throughout the screening process, disagreements between the two investigators were resolved through discussions between them."
6.	Did the review authors perform data extraction in duplicate?	NR	Not reported
7.	Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	Pages 17-114
8.	Did the review authors describe the included studies in adequate detail?	Yes	Pages 17-114
9.	Did the review authors use a satisfactory technique for assessing	Yes	Appraisal of Systematic Reviews (page 14):

	the risk of bias (RoB) in individual studies that were included in the review?		"The quality of all included systematic reviews was assessed by two independent investigators from the ERWG using 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). The use of sex- and gender-based analysis (SGBA) was also appraised."
10.	Did the review authors report on the sources of funding for the studies included in the review?	No	
11.	If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	N/A	Meta-analysis not performed
12.	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	N/A	Meta-analysis not performed
13.	Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	Yes	Pages 17-114
14.	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Pages 17-114
15.	If they performed quantitative synthesis did the review authors carry	N/A	Quantitative synthesis not performed

	out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?		
16.	Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	In separate report entitled *Update of Canada's Low-Risk Alcohol Drinking Guidelines:* *Disclosure of Affiliations and Interests*

Appendix 2. Search strategy for the systematic review

Database Name	Embase 1974 to 2024 via Ovid
Date search was run	08 April 2024

#1	'drinking behavior'/exp OR 'drinking behavior' OR 'alcoholic beverage'/exp OR 'alcoholic beverage' OR 'alcoholism'/exp OR 'alcoholism' OR 'alcohol intoxication'/exp OR 'alcohol intoxication' OR 'binge drinking'/exp OR 'binge drinking' OR 'fetal alcohol syndrome'/exp OR 'fetal alcohol syndrome'	274,018
#2	alcohol*.ab, ti	571,094
#3	#1 OR #2	655,689
#4	'meta analysis'/de OR 'systematic review'/de	590,744
#5	#3 AND #4	10,358
#6	#3 AND #4 AND [17-02-2021]/sd NOT [09-04-2024]/sd	4,109
#7	#3 AND #4 AND [17-02-2021]/sd NOT [09-04-2024]/sd AND ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim)	1,055
#8	#6 NOT #7	3,054

Appendix 3. Grey literature search strategy for the systematic review

Database	Search terms
Register of Australian Drug and Alcohol Research: https://catalogue.nla.gov.au/Record/2978698	Alcohol* [title]
National Drug and Alcohol Research Centre: http://ndarc.med.unsw.edu.au/	Alcohol
National Drug Research Institute: http://ndri.curtin.edu.au/	Alcohol*
National Institute of Health and Care Excellence: https://www.nice.org.uk/	alcohol*
Agency for Healthcare Research and Quality: http://www.ahrq.gov/	Alcohol*
Centers for Disease Control and Prevention: https://www.cdc.gov/	Alcohol*
World Health Organization: http://www.who.int/en/	Alcohol
National Institute on Alcohol Abuse and Alcoholism: https://www.niaaa.nih.gov/	No specific search; browsed website
International Prospective Register of Systematic Reviews :http://www.crd.york.ac.uk/PROSPERO/	MeSH DESCRIPTOR Alcohol-Related Disorders EXPLODE ALL TREES MeSH DESCRIPTOR Alcohol Drinking EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT MeSH DESCRIPTOR Alcoholic Beverages EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT MeSH DESCRIPTOR Alcoholism EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT MeSH DESCRIPTOR Alcoholic Intoxication EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT MeSH DESCRIPTOR Binge Drinking EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT MeSH DESCRIPTOR Fetal Alcohol Spectrum Disorders EXPLODE ALL TREES AND (Systematic Review OR Meta-Analysis):RT
Health Evidence Canada: http://www.healthevidence.org/	Limit: Date = Published from 2021 to date

	Topic Area = Addiction/Substance Use -> Alcohol Abuse/Use
U.S. Preventive Services Task Force: https://www.uspreventiveservicestaskforce.org/	alcohol*
Public Health England: https://www.gov.uk/government/organisations/public-health-england	alcohol* in Research and Statistics
Indigenous HealthInfoNet: http://www.healthinfonet.ecu.edu.au/	Browsed Alcohol and Other Drugs Knowledge Centre Alcohol
International Agency for Research on Cancer: https://www.iarc.fr/	Alcohol
World Cancer Research Fund: https://www.worldwidecancerresearch.org/	Alcohol*

Appendix 4. Data extraction template for the systematic review

Review details			Review methods				Review results			Methodological quality criteria			
Study author	Study year	Study design	Search dates	Population	Exposure	Outcome	Number of unique studies	Number of participants	Narrative summary of results	Comprehensive literature search	Characteristics of included studies in systematic reviews	Quality assessment of included studies in systematic reviews	Inclusion and exclusion criteria

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For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie