Draft Report:
Scientific Findings of the Alcohol Intake & Health Study for Public Comment

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Summary

- The Alcohol Intake and Health Study assessed relationships between alcohol use and health in the U.S., with a focus on morbidity and mortality (i.e., deaths and reduced life expectancy) from health conditions causally related to alcohol use.
- Most of the evidence evaluated in this report is from systematic reviews and meta-analyses of "observational" cohort studies. It did not include data from quasi-experimental (e.g., Mendelian randomization) studies or randomized controlled trials.
- We assessed relationships between different levels of alcohol consumption and the risk of dying from health conditions that are causally related to alcohol consumption in the U.S. We also modelled the total alcohol-specific mortality at different levels of consumption based on all alcohol-related conditions.
- Among the U.S. population, the risk of dying from alcohol use begins at low levels of average use. Higher levels of alcohol consumption are linked with progressively higher mortality risk. Depending on the level of use, men are at a similar risk of health harms from alcohol use compared to women.
- In the United States, males and females have a 1 in 1000 risk of dying from alcohol use if they consume more than 7 drinks per week. This risk increases to 1 in 100 if they consume more than 9 drinks per week.
- Males and females who consumed 1 drink per day had an increased risk of liver cirrhosis, esophageal cancer, oral cancer, and injuries, but a lower risk for ischemic stroke. In addition, females had a higher risk for liver cancer and a lower risk for diabetes mellitus when they drank 1 drink per day. However, drinking patterns shape risk. Specifically, even infrequent high per-occasion drinking may eliminate the lower levels of risk for ischemic stroke.
- Alcohol use is associated with increased mortality for seven types of cancer (colorectal, female breast, liver, oral cavity, pharynx, larynx, esophagus [squamous cell type]). Increased risk for these cancers begins with any alcohol use and increases with higher levels of use. Women experience a much greater risk of an alcohol-attributable cancer per drink consumed.
- 'Per occasion' alcohol use refers to how much alcohol is consumed within a short time period, as opposed to how much is consumed on average. Higher levels of per occasion use result in higher blood alcohol levels and higher risks for injuries. Risks increase starting at one drink per occasion and are particularly pronounced for women consuming more than three drinks and men consuming more than four drinks per occasion.
- For individuals who start consuming alcohol at age 15, the risk of an alcohol-attributable death between the ages of 15 and 20 varies by consumption level. The risk of an alcohol-attributable death increases linearly with alcohol consumption. For males, the risk of an alcohol-attributable death

ranges from 0.07 (95% CI: 0.05, 0.08) per 1000 for those who consume 1 drink per week, to 1.76 (95% CI: 1.42, 2.28) per 1000 for those who consume 3 drinks per day (i.e., 21 drinks per week). Similarly, for females, the risk increases from 0.03 (95% CI: 0.02, 0.04) per 1000 for those who consume 1 drink per week, to 0.75 (95% CI: 0.57, 1.06) per 1000 for those who consume 3 drinks per day (i.e., 21 drinks per week). Most of these alcohol-attributable deaths are caused by road traffic crashes, unintentional injuries, and intentional injuries. These deaths represent a substantial proportion of all deaths for individuals 15 to 20 years of age.

Introduction

Alcohol is one of the most widely used psychoactive substances in the United States. According to the 2023 National Survey on Drug Use and Health (NSDUH), 47.5% of Americans aged 12 or older (134.7 million people) used alcohol in the past month. These NSDUH data also show that 8.6% of individuals aged 12 to 20 (3.3 million people) reported binge drinking on 5 or more days in the past month compared to 23.7% of those aged 21 and older (58.1 million). The prevalence of alcohol consumption in adults has remained relatively stable over recent years, with slight fluctuations. However, certain subgroups show increases in alcohol use and alcohol-related deaths, such as females and middle-aged and older adults (1, 2). It is also noteworthy that between 1999 and 2021 alcohol beverage sales data suggest that per capita consumption rose by 13%. Notably, while the data suggest beer sales declined by 38%, they also suggest spirits sales rose by more than 50% and wine by more than 40% (3).

The NSDUH data also highlight the prevalence of alcohol use disorder (AUD) in the United States. In 2023, an estimated 28.9 million people aged 12 or older (10.2% of the population) met diagnostic criteria for AUD in the past year. This included 0.8 million adolescents aged 12 to 17 (2.9% of this age group), 5.1 million young adults aged 18 to 25 (15.1% of this age group), and 23.0 million adults aged 26 or older (10.3% of this age group) (4). These statistics underscore the substantial public health challenges associated with alcohol consumption in the United States—particularly among young adults—and emphasize the need for continued prevention and treatment efforts across all age groups.

Adult and Youth Drinking Patterns Are Linked

Research has established a clear relationship between adult and youth drinking patterns in the United States. A comprehensive study by Nelson et al. (2009) examined this relationship using state-level data from both the Youth Risk Behavior Survey (YRBS) and the Behavioral Risk Factor Surveillance System. Their analysis, which pooled data from 1993 to 2005, revealed significant correlations between youth and adult patterns of both past year drinking and binge drinking (5). This relationship was further investigated by Xuan et al. (2013), who analyzed YRBS data from 1999 to 2009, and found that state alcohol policies influenced both adult and youth binge drinking behaviors. Most notably, their research demonstrated that even a modest 5 percent increase in state-level adult binge drinking prevalence was associated with a 12 percent increase in the likelihood of youth alcohol consumption (6). These findings underscore the strong correlation between adult drinking behaviors and youth alcohol consumption patterns (7).

At the population level, an average of 178,000 individuals (of all ages) in the United States died annually from excessive alcohol use[1] in 2020 and 2021—making it a leading preventable cause of death in the United States (8). Alcohol also plays a role in many drug overdoses; there was a 4.6-fold increase in combined alcohol and opioid poisoning deaths between 2000 and 2019, a total increase of 5,856 deaths across this time period (9). Deaths related to excessive alcohol use mostly affect working-age people (i.e., those aged 20 to 64 years). From 2015 through 2019, alcohol consumption caused on average an estimated 89,700 deaths annually among people in this age group, accounting for two-thirds of the total deaths from excessive alcohol use. These deaths (64,998 among males and 24,699 among females) represented 12.9% of all deaths among working-age people (15.0% of all deaths among males and 9.4% of all deaths among females) (10). The economic burden of excessive alcohol use was estimated at $249 billion in 2010, when it was most recently assessed (11).

Purpose of this Report

In 2022, the Alcohol Intake & Health Study was devised and approved by the Interagency Coordinating Committee on the Prevention of Underage Drinking (ICCPUD). To conduct this study, the ICCPUD convened a Scientific Review Panel[2] (SRP) to analyze the current scientific evidence on youth and adult alcohol intake and health risks. The SRP was comprised of six external scientists with expertise in topics that include alcohol epidemiology, alcohol's health effects, cancer epidemiology, biostatistics, meta-analyses, and systematic reviews. The purpose of the SRP was to develop and apply a methodology to assess the relationship between alcohol intake and related health conditions using current best practices. In particular, the SRP focused on four areas: 1. Chronic alcohol use and the development of health conditions, 2. The relationship between alcohol intake and injuries, 3. Lifetime risks of alcohol-attributable mortality and morbidity by alcohol intake, and 4. The burden of alcohol intake and related health conditions in the United States.

Alcohol-attributable Health Conditions Addressed in This Study

Research causally links alcohol consumption, including non-excessive and excessive use, with more than 200 health conditions[3] (14) including infectious diseases, malignant neoplasms, cardiovascular diseases, digestive diseases, mental and behavioral disorders, metabolic disorders, and injuries. This study specifically addresses the potential links between alcohol intake and multiple conditions that can lead to

[1] "Excessive alcohol use," as defined by the Centers for Disease Control and Prevention, includes binge drinking, heavy drinking, and any drinking by pregnant females or people younger than 21 (see https://www.cdc.gov/alcohol/about-alcohol-use/index.html).
[2] The members of the Scientific Review Panel are Drs. Katherine Keyes, Priscilla Martinez, Adam J. Milam, Jürgen Rehm, Timothy S. Naimi, and Kevin Shield.
[3] Conditions defined by the three-digit codes of the International Statistical Classification of Diseases and Related Health Problems, 10th revision, (ICD-10).

death in order to understand the health impacts of the number of alcoholic beverages consumed in a single drinking occasion (i.e., per-occasion drinking), including but not limited to heavy and binge drinking. These conditions include:

- infectious diseases, including tuberculosis, pneumonia, HIV, and coronavirus (15);
- cancers, including breast, mouth and throat, esophagus (squamous type), larynx, liver, and colon and rectum (16);
- cardiovascular diseases, including ischemic heart disease, ischemic stroke, atrial fibrillation, and heart failure (17);
- liver cirrhosis, pancreatitis, and diabetes (18-20);
- neurological diseases, including epilepsy(21); and
- injuries (22, 23).

The impact of alcohol use on health is complex and multifactorial. For example, with respect to injuries and the majority of diseases, there is evidence that alcohol use has no protective effect at any level of consumption (24). However, for conditions such as ischemic heart disease, ischemic stroke, certain cancers (e.g., kidney and thyroid), and diabetes mellitus, there is mixed research about the potential protective effect on disease occurrence and mortality for people who consume relatively low amounts of alcohol and who do not engage in binge drinking (i.e., consuming 5 or 4 or more standard drinks [each with 14 grams of ethanol] during one drinking occasion for males and females, respectively) (25). However, Mendelian randomization studies, including those using advanced methodologies, find no protection at low levels of consumption for ischemic heart disease, ischemic stroke, or diabetes mellitus (26-28).

This study modeled disease-, injury-, and condition-specific relative risk (RR) curves to estimate the burden of disease attributable to alcohol use; the primary focus of these analyses was on morbidity and mortality from conditions that are considered causally related to alcohol. This study assessed the health impacts caused by ethanol in alcohol beverages and did not distinguish between impacts caused by different types of alcohol-containing products (e.g., beer, wine, spirits, and other alcohol beverages). Since health impacts caused by beer, wine, spirits, and other alcohol beverages are likely based on ethanol content regardless of the form in which the ethanol is consumed, this study focused on standard drinks consumed instead of specific types of alcohol beverages (29).

Methods

The SRP, selected by an interagency nomination and scientific vetting process conducted by the ICCPUD, developed the multi-method approach summarized here to formulate data on (i) RRs related to short- and long-term risks of morbidity and mortality, (ii) RRs related to the short-term risk of injury or acute illness due to per-occasion drinking, (iii) alcohol use among specific populations (e.g., pregnant persons, underage youth), and (iv) situations and individual circumstances that can be hazardous when drinking alcohol (e.g., driving, swimming).

Based on the current practices of the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and the Institute for Health Metrics and Evaluation (IHME) (30-32), this study modeled absolute risk curves of alcohol-attributable mortality and morbidity from conditions considered causally related to alcohol consumption based on a person's age, sex, and alcohol use. Of note, no modeling is required for causes of death that are solely (100%) attributable to alcohol use (e.g., alcohol cardiomyopathy).

These risks can then be combined to estimate the risk for total alcohol-specific mortality. This method does not depend on all-cause mortality studies, so it can be applied to the actual distribution of causes of death in the United States. In addition, this method can also model risk relationships between alcohol use and other indicators of morbidity and mortality (e.g., years of potential life lost, disability-adjusted life years).

Consequently, we used cause-specific modeling to estimate the lifetime risk of mortality and morbidity. Separate models examined risks from any alcohol consumption as well as different levels of average alcohol consumption. The risk curves were generated based on the average amount of pure alcohol (i.e., ethanol) consumed. People who consumed alcohol were defined as those who consumed at least one standard drink (14 grams of alcohol) in the past year. The modeling examined the following outcomes:

- deaths;
- premature deaths (i.e., deaths that occur among those <70 years of age);
- years of potential life lost (YPLL);
- years lived with disability (YLD: a measure of disease occurrence and the disability caused by the disease);
- disability adjusted years of potential life lost (a combination of both YPLL and YLD).

Models only included diseases and injuries that met three criteria: (i) the disease or injury is causally related to alcohol use, (ii) a dose-response risk function is available for the risk relationship between alcohol consumption (measured in grams per day) and the disease or injury of interest, and (iii) either death or morbidity is measured specifically for the disease or injury causally related to alcohol use. We treated specific types of cancer as separate outcomes because the association between alcohol and cancer varies at different sites of the body.

The process to estimate alcohol-specific risk relationships comprised two steps (Figure 1). First, we performed a systematic scoping review of existing systematic reviews and meta-analyses on the relationship between alcohol consumption and the occurrence of disease and injury for diseases and injuries causally related to alcohol. Experts used these systematic reviews and meta-analyses to identify the most appropriate risk relationship between alcohol consumption and each disease or injury. Second, we applied the obtained risk relationships to data on alcohol consumption, diseases, and injuries in the United States population. These models compared risks observed with specific levels of alcohol consumption (e.g., 1 or 2 drinks per day) to risks observed among lifetime abstainers (i.e., people who have never consumed alcohol). Lifetime abstainers were selected as the reference group to limit abstainer bias, which can arise when studies combine lifetime abstainers with former drinkers who may have quit after becoming sick or experiencing some health effects related to their alcohol use. Each of these steps is described in greater detail in the following sections.

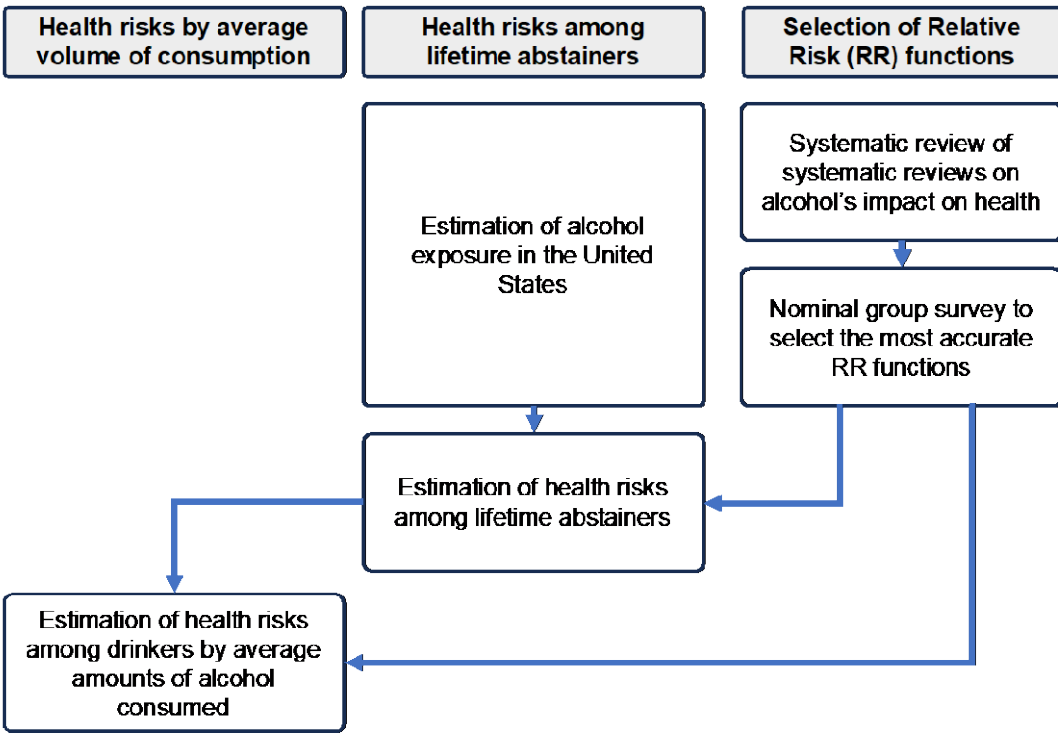

Figure 1. Flow chart for estimating the relationship between average volume of alcohol consumed and health consequences.

Data Sources for Alcohol Consumption, Morbidity, and Mortality in the United States

Table 1 lists the data sources used to obtain the information used in the models that are described below.

Table 1. Data sources for alcohol consumption, morbidity and mortality and injuries

Data	Source
Alcohol Consumption	
Alcohol consumption	National Alcohol Survey, National Survey on Drug Use and Health (NSDUH), National Health Interview Survey (NHIS), National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III), and Behavioral Risk Factor Surveillance System (BRFSS)
Morbidity and Mortality	
Number of deaths that occurred in United States by age, sex, and cause	National Vital Statistics System
Cancer incidence data	Centers for Disease Control and Prevention's WONDER database
Population by age and sex	U.S. Census Bureau
Disease incidence and YLD	Institute for Health Metrics and Evaluation's Global Burden of Disease study
Life tables by sex	Centers for Disease Control and Prevention's National Center for Health Statistics
Injuries	
BAC as a marker for alcohol-attributable traffic injury deaths	Fatality Analysis Reporting System (FARS), National Highway Traffic Safety Administration (NHTSA)
BAC information on violent deaths (assaults and self-harm)	Centers for Disease Control and Prevention's Web-based Injury Statistics Query and Reporting System (WISQARS), National Violent Death Reporting System (NVDRS)
Proportion of injuries with a BAC at or above 0.10 g/dL for the United States	Systematic review and meta-analysis (36).

We modeled past-year drinking prevalence among the United States' population using the population surveys listed in Table 1. Survey estimates of per capita consumption only cover approximately half of the alcohol sold in stores, and accurately modeling risk relationships hinges on knowing true levels of exposure to alcohol (37, 38). Therefore, we corrected survey data for under-coverage of alcohol use before using the data to model the number of alcohol-attributable deaths in the United States. To do this, we obtained (38) data on adult per capita sales from the Alcohol Epidemiologic Data System as a proxy for per capita consumption levels (39). The World Health Organization provided estimates of unrecorded adult per capita consumption (e.g., moonshine, etc.) (40). We upshifted mean consumption among drinkers in United States population surveys by age (15 to 24, 25 to 34, 35 to 49, 50 to 64, ≥65 years of age) and sex to match 80% of alcohol per capita consumption (APC). Survey estimates were adjusted to 80% of APC rather than 100% to account for (i) alcohol that was sold but not consumed, and (ii) the

underreporting of alcohol consumption in observational studies from which the RR estimates used in this study were obtained. The distribution of alcohol consumption among past year drinkers was then modeled using a gamma distribution. Following the methods of Rehm et al., 2010 and Kehoe et al., 2012, the mean of the gamma distribution was used to predict the standard deviation (37, 41).

Systematic Review of Meta-analyses to Identify Risk Relationships

Meta-analyses used in the modeling process were selected by panels of experts in the distinct areas of (i) cancer, (ii) cardiovascular diseases, (iii) digestive conditions, (iv) neurological disorders, and (v) infectious diseases. The experts were consulted to determine the RR estimates for each condition causally related to alcohol use. The sampling frame of experts was based on the authors who have published the largest number of first and last author scientific publications concerning the noted disease areas (determined by performing a PubMed Search) in the past 10 years. These authors were asked to participate in the expert group panels for their respective area of expertise. Quota sampling was used to establish expert group panels to ensure diversity and representation based on geographic location, sex, race, and ethnicity.

All panels provided input on the magnitude of the underreporting of alcohol consumption in observational studies, and on specific populations and situations and individual circumstances where the consumption of alcohol is hazardous. During the expert panel consultations, each expert was provided with the results of the preregistered systematic scoping review. The experts then completed a questionnaire in which they selected the most accurate RR for each condition to be used in the current modeling study and provided a rationale for the chosen RR. The results of these questionnaires were used to determine which RRs to include in the modeling study. The results of the selection of RRs were summarized by sex. When an expert panel selected RRs which were not sex specific, the RRs were assumed to be applicable to both males and females.

Estimation of The Burden of Disease in the United States in 2022 Attributable to Alcohol Use

Population-attributable fractions (PAFs) express the proportion of the risk of death from a particular condition that is caused by alcohol consumption. These attributable fractions were generated using a Levin-based method that pools data on alcohol exposure (adjusted using per capita alcohol sales data to account for the underreporting in survey data) with the associated RR estimates from the identified systematic reviews by type of condition (43).

The number of alcohol-attributable deaths was calculated using the corresponding disease and injury specific PAF applied to the death estimates by sex, age, and cause. Data on disease- and injury-specific PAFs were available by sex and age (15 to 24, 25 to 34, 35 to 49, 50 to 64, ≥65 years of age). Data on disease- and injury-specific mortality and population were available by sex and age (0, 1 to 4, 5 to 9 …. 90 to 94, ≥65 years of age). The risk of death for lifetime abstainers (i.e., people who have not consumed at least 1 standard drink of alcohol) for specific health conditions and age was calculated by taking the total alcohol-attributable deaths and subtracting that number from the total number of deaths, which was then divided by the total population of United States. All such calculations were completed by age (0, 1 to 4, 5 to 9 …. 90 to 94, ≥65 years of age) and sex.

A comparative risk assessment methodology was utilized to estimate the burden of disease in 2022 attributable to alcohol use. These estimations were based on the theoretical minimal risk exposure level (TMREL) of lifetime abstention from alcohol use. The alcohol-attributable health burden estimates were based on alcohol consumption prevalence data from 2022 for all diseases causally associated with alcohol use, except for cancer where 2012 data were used. For diseases which were 100% attributable to alcohol, the PAF was assumed to be 1.0 because the condition would not occur without alcohol.

Relative risks from the systematic review of meta-analyses were combined with estimates of the risk of mortality and morbidity for lifetime abstainers to estimate lifetime risk curves. For injuries, the proportion of injuries where the blood alcohol concentration (BAC) was at or above 0.10 g/dL (obtained from NHTSA, NVDRS and a systematic review by Alpert and colleagues (36)) was used as an estimate of the fraction of injuries attributable to alcohol consumption. A comparative risk assessment methodology was used to estimate the risk of mortality and morbidity for lifetime abstainers. Lifetime risk curves were calculated by estimating alcohol-attributable mortality and morbidity risk by cause, age, and sex. The life-year specific alcohol-attributable mortality risks were multiplied by the YPLL for each cause of death. The lifetime risk curves also accounted for competing causes of death (i.e., deaths not attributable to alcohol use).

Estimation of the risk relationship between alcohol use and injury

To estimate the risk relationship between alcohol use and injury, data on the proportion of injuries where there was a BAC at or above 0.10 g/dL (obtained from NHTSA, NVDRS and a systematic review by Alpert and colleagues) were combined with survey data on alcohol use. The use of a BAC of 0.10 g/dL as a threshold for defining alcohol-attributable injuries (for conditions that are not 100% alcohol attributable) is based on the findings of RR function from case crossover studies (22, 23). While a

proportion of injuries that occur among people who have a BAC below 0.10 g/dL may also be causally associated with alcohol (in particular among people with a BAC between 0.03 to 0.09 g/dL) (42), these injuries are not modeled due to there being less certainty as to whether they are attributable to alcohol use.

The estimation of the RRs for injuries in the United States is based on a two-step process. The first step is to determine the shape of the risk curve between alcohol use and the risk of injuries. The second step in the estimation of the RRs for people in the United States who drink (i.e., people who have consumed alcohol in the past year; RR_D) is based on the average amount of alcohol consumed per day (operationalized as x). The process used to estimate the RR_D is based on data regarding the PAFs of injuries (using toxicology reports on BAC as a proxy) and data on alcohol use.

Lifetime risks of alcohol-attributable mortality and morbidity

The lifetime risks of experiencing alcohol-attributable mortality and morbidity were estimated based on a cause-specific approach. The lifetime risks of experiencing alcohol-attributable mortality and morbidity are the estimated absolute risk of alcohol consumption at the population level. To account for under coverage of alcohol consumption in medical epidemiology studies, we used a correction factor of 0.9 (i.e., we assumed that on average epidemiological measures of alcohol consumption underestimated a person's alcohol consumption by 10%) (see: (44)).

Estimating age-, sex-, and cause-specific alcohol attributable mortality

Cause-specific alcohol-attributable mortality risk (Risk_D_AA) for a given life year was estimated by multiplying Risk_D_LA (see Formula A2 in the appendix) by the corresponding RR given an age, sex, cause, and average daily alcohol consumption amount (see Formula A4in the appendix).

Estimating cause-specific alcohol-attributable morbidity

Cause-specific alcohol-attributable morbidity (measured in YLD) risk was estimated by multiplying Risk_YLD_LA (see Formula A3 in the appendix) by the corresponding RR given an age, sex, cause, and average daily alcohol consumption amount (see Formula A5 in the appendix).

Estimating total alcohol-attributable mortality risk and morbidity risk for a given life year

Total alcohol-attributable mortality risk and morbidity risk for a given life year were estimated by summing all cause-specific alcohol-attributable mortality risk and morbidity risk for a given life year, respectively

(see Formulas A6 to A12 in the appendix). Estimates of lifetime risks of alcohol-attributable mortality and morbidity accounted for competing causes of death (i.e., deaths which are not attributable to alcohol use); to account for competing causes of death, the probability of survival for a given life year was estimated based on a person's sex and on average daily alcohol consumption.

Estimating age-specific mortality risk

The age-specific mortality risk was estimated as the sum of the risk of an alcohol-attributable death and the risk of a non-alcohol attributable death. Based on age–specific mortality risk, we estimated the probability of being alive at a given life course age (see Formula A8 in the appendix).

Estimating total lifetime risk of an alcohol-attributable death

The total lifetime risk of an alcohol-attributable death was estimated by summing the one-year age-specific alcohol-attributable mortality risks. Each risk was weighted using the proportion of people alive in the population at the end of a given life year based on their sex and on average daily alcohol consumption (see Formula A9 in the appendix).

We also estimated the morbidity associated with these alcohol-attributable deaths. To estimate the lifetime risk of alcohol-attributable YPLL, we weighted the alcohol-attributable mortality risks by the YPLL for each cause of death and the proportion of people alive in the population at the end of a given age based on their sex and on average daily alcohol consumption (see Formula A10 in the appendix). We then summed these weighted risks. We used an analogous process to estimate YLD risks (see Formula A11 in the appendix). The life risk of disability-adjusted life years (DALYs) lost was estimated by summing the lifetime risks of alcohol YPLL and YLD (see Formula A12 in the appendix).

Estimating alcohol-attributable cancer risk for a given life year

Alcohol–attributable cancer risk for a given life year was estimated by summing alcohol-attributable cancer incidence risks for each type of cancer and life year, respectively (see Formulas A10 and A11). Estimates of lifetime risks of alcohol-attributable cancer incidence accounted for survival. This was achieved by estimating the probability of survival for a given life year based on a person's sex and on average daily alcohol consumption.

Alcohol and health risks that occur from short-term drinking occasions

Researchers can estimate alcohol consumption per occasion or on average. Per-occasion alcohol use is based on consumption during particular times (e.g., 2 hours, 1 day) or occasions. By contrast, average consumption is determined by dividing total consumption by time (e.g., number of standard drinks consumed per year). The formulas in the previous section all relied on average alcohol consumption. However, per-occasion consumption is more strongly related to consumption patterns and provides a proxy measure for BACs that might be reached based on a particular level of per-occasion consumption. Per-occasion consumption is often measured as binge or heavy episodic drinking (i.e., 5 or more drinks for males, or 4 or more drinks for females), which generally results in BACs that can produce impairment (e.g., $\geq$0.08%). Understanding per-occasion consumption is particularly important when estimating "acute" outcomes, such as injuries and acute pancreatitis (22, 23), that can be caused by high BACs. However, high per-occasion consumption can also increase the risk of infectious diseases (45), female breast cancer (46), ischemic heart disease and ischemic stroke (47), diabetes mellitus (20), epilepsy (21, 48), and liver cirrhosis (49). Thus, studies that focus exclusively on average alcohol consumption may miss the risks associated with high per-occasion consumption by making people who regularly drink low volumes appear similar to those who drink heavily but infrequently. Consequently, we reviewed available data on per-occasion consumption and disease and injury risk.

Multiple sources of data were used to produce a narrative review of the health impacts of per-occasion alcohol use, namely: (i) results from the systematic review of meta-analyses and systematic reviews that summarize how drinking patterns affect the risk of disease and injury occurrence, (ii) results from a reanalysis of United States' emergency department case-cross-over studies that examined the relationship between alcohol use and injury occurrence (22, 23), and (iii) results from roadside survey studies where the BACs of road injury decedents were compared to those of drivers randomly selected from the same road on the same day and at the same hour as the fatal crash case (50, 51).

Collecting and generating evidence on the effects of alcohol use among specific populations, and situations and individual circumstances where consuming alcohol is hazardous.

The study also synthesized the available evidence on the effects of alcohol use among specific populations (e.g., pregnant persons, underage youth), and situations and individual circumstances where consuming alcohol is hazardous.

Results

Systematic review of alcohol use and the risk of alcohol-related conditions

The search strategy yielded 7294 publications after duplicates were excluded. Based on title and abstract screening, 7003 of these studies were excluded, and 291 underwent full-text assessments. After completion of the full-text assessments, a total of 56 unique systematic reviews were included in the current review (See Figure 2). Despite a previously established causal relationship, no systematic reviews on the direct relationship between alcohol consumption and the risk of HIV/AIDS, other sexually transmitted diseases, cervical cancer, or depression were found.

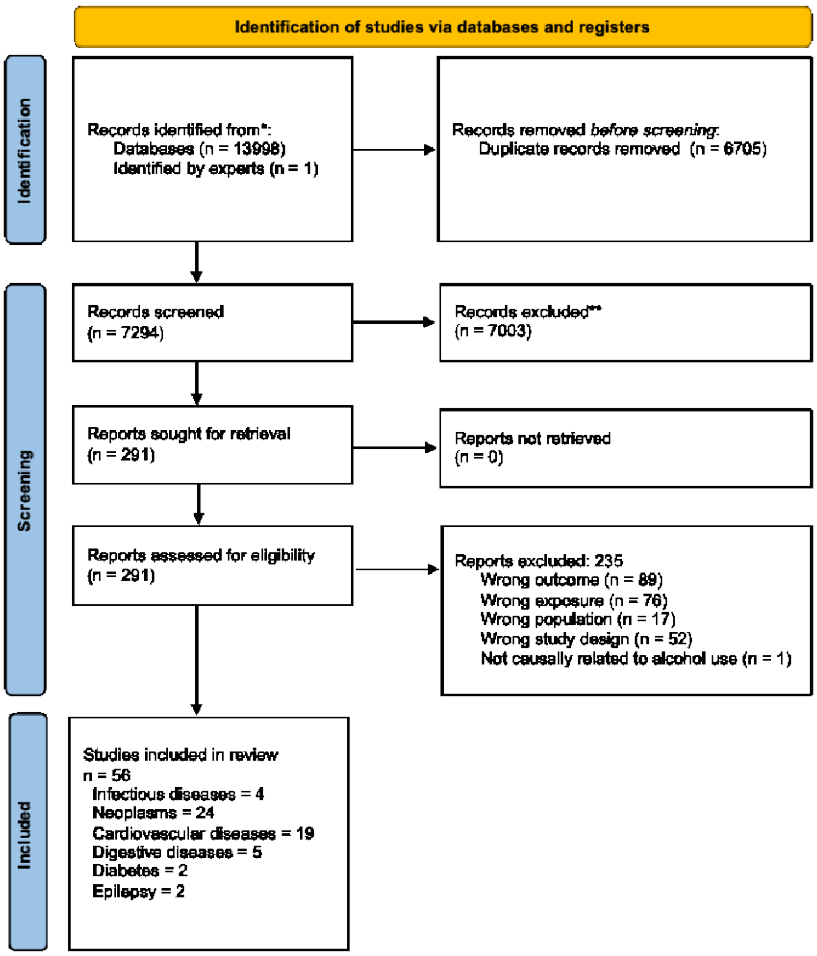

Figure 2. Systematic search results for systematic reviews and meta-analyses on the risk relationship between alcohol consumption and disease occurrence*

* Relative risks for injuries were estimated using data from Fatality Analysis Reporting System (FARS), National Highway Traffic Safety Administration (NHTSA), Centers for Disease Control and Prevention's National Violent Death Reporting System (NVDRS), and a systematic review and meta-analysis by Alpert et al., (32).

Table 2. Results of the systematic review and expert study selections

Disease	Systematic reviews found	Study selected	Outcome definition	Dates search was Conducted	Analysis selected	Studies included
Communicable, maternal, neonatal, and nutritional diseases						
Tuberculosis	2	Simou et al., 2018 (52)	Incidence	January 2005 to April 2018	Meta-analysis - continuous RR	2 case-control, 1 cohort study
Pneumonia	2	Simou et al., 2018 (53)	Incidence	December 1985 to December 2017	Meta-analysis - continuous RR	4 case-control, 1 cohort study
Non-communicable diseases						
Neoplasms						
Oral cavity and Pharyngeal cancer (excluding nasopharynx)	6	WCRFI, 2018 (54)	Incidence and mortality	January 1, 2006 to March 1, 2015	Oral cavity: Meta-analysis - continuous RR	5 cohort studies
					Pharyngeal cancer (excluding nasopharynx): Meta-analysis by sex - continuous RR	4 cohort studies for males / 5 cohort studies for females
Laryngeal cancer	4	WCRFI, 2018 (54)	Incidence and mortality	January 1, 2006, to April 30 2015	Meta-analysis by sex - continuous RR	4 cohort studies for males / 5 cohort studies for females
Esophageal cancer	8	WCRFI, 2018 (55)	Incidence and mortality	January 1, 2006 to February 28,2013	Meta-analysis by sex - continuous RR	11 cohort studies for males / 4 cohort studies for females
Colon and rectum cancer	6	Jun et al., 2023 (56)	Incident and mortality	up to July 2021	Meta-analysis by sex - categorical RR	22 cohort studies for males / 15 cohort studies for females
Liver cancer	5	WCRFI, 2015 (57)	Incidence and mortality	January 1, 2006 to March 31, 2013	Meta-analysis by sex - continuous RR	8 cohort studies for males / 4 cohort studies for females
Female breast cancer	6	Sohi et al., 2024 (46)	Incidence	Up to November 15, 2023	Meta-analysis, premenopausal breast cancer - continuous RR	11 cohort studies
					Meta-analysis, postmenopausal breast cancer - continuous RR	8 cohort studies
Cardiovascular diseases						
Ischemic heart disease	4	Zhao et al., 2017 (58)	Mortality	Up to June 30, 2016	Studies in which heart disease at baseline was controlled for, meta-regression adjusting for if the abstainer biases, sex of study population, alcohol measure accuracy, country, and whether studies controlled for social and smoking status - categorical RR	18 cohort studies
Ischemic stroke	4	Larsson et al., 2016 (59)	Incidence	January 1966 to September 1, 2016	Meta-analysis - categorical RR	25 cohort studies
Intracerebral hemorrhage and subarachnoid hemorrhage	4	Zhang et al., 2014 (60)	Incidence and mortality	Up to July 2013	Meta-analysis - categorical RR	11 cohort studies
Hypertensive heart disease	4	Cecchini et al., 2024 (61)	Incidence	Up to February 20, 2024	Meta-analysis by sex - continuous RR	18 cohort studies for males / 12 cohort studies for females
Atrial fibrillation and flutter	6	Jiang et al., 2022 (62)	Incidence	Up to June 2022	Meta-analysis by sex- continuous RR	7 cohort studies for males / 8 cohort studies for females
Digestive diseases						

Disease	Systematic reviews found	Study selected	Outcome definition	Dates search was Conducted	Analysis selected	Studies included
Cirrhosis and other chronic liver diseases	4	Llamosas-Falcon et al., 2022 (49)	Incident and mortality (RR selected was for mortality only)	Up to January 14, 2022	Meta-regression (adjusting for sex, cause of liver cirrhosis, quality score) - continuous RR	9 cohort studies for males / 4 cohort studies for females
Pancreatitis	1	Samokhvalov et al., 2015 (63)	Incidence	January 2009 to May 2015	Meta-analysis- continuous RR	5 case-control studies, 2 cohort studies
Diabetes mellitus	2	Llamosas-Falcón et al., 2023 (64)	Incident and mortality	Up to July 6, 2022	Meta-regression (adjusting for age, sex, Newcastle-Ottawa Scale score and country of residency) - continuous RR	40 cohort studies for males / 29 cohort studies for females
Epilepsy	2	Woo et al., 2022 (65)	Incidence	Up to January 25, 2021	Meta-analysis- continuous RR	6 case-control, 2 cohort studies

The health impact of consuming an average of 1, 2 and 3 standard drinks per day

This section addresses the question, "*What is the association between chronic alcohol use and the development of health conditions?*" To address this question, this section summarizes associations between alcohol consumption and 22 (males) to 23 (females) health conditions and injuries. It reports risks associated with consuming an average of 1, 2, or 3 alcoholic drinks per day. Results are provided separately for males and females; results for both males and females (combined) are available in the appendix.

The health impact of consuming an average of 1, 2 and 3 standard drinks per day for males[4]

At 1 standard drink per day (14g/day) among males, we observed the highest RRs for esophageal cancer (RR = 1.51 (95% CI: 1.32, 1.71)) and liver cirrhosis (RR = 1.37 (95% CI: 1.18, 1.62)). Risks for injuries, such as unintentional injuries (1.29 (95% CI: 1.04, 1.74)) and road injuries (RR = 1.20 (95% CI: 1.17, 1.25)), were also significantly increased, as was the risk for oral cancer (RR = 1.22 (95% CI: 1.13, 1.32)). In contrast, alcohol was associated with lowered risk for ischemic stroke (RR = 0.92 (95% CI: 0.87, 0.97)) at 1 standard drink per day. There was no difference in risk for ischemic heart disease (RR = 0.87 (95% CI: 0.71, 1.06) or hemorrhagic stroke (RR = 0.96 (95% CI: 0.74, 1.24)) at 1 standard drink per day (see Figures 3 to 6).

At 2 standard drinks per day (28g/day), liver cirrhosis showed a 53% increase relative to the risk seen for 1 standard drink per day, rising to an RR of 2.10 (95% CI: 1.68, 2.65). Similarly, the risk for esophageal cancer increased by 51% (RR = 2.27 (95% CI: 1.75, 2.94)). Risks for injuries also escalated at 2 versus 1 standard drink per day, with RRs for unintentional injuries rising from 1.29 (95% CI: 1.04, 1.74) to 1.68

[4] Confidence intervals for RRs were constructed using a set of 1000 simulations.

(95% CI: 1.08, 3.04), and for road injuries increasing from 1.20 (95% CI: 1.17, 1.25) to 1.43 (95% CI: 1.36, 1.56). At 2 standard drinks per day, alcohol consumption increased the risk for ischemic stroke (RR = 1.08 (95% CI: 1.01, 1.15)). There was no difference in risk for ischemic heart disease (RR = 0.92 (95% CI: 0.75, 1.14)) or hemorrhagic stroke (RR = 1.21 (95% CI: 0.85, 1.73)).

At 3 standard drinks per day (42g/day), risk estimates became more pronounced, with esophageal cancer (RR = 3.42 (95% CI: 2.31, 5.04)) and liver cirrhosis (RR = 3.58 (95% CI: 2.90, 4.48)), compared to people who abstain from alcohol. Unintentional injuries increased nearly 68% relative to the increased risk for 1 drink per day, with an RR of 2.17 (95% CI: 1.12, 5.29). Consuming 3 standard drinks per day showed no difference in risk for ischemic heart disease (RR = 0.92 (95% CI: 0.75, 1.14)) or hemorrhagic stroke (RR = 1.29 (95% CI: 0.98, 1.71)). There was a significant increase in risk for ischemic stroke (RR = 1.08 (95% CI: 1.01, 1.15)).

The health impact of consuming an average of 1, 2 and 3 standard drinks per day for females

Among females, compared to alcohol abstention, consuming 1 standard drink per day (14g/day) resulted in an observed highest increase in RRs for liver cirrhosis (RR = 2.33 (95% CI: 1.74, 3.17)), esophageal cancer (RR = 1.37 (95% CI: 1.20, 1.55)), and liver cancer (RR = 1.28 (95% CI: 1.06, 1.52)); there was no difference in risk for pharyngeal cancer (RR=1.37 (95% CI: 0.99, 1.90)). Risks for injuries, such as unintentional injuries (RR = 1.29 (95% CI: 1.04, 1.74)) and road injuries (RR = 1.20 (95% CI: 1.16, 1.28)), were also elevated, alongside oral cancer (RR = 1.22 (95% CI: 1.13, 1.32)). In contrast, diabetes mellitus (RR = 0.70 (95% CI: 0.65, 0.75)) and ischemic stroke (RR = 0.92 (95% CI: 0.87, 0.97)) showed lowered risk. There was no difference in risk for ischemic heart disease (RR = 0.87 (95% CI: 0.71, 1.06)) or hemorrhagic stroke (RR = 0.96 (95% CI: 0.74, 1.24)) at 1 standard drink per day.

At 2 standard drinks per day (28g/day), risks increased substantially for multiple outcomes. Liver cirrhosis showed a 31% increase relative to the risk observed for1 standard drink per day, rising to an RR of 5.38 (95% CI: 3.81, 7.73). Risks for injuries were also higher for 2 standard drinks per day than were observed for 1 standard drink per day, with RRs for unintentional injuries rising from 1.29 (95% CI: 1.04, 1.74) to 1.68 (95% CI: 1.08, 3.04) and for road injuries increasing from 1.20 (95% CI: 1.16, 1.28) to 1.45 (95% CI: 1.34, 1.63). At 2 drinks per day, lowered risk was seen for diabetes (RR = 0.74 (95% CI: 0.67, 0.81)). At 2 drinks per day, there was a significant increase in risk for ischemic stroke (RR = 1.08 (95% CI: 1.01, 1.15)). There was no difference in risk for pharyngeal cancer (RR = 1.87 (95% CI: 0.97, 3.60)), ischemic heart disease (RR = 0.92 (95% CI: 0.75, 1.14)), or hemorrhagic stroke (RR = 1.21 (95% CI: 0.85, 1.73)).

At 3 standard drinks per day (42g/day), risk estimates became more pronounced, with liver cirrhosis (RR = 10.67 (95% CI: 7.78, 14.63)) showing sharp increases compared to the risk observed at 1 standard drink per day. The RR for unintentional injuries at 3 standard drinks per day increased 68% when compared to the risk at 1 standard drink per day, with an RR of 2.17 (95% CI: 1.12, 5.29). At 3 drinks per day, lowered risk was seen for diabetes (RR = 0.79 (95% CI: 0.69, 0.90)) when compared to the risk for abstainers; there was no difference in risk for ischemic heart disease (RR = 0.92 (95% CI: 0.75, 1.14)). Alcohol's impact on all other assessed conditions was associated with increased risk.

The health impact of consuming an average 1, 2 and 3 standard drinks per week

To assess the risk associated with lower levels of regular alcohol consumption and the development of health conditions, this section summarizes associations between consuming an average of 1, 2, or 3 alcoholic drinks per week and the same health conditions and injuries included in the previous section. Results are provided separately for males and females, and results for both males and females (combined) are available in the appendix.

The health impact of consuming an average 1, 2 and 3 standard drinks per week for males

For males, compared to abstention, consumption of 1-3 standard drinks per week is predominantly associated with increased risk for most health conditions, with risk increasing at higher levels of consumption.

At 1 standard drink per week (2g/day), alcohol consumption was associated with lowered risk for one condition and increased risk for 18 conditions compared to abstention. We observed lower risk for ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)). There was no difference in risk for diabetes mellitus at this level of consumption relative to abstention (RR = 1.00 (95% CI: 1.00, 1.00)). Among the disease conditions for which 1 standard drink per week resulted in increased risk, the highest RRs were observed for colorectal cancer (RR = 1.16 (95% CI: 1.04, 1.28)), esophageal cancer (RR = 1.06 (95% CI: 1.04, 1.08)), and liver cirrhosis (RR = 1.04 (95% CI: 1.02, 1.07)). Risks for injuries, such as unintentional injuries (RR = 1.04 (95% CI: 1.01, 1.08)) and road injuries (RR = 1.03 (95% CI: 1.02, 1.03)), were also elevated. Conversely, conditions such as liver cancer (RR = 1.01 (95% CI: 1.00, 1.01)), pancreatitis (RR = 1.01 (95% CI: 1.00, 1.02)), and pneumonia (RR = 1.01 (95% CI: 1.01, 1.01)) showed minimal risk increases at 1 standard drink per week.

At 2 standard drinks per week (4g/day), the lowered risk for ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)) remained unchanged from 1 standard drink per week (due to the use of categorical risk functions for these conditions). Risks for conditions for which there was an increased risk at lower levels of consumption (i.e., 1 standard drink per week) all increased slightly, except for colorectal cancer which remained unchanged (RR = 1.16 (95% CI: 1.04, 1.28)) (due to the use of categorical risk functions for this condition). We observed more pronounced increases in risk for esophageal cancer (RR = 1.12 (95% CI: 1.08, 1.17)), liver cirrhosis (RR = 1.09 (95% CI: 1.04, 1.15)), unintentional injuries (RR = 1.08 (95% CI: 1.01, 1.17)) and road injuries (RR = 1.05 (95% CI: 1.05, 1.07)). Diabetes mellitus (RR = 1.00 (95% CI: 1.00, 1.01)) showed no risk effect, while liver cancer (RR = 1.01 (95% CI: 1.00, 1.02)), pancreatitis (RR = 1.02 (95% CI: 1.00, 1.04)) and pneumonia (RR = 1.02 (95% CI: 1.02, 1.02)) continued to exhibit relatively lower risks.

At 3 standard drinks per week (6g/day), the lowered risk for ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)) remained present. The highest risks continued to be observed for esophageal cancer (RR = 1.19 (95% CI: 1.13, 1.26)), liver cirrhosis (RR = 1.14 (95% CI: 1.06, 1.23)), unintentional injuries (RR = 1.12 (95% CI: 1.02, 1.27)) and road injuries (RR = 1.08 (95% CI: 1.07, 1.10)). Diabetes mellitus (RR = 1.01 (95% CI: 1.00, 1.01)), liver cancer (RR = 1.02 (95% CI: 1.01, 1.03)), and pneumonia (RR = 1.03 (95% CI: 1.02, 1.04)) continued to show comparatively lower risks.

The health impact of consuming an average 1, 2 and 3 standard drinks per week for females

For females, compared to abstention consuming alcohol consumption at 1 to 3 standard drinks per week is predominately associated with increased risk for the assessed health conditions, with risk increasing at higher levels of consumption.

At 1 standard drink per week (2 g/day), alcohol lowered the risk for two conditions and raised it for 19 conditions. Reduced risk was present for diabetes mellitus (RR = 0.93 (95% CI: 0.91, 0.94)) and ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)). There was no significant association with colorectal cancer (RR = 1.00 (95% CI: 0.97, 1.04)), atrial fibrillation and flutter (RR = 1.01 (95% CI: 0.99, 1.02)), hypertension (RR = 1.00 (95% CI: 0.97, 1.03), ischemic heart disease (RR = 0.87 (95% CI: 0.71, 1.06)) or hemorrhagic stroke (RR = 0.96 (95% CI: 0.74, 1.24)) at this level of consumption relative to lifetime abstention. Among the disease conditions with greater risk at 1 standard drink per day, the highest RRs were observed for liver cirrhosis (RR = 1.13 (95% CI: 1.07, 1.19)), pharyngeal cancer (RR = 1.05 (95% CI: 1.00, 1.10)), esophageal cancer (RR = 1.05 (95% CI: 1.03, 1.06)), laryngeal cancer (RR = 1.04 (95% CI: 1.01, 1.08)) and unintentional injuries (RR = 1.04 (95% CI: 1.01, 1.08)). Conversely, conditions such as

premenopausal female breast cancer (RR = 1.01 (95% CI: 1.00, 1.01)), pancreatitis (RR = 1.01 (95% CI: 1.00, 1.02)), and pneumonia (RR = 1.01 (95% CI: 1.01, 1.01)) showed relatively smaller increased risks compared to other conditions.

At 2 standard drinks per week (4 g/day), the lowered risk for diabetes mellitus (RR = 0.86 (95% CI: 0.82, 0.89)) was more pronounced, and those for ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)); ischemic heart disease (RR = 0.87 (95% CI: 0.71, 1.06)) and hemorrhagic stroke (RR = 0.96 (95% CI: 0.74, 1.24)) remained unchanged (due to the use of categorical risk functions for these conditions). The risk for all conditions for which there was increased risk at 1 standard drink per week all increased slightly, except for liver cirrhosis which demonstrated a more substantial increase from an RR of 1.13 (95% CI: 1.07, 1.19) to 1.27 (95% CI: 1.15, 1.41). Premenopausal female breast cancer (RR = 1.02 (95% CI: 1.00, 1.03)), pancreatitis (RR = 1.02 (95% CI: 1.00, 1.04)), and pneumonia (RR = 1.02 (95% CI: 1.02, 1.02)), continued to exhibit relatively smaller risks compared to other conditions. The association with atrial fibrillation and flutter (RR = 1.02 (95% CI: 0.99, 1.04)) and hypertension (RR = 1.00 (95% CI: 0.93, 1.09) remained non-significant.

At 3 standard drinks per week (6 g/day), the lowered risks for diabetes mellitus (RR = 0.80 (95% CI: 0.75, 0.84)) and ischemic stroke (RR = 0.90 (95% CI: 0.85, 0.95)) became more pronounced, while those for ischemic heart disease (RR = 0.87 (95% CI: 0.71, 1.06)) and hemorrhagic stroke (RR = 0.96 (95% CI: 0.74, 1.24)) remained relatively stable. The risk for all conditions for which there was an increased risk at 1 standard drink of alcohol per week continued to increase slightly as consumption increased. The only exception was liver cirrhosis, which increased more substantially from a RR of 1.27 (95% CI: 1.15, 1.41) to 1.43 (95% CI: 1.24, 1.67). Premenopausal female breast cancer (RR = 1.02 (95% CI: 1.01, 1.04)), and pneumonia (RR = 1.03 (95% CI: 1.02, 1.04)), remained relatively stable, with pancreatitis (RR = 1.03 (95% CI: 1.02, 1.04)) showing a slightly more pronounced increase in risk when compared to the risk observed at lower levels of drinking per week. There was no difference in risk for atrial fibrillation and flutter (RR = 1.02 (95% CI: 0.98, 1.07)) or hypertension (RR = 1.01 (95% CI: 0.91, 1.11)).

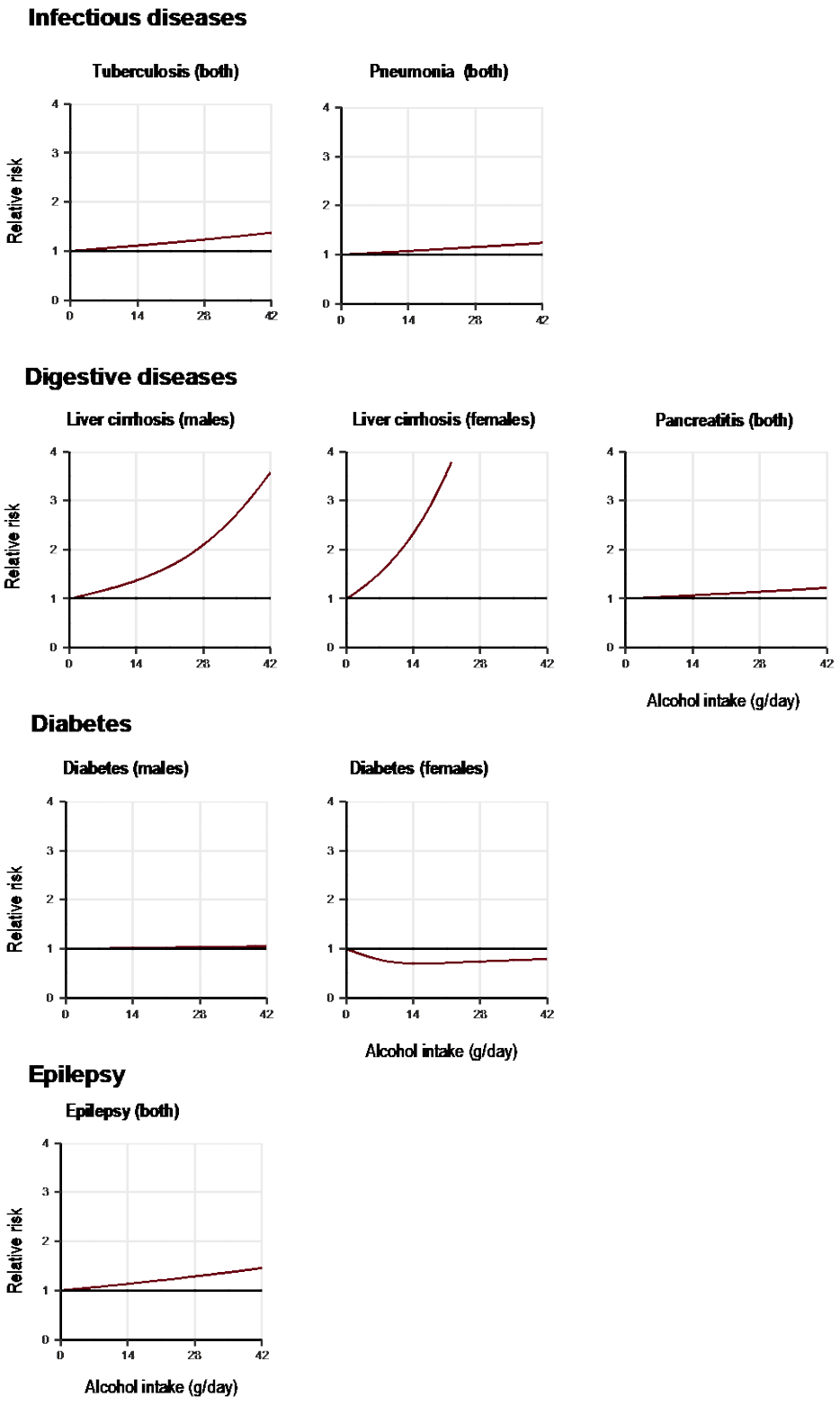

Figure 3. Relative risk functions for alcohol intake and infectious diseases, digestive diseases, diabetes and epilepsy

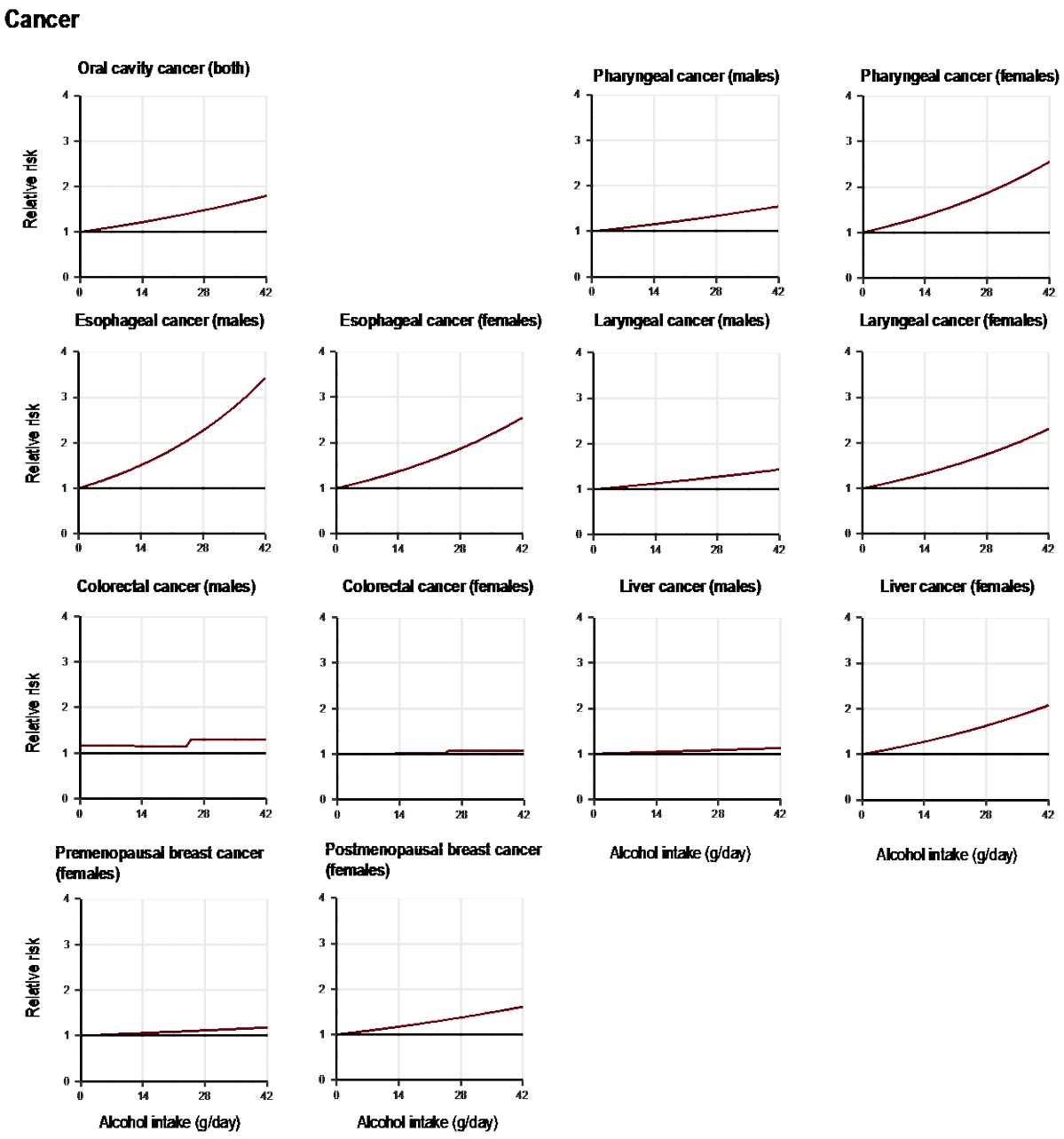

Figure 4. Relative risk functions for alcohol intake and cancer

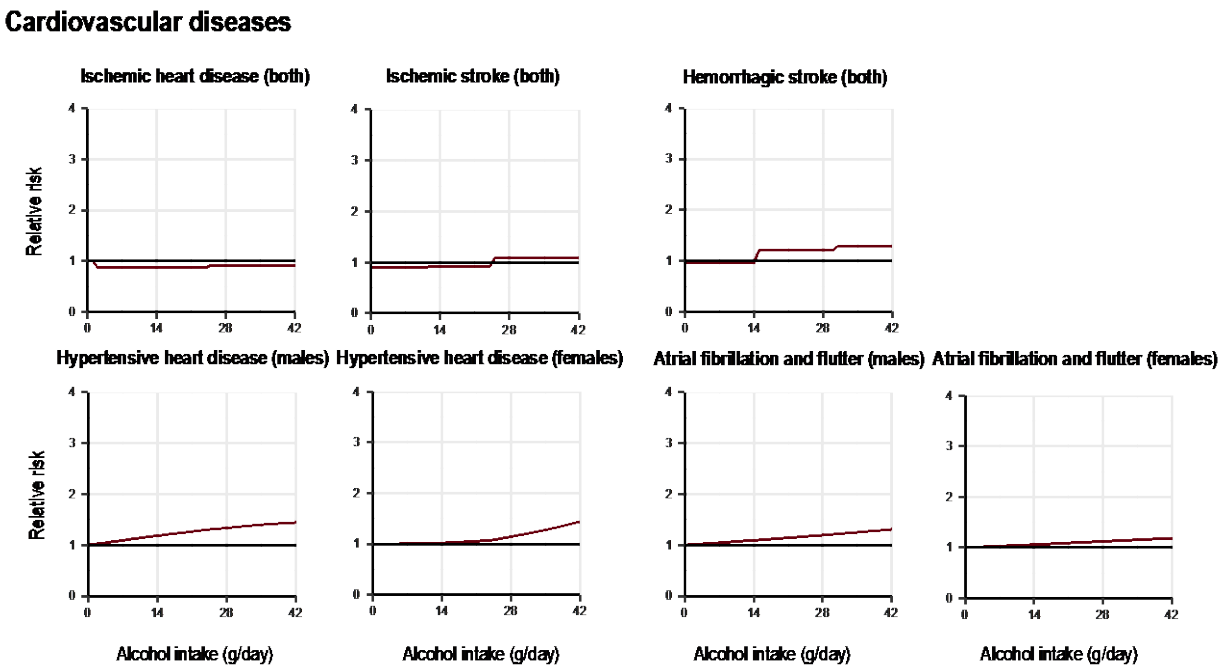

Figure 5. Relative risk functions for alcohol intake and cardiovascular disease

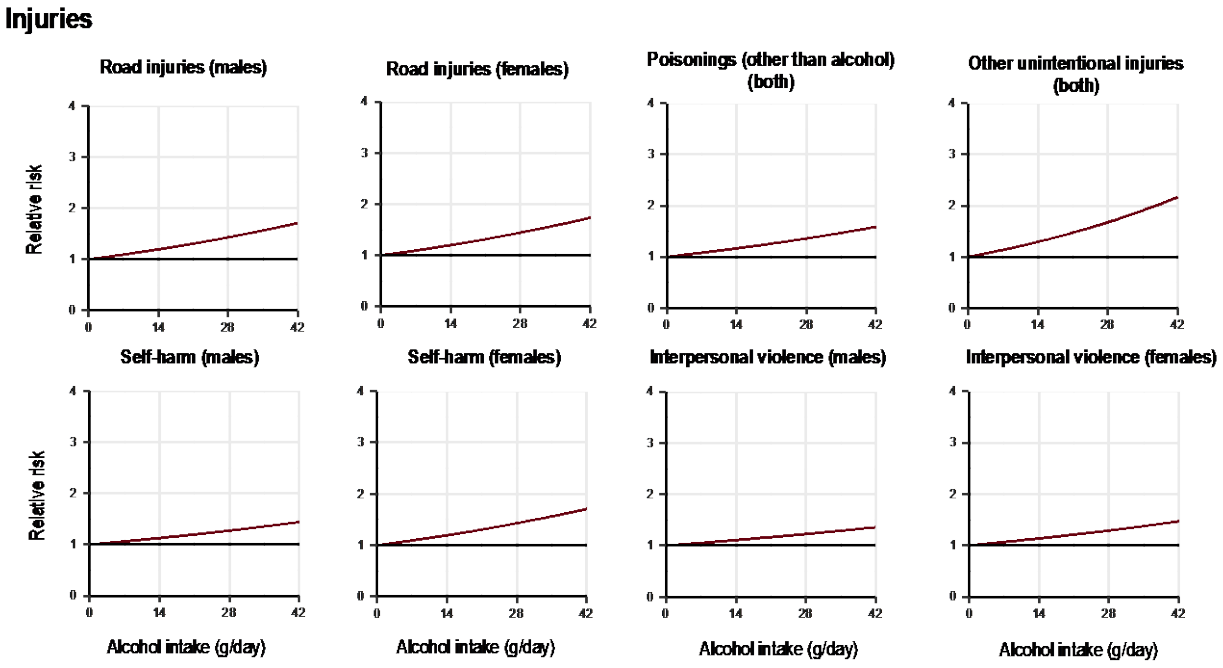

Figure 6. Relative risk functions for alcohol intake and injury

Associations between average alcohol consumption and indicators of morbidity and mortality

This section answers the question, "*What is the lifetime risk of alcohol-attributable morbidity and mortality by alcohol intake?*" Specifically, this section reports findings related to the associations between average daily and weekly alcohol consumption levels and the risk of alcohol-attributable cancer, death, and premature (age < 70 years) death over the lifetime.

Lifetime risk of an alcohol-attributable death at different levels of average alcohol consumption

Among males, a 1 in 1000 risk of a lifetime alcohol-attributable death occurred among those who drank more than 6.5 standard drinks per week (95% CI: <1, 13.5 drinks per week). This lifetime risk rose to 1 in 100 people above 8.5 drinks per week (95% CI: 1, 14 drinks per week) (see Figure 7). Among females, a lifetime risk of an alcohol-attributable death of 1 per 1000 people occurred when consuming more than 7 standard drinks per week (95% CI: <1 to 11.5 drinks per week). The 1 in 100 risk threshold for females was the same as for males: above 8.5 drinks per week (95% CI: 2.5 to 13 drinks per week). The lifetime risk of an alcohol-attributable death at different levels of average alcohol consumption by cause is displayed in Figure 8.

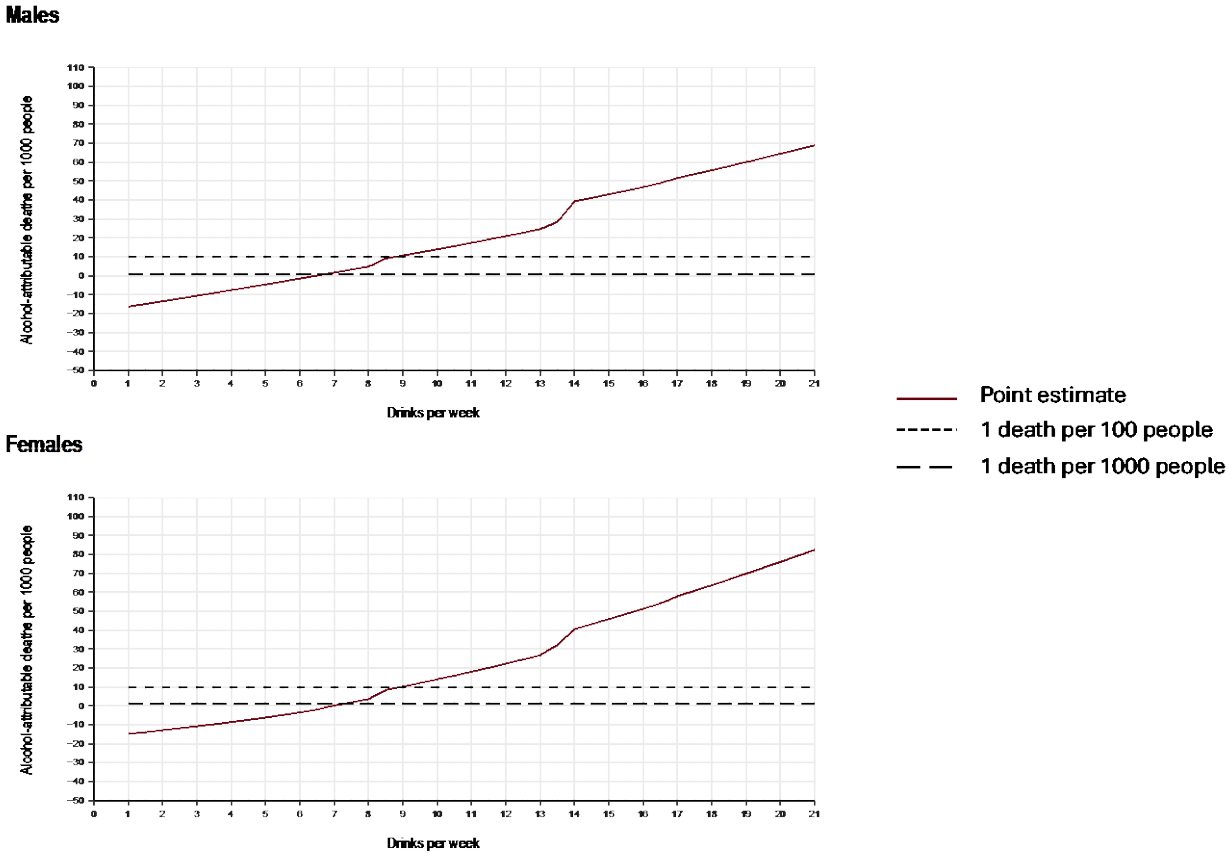

Figure 6. Lifetime risk of an alcohol-attributable death among males and females for differing levels of alcohol consumption

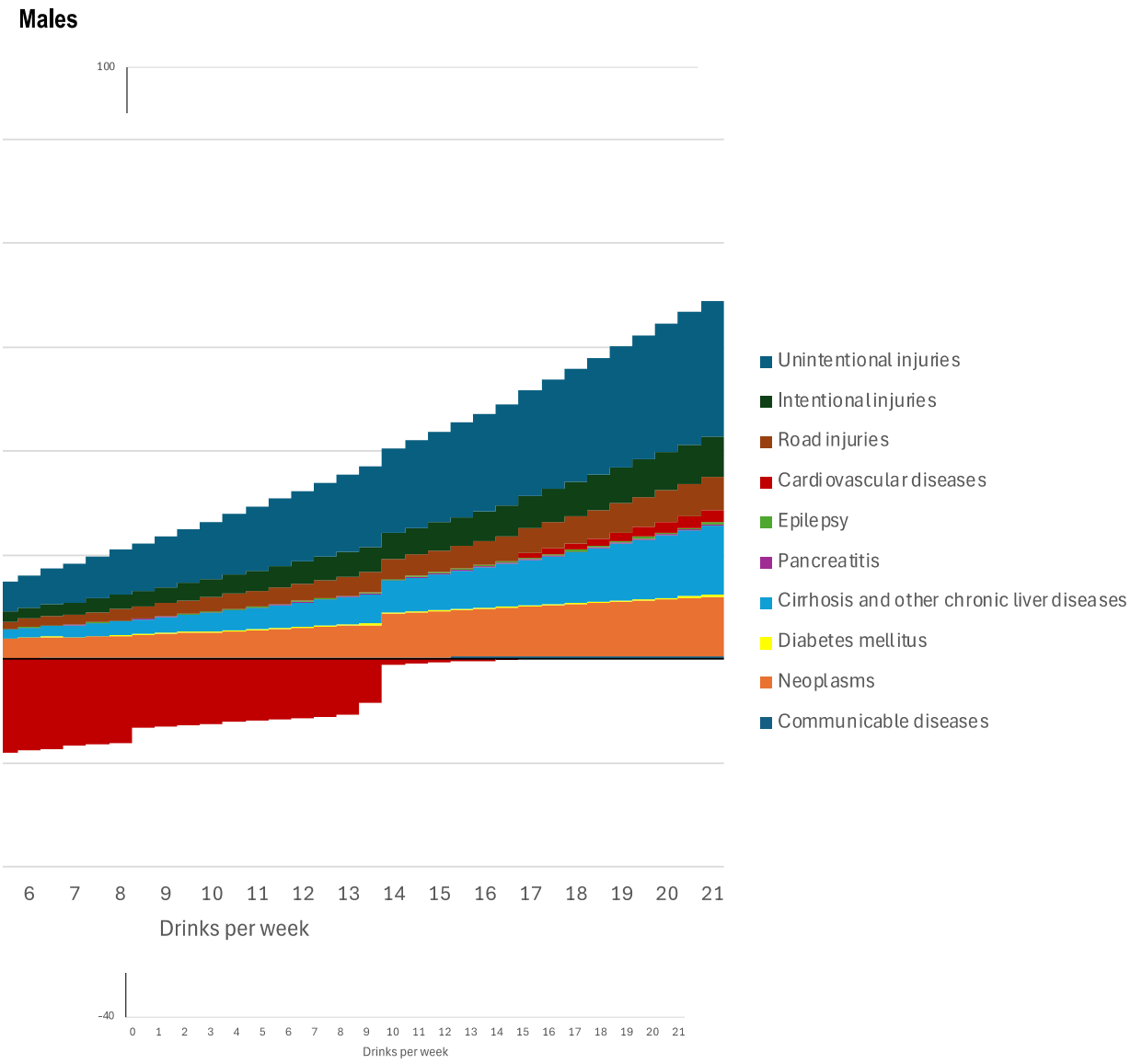

Figure 7. Lifetime risk of an alcohol-attributable death among males and females by cause for differing levels of alcohol consumption

Lifetime risk of an alcohol-attributable death by age

Table 3 outlines the lifetime risk of an alcohol-attributable death at different levels of average alcohol consumption, stratified by age of death. Overall, for males and females, the increase in risk of mortality due to alcohol occurred at younger ages, while the lowered risk of mortality due to alcohol occurred at older ages. Furthermore, even at low levels of consumption (i.e., 1 drink per week), alcohol had a significant negative impact on the health of individuals 15 to 39 years of age. Based on the analysis of age specific risks of an alcohol-attributable death, at no age was there a significant net benefit of alcohol consumption on all-cause mortality.

Table 3. Lifetime risk of an alcohol-attributable death for differing levels of alcohol consumption, stratified for age of death

Sex	Age (years)	Drinks per week					
		1	2	3	7	14	21
Males	15 to 19	0.05 (0.04, 0.06)	0.10 (0.09, 0.13)	0.16 (0.13, 0.19)	0.38 (0.32, 0.47)	0.82 (0.68, 1.04)	1.33 (1.08, 1.71)
	20 to 24	0.08 (0.06, 0.10)	0.17 (0.13, 0.21)	0.25 (0.20, 0.32)	0.62 (0.50, 0.79)	1.35 (1.07, 1.75)	2.18 (1.71, 2.88)
	25 to 29	0.10 (0.06, 0.13)	0.21 (0.15, 0.28)	0.32 (0.24, 0.42)	0.80 (0.61, 1.05)	1.75 (1.34, 2.34)	2.84 (2.15, 3.87)
	30 to 39	0.17 (0.00, 0.34)	0.44 (0.23, 0.65)	0.70 (0.44, 1.00)	1.83 (1.30, 2.50)	4.18 (3.10, 5.78)	6.88 (5.09, 9.65)
	40 to 49	-0.10 (-0.77, 0.56)	0.19 (-0.49, 0.84)	0.48 (-0.22, 1.18)	1.71 (0.86, 2.62)	4.61 (3.27, 6.30)	7.75 (5.81, 10.58)
	50 to 59	-0.82 (-2.82, 1.10)	-0.47 (-2.47, 1.42)	-0.12 (-2.13, 1.79)	1.36 (-0.71, 3.31)	5.46 (3.14, 8.14)	9.52 (6.75, 12.94)
	60 to 69	-2.13 (-6.37, 1.86)	-1.72 (-5.95, 2.23)	-1.30 (-5.57, 2.61)	0.46 (-3.83, 4.46)	6.12 (1.87, 10.85)	11.12 (6.55, 16.37)
	70 plus	-13.66 (-36.71, 7.46)	-12.37 (-35.56, 8.44)	-11.06 (-34.26, 9.41)	-5.47 (-28.59, 14.57)	15.04 (-6.71, 35.66)	27.30 (5.58, 48.33)
	Total	-16.30 (-46.57, 11.41)	-13.46 (-43.99, 13.80)	-10.56 (-40.92, 16.42)	1.70 (-28.77, 29.08)	39.34 (9.65, 69.62)	68.92 (37.51, 101.23)
Females	15 to 19	0.02 (0.02, 0.03)	0.04 (0.03, 0.06)	0.06 (0.05, 0.09)	0.16 (0.13, 0.21)	0.35 (0.27, 0.48)	0.58 (0.44, 0.81)
	20 to 24	0.03 (0.02, 0.04)	0.06 (0.05, 0.08)	0.09 (0.07, 0.13)	0.24 (0.18, 0.32)	0.53 (0.40, 0.72)	0.87 (0.65, 1.22)
	25 to 29	0.03 (0.02, 0.05)	0.08 (0.05, 0.11)	0.12 (0.09, 0.16)	0.31 (0.23, 0.42)	0.71 (0.54, 0.99)	1.21 (0.91, 1.72)
	30 to 39	0.07 (0.00, 0.14)	0.18 (0.10, 0.28)	0.30 (0.19, 0.44)	0.85 (0.61, 1.18)	2.17 (1.65, 2.98)	3.91 (3.01, 5.42)
	40 to 49	-0.05 (-0.29, 0.21)	0.09 (-0.16, 0.38)	0.25 (-0.02, 0.56)	0.99 (0.58, 1.52)	3.08 (2.36, 4.17)	5.87 (4.66, 7.93)
	50 to 59	-0.34 (-1.02, 0.41)	-0.12 (-0.80, 0.66)	0.12 (-0.58, 0.93)	1.32 (0.46, 2.39)	5.02 (3.78, 6.77)	9.92 (7.96, 12.76)
	60 to 69	-1.08 (-2.70, 0.69)	-0.80 (-2.43, 1.00)	-0.49 (-2.09, 1.31)	1.16 (-0.57, 3.25)	6.72 (4.48, 9.55)	13.79 (10.87, 17.66)
	70 plus	-13.48 (-30.26, 4.23)	-12.47 (-29.19, 5.30)	-11.34 (-28.08, 6.52)	-4.87 (-22.22, 13.88)	21.95 (3.61, 40.93)	46.28 (25.55, 65.84)
	Total	-14.79 (-34.02, 5.57)	-12.93 (-32.42, 8.00)	-10.88 (-30.25, 10.57)	0.15 (-19.37, 21.90)	40.53 (18.49, 63.28)	82.43 (57.78, 108.45)

Risk of an alcohol-attributable death for people 15 to 20 year of age

For individuals who start consuming alcohol at age 15, the risk of an alcohol-attributable death between the ages of 15 and 20 varies by consumption level, as outlined by cause in Table 4. The risk of an alcohol-attributable death increases linearly with alcohol consumption. For males, the risk of an alcohol-attributable death ranges from 0.07 (95% CI: 0.05, 0.08) per 1000 for those who consume 1 drink per week, to 1.76 (95% CI: 1.42, 2.28) per 1000 for those who consume 3 drinks per day (i.e., 21 drinks per week). Similarly, for females, the risk increases from 0.03 (95% CI: 0.02, 0.04) per 1000 for those who consume 1 drink per week, to 0.75 (95% CI: 0.57, 1.06) per 1000 for those who consume 3 drinks per day (i.e., 21 drinks per week). Most of these alcohol-attributable deaths are caused by road traffic crashes, unintentional injuries, and intentional injuries. These deaths represent a substantial proportion of all deaths for individuals 15 to 20 years of age. For males, alcohol-attributable deaths account for 1.3% (95% CI: 1.1%, 1.7%) of all deaths for those consuming 1 drink per week, and 26.5% (95% CI: 21.3%, 34.3%) for those consuming 21 drinks per week. For females, the proportions are 1.3% (95% CI: 1.0%, 1.7%) for those consuming 1 drink per week, and 26.9% (95% CI: 20.5%, 37.9%) for those consuming 21 drinks per week (see Figure 9).

Table 4. Risk of an alcohol-attributable death for differing levels of alcohol consumption stratified by cause for underage drinks (i.e., people 15 to 20 years of age)

Sex	Cause	Drinks per week					
		1	2	3	7	14	21
Male	Communicable diseases	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Neoplasms	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Diabetes mellitus	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Cirrhosis and other chronic liver diseases	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.01 (0.01, 0.01)
	Pancreatitis	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Epilepsy	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.01)	0.01 (0.01, 0.01)	0.02 (0.01, 0.02)
	Cardiovascular diseases	0.00 (-0.01, 0.00)	0.00 (-0.01, 0.00)	0.00 (-0.01, 0.00)	0.00 (-0.01, 0.00)	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)
	Road injuries	0.02 (0.02, 0.03)	0.04 (0.04, 0.05)	0.06 (0.05, 0.08)	0.15 (0.13, 0.19)	0.33 (0.28, 0.43)	0.55 (0.46, 0.72)
	Unintentional injuries	0.02 (0.01, 0.02)	0.03 (0.02, 0.05)	0.05 (0.02, 0.07)	0.12 (0.06, 0.17)	0.27 (0.12, 0.39)	0.44 (0.19, 0.67)
	Intentional injuries	0.03 (0.03, 0.04)	0.06 (0.05, 0.08)	0.09 (0.08, 0.12)	0.22 (0.19, 0.28)	0.47 (0.40, 0.61)	0.75 (0.62, 0.97)
	Total	0.07 (0.05, 0.08)	0.14 (0.11, 0.17)	0.21 (0.17, 0.26)	0.51 (0.42, 0.63)	1.09 (0.89, 1.39)	1.76 (1.42, 2.28)
Female	Communicable diseases	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Neoplasms	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Diabetes mellitus	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Cirrhosis and other chronic liver diseases	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.01 (0.00, 0.01)	0.01 (0.01, 0.02)
	Pancreatitis	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
	Epilepsy	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.01 (0.00, 0.01)	0.01 (0.01, 0.02)
	Cardiovascular diseases	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)
	Road injuries	0.01 (0.01, 0.01)	0.02 (0.02, 0.03)	0.03 (0.02, 0.04)	0.08 (0.06, 0.10)	0.17 (0.13, 0.24)	0.27 (0.21, 0.40)
	Unintentional injuries	0.01 (0.00, 0.01)	0.01 (0.01, 0.02)	0.02 (0.01, 0.03)	0.05 (0.03, 0.07)	0.11 (0.05, 0.17)	0.18 (0.08, 0.29)
	Intentional injuries	0.01 (0.01, 0.01)	0.02 (0.02, 0.03)	0.03 (0.03, 0.04)	0.08 (0.06, 0.10)	0.17 (0.13, 0.23)	0.27 (0.20, 0.39)
	Total	0.03 (0.02, 0.04)	0.05 (0.04, 0.07)	0.08 (0.07, 0.11)	0.21 (0.16, 0.28)	0.46 (0.35, 0.63)	0.75 (0.57, 1.06)

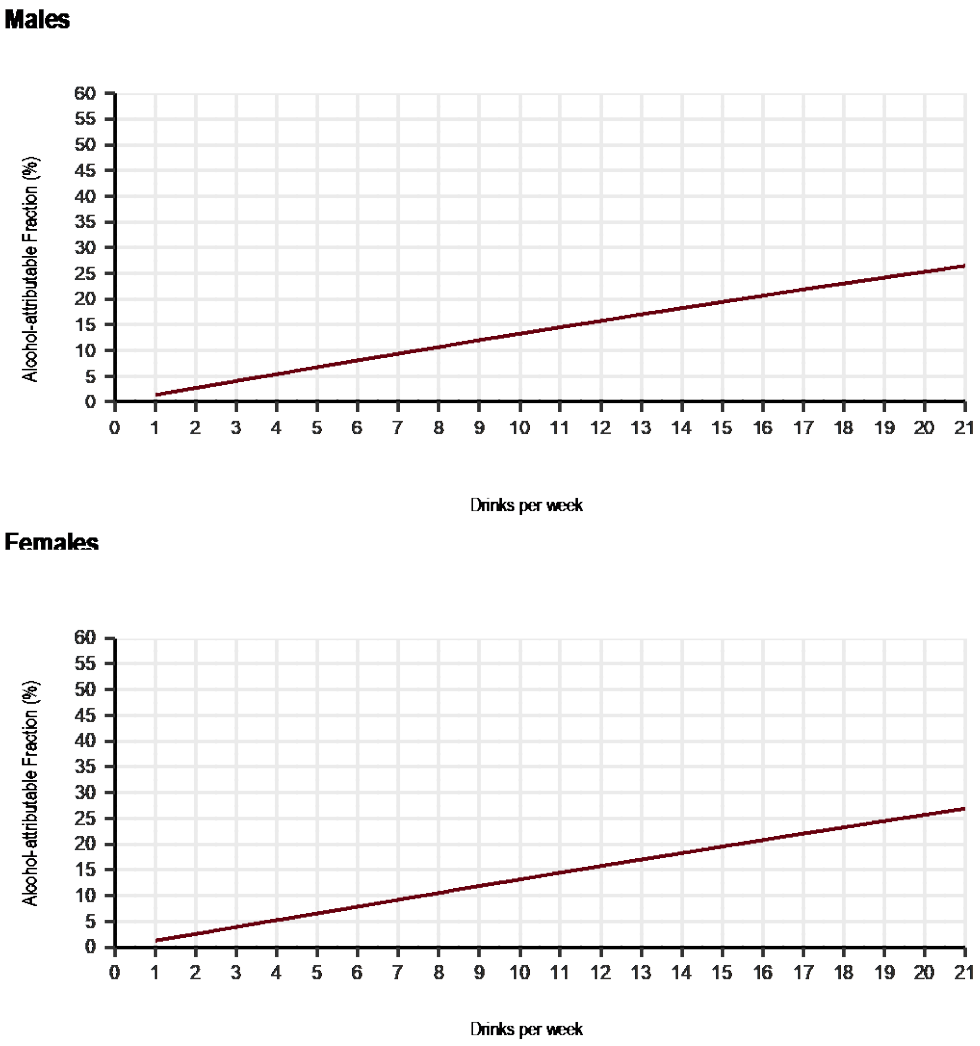

Figure 8. Alcohol-attributable fractions among males and females 15 to 20 years of age by level of alcohol consumption

Risk of premature (age <70 years) alcohol-attributable death at different levels of average alcohol consumption

Among males, the risk of an alcohol-attributable premature death of 1 in 1000 occurred above a consumption level of 3 standard drinks per week (95% CI: <1 to 7.5 drinks per week), while the risk of an alcohol-attributable premature death of 1 in 100 occurred above 8 drinks per week (1 drink per day; 95% CI: 4.5 to 12.5 drinks per week). Among females, the risk of a lifetime alcohol-attributable premature death at or above 1 in 1000 occurred at a consumption level above 3.5 standard drinks per week (95% CI: <1 to 6 drinks per week), while the risk of an alcohol-attributable premature death of 1 in 100 occurred above 9.5 drinks per week (95% CI: 7.5 to 12.0 drinks per week) (see Figure 10).

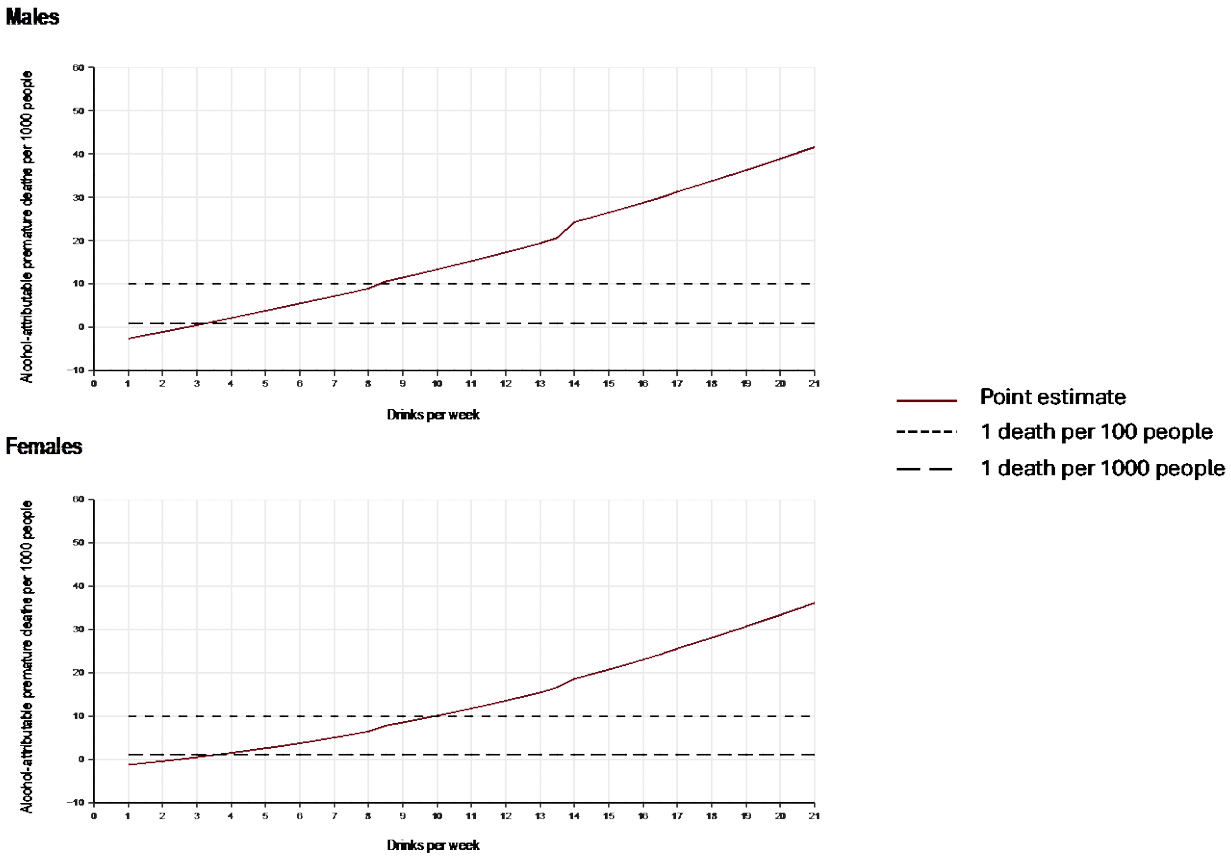

Figure 9. Risk of a premature alcohol-attributable death among males and females for differing levels of alcohol consumption

Years of potential life lost and disability adjusted years of life lost at different levels of average alcohol consumption

Among males and females who drink alcohol, the lowest risk of an alcohol-attributable premature death, death, YPLL, and DALYs lost occurred among people who consumed 1 drink per week, with the risk of an alcohol-attributable premature death, death, YPLL, and DALYs lost increasing as amounts of alcohol consumed increased.

Based on combining data from lifetables and all-cause mortality data from vital statistics, we estimate that on average 15 years of life are lost per death in the United States. Among males, the risk of 15 alcohol-attributable YLL per 1000 people occurred at a consumption level above 3 standard drinks per week (95% CI: <1 to 8 drinks per week), while the risk of 15 alcohol-attributable YLL per 100 lifetimes occurred above 5.5 drinks per week (95% CI: <1 to 10 drinks per week). Among females, the risk of 15 alcohol-attributable YLL per 1000 people occurred at a consumption level above 4 standard drinks per week (95%

CI: <1 to 7.5 drinks per week), while the risk of 15 alcohol-attributable YLL per 100 people occurred above 6.5 drinks per week (95% CI: 2.5 to 9.5 drinks per week) (see Figure 11).

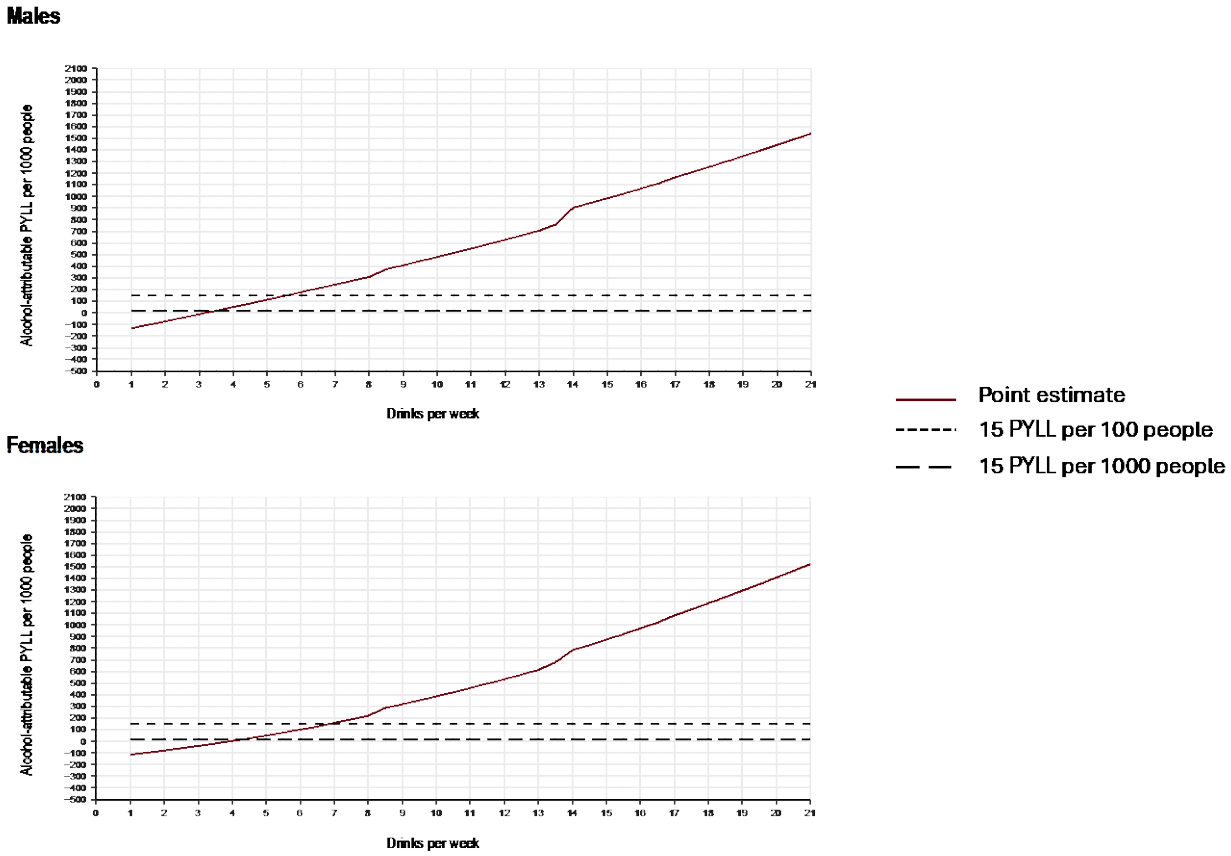

Figure 10. Lifetime risk of an alcohol-attributable year of potential life lost (YPLL) among males and females for differing levels of alcohol consumption

Among females, the risk of 15 lifetime alcohol-attributable DALYs lost per 1000 people occurred at a consumption level above 2.5 standard drinks per week (95% CI: <1 to 6.5 drinks per week), while the risk of 15 alcohol-attributable DALYs lost per 100 people occurred above 4.5 drinks per week (95% CI: <1 to 8 drinks per week). Among females, the risk of lifetime 15 alcohol-attributable DALYs lost per 1000 people occurred at a consumption level above 6.5 standard drinks per week (95% CI: <1 to 9.5 drinks per week), while the risk of 15 alcohol-attributable DALYs lost per 100 people occurred above 8 drinks per week (95% CI: 5 to 11 drinks per week) (see Figure 12).

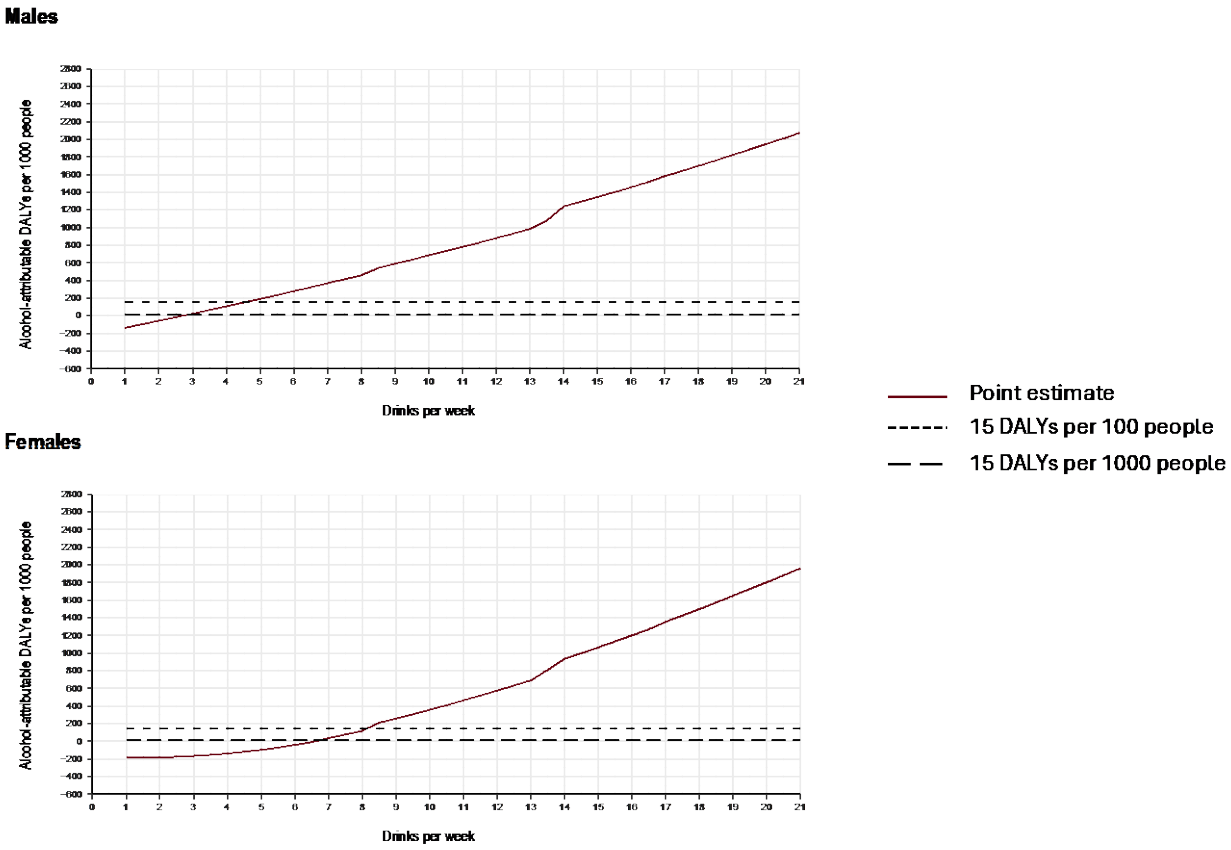

Figure 11. Lifetime risk of an alcohol-attributable disability adjusted years of life (DALYs) lost among males and females for differing levels of alcohol consumption

We also examined the impact of alcohol consumption at the upper limits of the 2020-2025 Dietary Guidelines for Americans on lifetime risks of alcohol-attributable premature death, YPLL, and DALYs lost. These guidelines recommend limits of two drinks or less per day for males and one drink (14g) or less per day for females of legal drinking age (66). For males, at 2 standard drinks per day, there were an estimated 39.3 (95% CI: 9.6, 69.6) alcohol-attributable deaths per 1000 people, 24.3 (95% CI: 15.4, 34.9) premature alcohol-attributable deaths per 1000 people, 903.9 (95% CI: 532.9, 1326.9) alcohol-attributable YPLL per 1000 people, and 1238.8 (95% CI: 787.7, 1673.7) alcohol-attributable DALYs lost per 1000 people. For females, at alcohol consumption of 1 drink per day, we observed a health impact of 0.1 (95% CI: -19.4, 21.9) alcohol-attributable deaths per 1000 people , 5.0 (95% CI: 1.8, 8.9) alcohol-attributable premature deaths per 1000 people , 159.8 (95% CI: -28.9, 386.1) alcohol-attributable YPLL per 1000 people , and 37.4 (95% CI: -216.7, 291.0) alcohol-attributable DALYs lost per 1000 people.

The impacts of alcohol consumption on lifetime cancer risk

Among males who consumed 1, 2 and 3 drinks *per week,* their lifetime risk of an alcohol-attributable cancer was 5.6 (95% CI: 1.7, 9.2), 6.1 (95% CI: 2.1, 9.7), and 6.6 (95% CI: 2.7, 10.2) per 1000 people, respectively. For males who consumed 1, 2 and 3 drinks *per day,* their lifetime risk of an alcohol-attributable cancer was 8.2 (95% CI: 6.5, 10.1), 17.2 (95% CI: 14.7, 19.8), and 22.6 (95% CI: 19.0, 26.3) per 1000 respectively. Among females who consumed 1, 2 and 3 drinks *per week,* their lifetime risk of an alcohol-attributable cancer was 2.6 (95% CI: 1.4, 3.8), 5.2 (95% CI: 3.9, 6.6), and 7.9 (95% CI: 6.4, 9.5) per 1000 people respectively. For females who consumed 1, 2 and 3 drinks *per day,* their lifetime risk of an alcohol-attributable cancer was 19.5 (95% CI: 10.6, 29.8), 43.0 (95% CI: 37.2, 49.7), and 66.9 (95% CI: 57.5, 77.5) per 1000 respectively. Compared to males, the rate ratio of developing an alcohol-attributable cancer for females who consumed 1, 2, and 3 drinks per day was 2.4, 2.5, and 3.0, respectively (see Figure 13). The lifetime risks of an alcohol-attributable cancer among males and females for differing levels of alcohol consumption by cancer site are outlined in Figures 14 and 15.

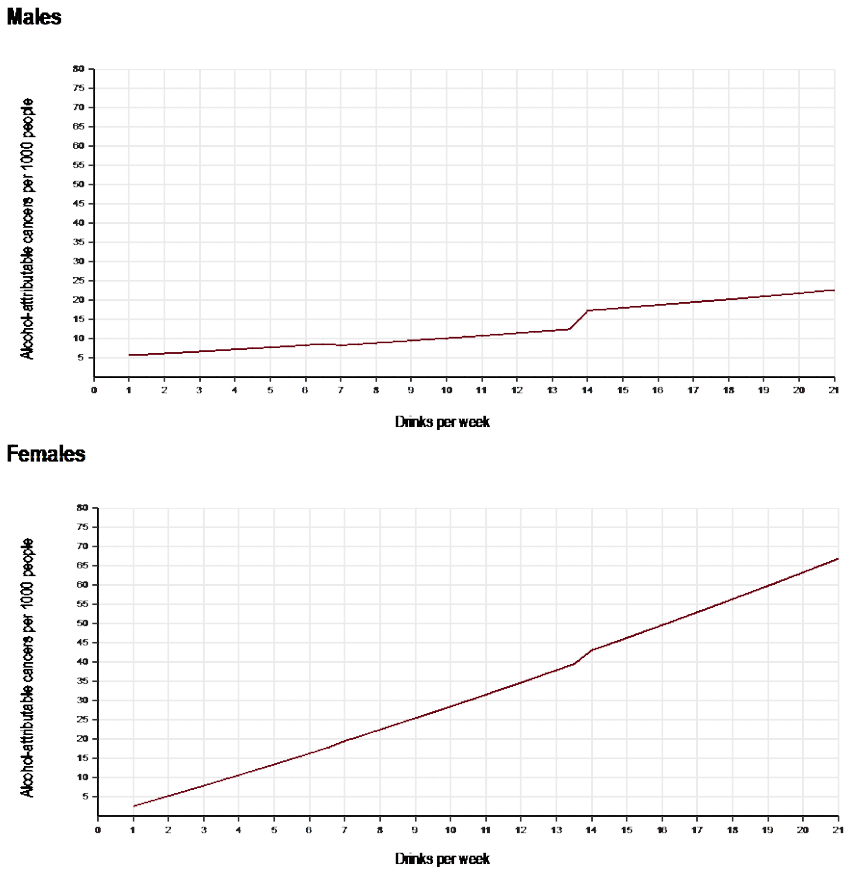

Figure 12. Lifetime risk of an alcohol-attributable cancer among males and females for differing levels of alcohol consumption

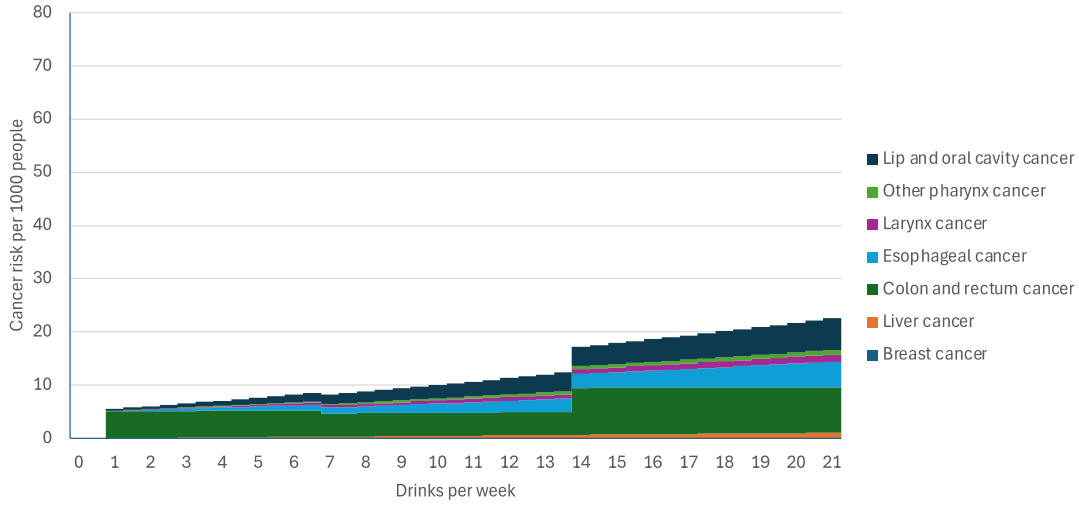

Figure 13. Lifetime risk of an alcohol-attributable cancer among males for differing levels of alcohol consumption by cancer site

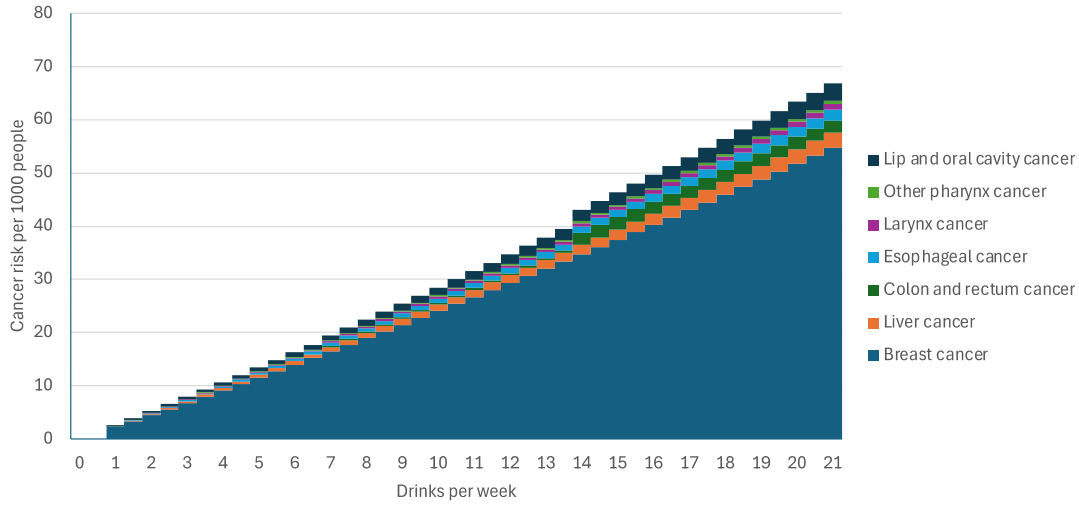

Figure 14. Lifetime risk of an alcohol-attributable cancer among females for differing levels of alcohol consumption by cancer site

The health impacts of per-occasion alcohol consumption (i.e., drinking patterns) on disease risk

This study found that patterns of alcohol consumption impact the risk of contracting infectious diseases, developing non-communicable diseases, and experiencing injuries. Many of the studies included in the review refer to thresholds of per-occasion consumption of five or more drinks for males and four or more

drinks for females per drinking occasion. At these or higher levels, most people will have impairment-level BACs of 0.08% or higher. This pattern of consumption is referred to as binge drinking or heavy episodic drinking.

The following section summarizes evidence from systematic reviews, collective re-analyses of emergency department case-crossover studies, and United States' roadside survey studies found on the relationship between drinking patterns and alcohol-related outcomes.

Impact of drinking patterns on cancer risk

A systematic review by Sohi et al. included two studies that showed engaging in past year binge drinking increased female breast cancer risk compared to not engaging in binge drinking (46, 67, 68). Furthermore, Sohi et al. found two studies that showed consuming more drinks during a single occasion was associated with a higher risk of female breast cancer (46, 69, 70). However, there is a lack of evidence that other cancer outcomes are impacted by levels of drinking.

Impact of drinking patterns on cardiovascular disease risk

A systematic review by Roerecke et al. identified seven studies providing data on the risk of ischemic heart disease from binge drinking (60g or 4.3 standard drinks per occasion) while average alcohol consumption was low to moderate (<30 g or 2.1 standard drinks day) (47). Compared with lifetime abstainers, the pooled RR for ischemic heart disease incidence was 0.64 (95% CI 0.53, 0.71) for people who drank moderately with no binge drinking occasions, and 1.12 (95% CI 0.91, 1.37) for people who consumed the same average amount and engaged in binge drinking. These findings suggest that binge drinking, even in the context of overall moderate alcohol use, can have a meaningful negative impact on heart health.

A systematic review by Mostofsky et al. found that high amounts of alcohol use were associated with higher cardiovascular risk (myocardial infarction, ischemic stroke and hemorrhagic stroke) in the following day (6 to 9 drinks: RR = 1.3 to 2.3) and week (19 to 30 drinks: RR =2.3 to 6.2) (71).

Impact of drinking patterns on liver disease risk

A systematic review by Llamosas-Falcón on drinking patterns and liver cirrhosis found that daily drinking was associated with a significant increase in the risk of liver cirrhosis compared to non-daily drinking (31).

Impact of drinking patterns on injuries

The relationship between BAC, consumption level, and injury risk is consistently dose-dependent, with increases in BAC corresponding to higher odds of injury. A systematic review by Taylor and Rehm (2012) identified a 1.74-fold increase in the odds of fatal motor vehicle crashes for every 0.02% BAC increment (approximately 1 standard drink), with an odds ratio (OR) of 13.0 (95% CI: 11.1, 15.2) at the legal BAC limit of 0.08% (73). Taylor et al. (2010) further highlighted non-linear risk escalations with ORs reaching 52.0 (95% CI: 34.5, 78.3) at 120g (approximately 8.5 standard drinks) consumed three hours before a motor vehicle crash. Importantly, injury risks were significant even at moderate consumption levels, with non-motor vehicle injuries (OR: 1.79, 95% CI: 1.59, 2.00) and motor vehicle injuries (OR: 2.20, 95% CI: 2.03, 2.09) linked to moderate doses (24g/day or about 1.7 drinks/day – the estimated conversion from BAC). These findings emphasize the broad risk spectrum for unintentional injuries at all BAC levels above zero (74).

Motor vehicle crashes are the prominent injury resulting from an elevated BAC. The 2013–2014 National Roadside Survey documented a declining prevalence of alcohol-positive drivers over several decades, particularly among those with BAC levels exceeding 0.08% (75). However, younger drivers (<20 years) showed no substantial reduction in alcohol-related crash risks, indicating demographic-specific vulnerabilities. Høye and Hesjevoll (2023) reinforced these findings through their analysis of 60 studies. The risk of crashes and injuries increases nearly exponentially with rising BAC levels, especially for serious crashes compared to other crashes (BAC range: 0.01% to 0.20%) (76).

The relationship between BAC and injury risk varies by injury type, with intentional injuries showing stronger associations with alcohol use than do unintentional injuries. For suicide attempts, the most comprehensive meta-analysis to date found a common OR of 6.97 (95% CI: 4.77, 10.17) for any acute alcohol use. Using four studies, 'low levels of acute drinking' resulted in an OR of 2.71 (95% CI: 1.56, 4.71) and 'high levels' had an OR of 37.18 (95% CI: 17.38, 79.53) (77). Furthermore, it should be noted that from 2003 to 2018 in the United States, the proportion of suicides that were alcohol-involved (i.e., BAC ≥ 0.08 g/dL) were found to have significantly increased on average annually for females of all age groups and for middle-aged males (78). Furthermore, alcohol use preceding death by suicide increased among females more than it did among males during the same time period (78).

The perpetrators of physical violence in most studies had higher BAC levels than the victims of the physical violence; for a recent review of alcohol use by perpetrators and violence see (80). A systematic review of alcohol use by perpetrators and violence estimated that in the United States the prevalence of

physical violence from others' drinking was 5.5% (95% CI: 4.4%, 6.7%) among males and 3.4% (95% CI: 2.6%, 4.2%) among females (80). Furthermore, the 2010–2012 National Intimate Partner and Sexual Violence Survey found that in the United States the prevalence of sexual violence caused from others' drinking was 4.5% (95%: 4.2%, 4.8%) among males and 10.1% (95% CI: 9.7%, 10.4%) among females, and the prevalence of intimate partner violence caused from others' drinking was 3.6% (95% CI: 3.4%, 2.8%) (82).

Overall, the above-cited research patterns suggest that alcohol's impairment effects exacerbate the likelihood of intentional injuries or violence due to alcohol's role in aggression and impaired decision-making.

Demographic factors, particularly sex and age, significantly shape the relationship between BAC and injury risks. Pelletti et al. (2024) highlighted a notable sex gap in alcohol-related driving risks, particularly among drivers involved in crashes, with male drivers showing a significantly higher alcohol-positive rate (30.7%, 95% CI: 26.8, 35.0) compared to female drivers (13.2%, 95% CI: 10.7, 16.1) (83). Taylor et al. (2010) also noted that intentional injuries, including violence, were more strongly linked to alcohol use among males than females (74). Age disparities were evident in the 2013–2014 National Roadside Survey, which showed stable alcohol-positive rates among young drivers (<20 years) despite broader declines among adult drivers over time. These findings underscore the disproportionate burden of alcohol-related injuries on young males and the need for targeted prevention strategies.

The impact of alcohol use on injuries can also be observed by testing for BAC among injury fatalities. Alpert et al. (2022) performed a systematic review of studies in North America that quantified alcohol-attributable fractions (AAFs) for fatal injuries, with the highest AAFs observed for railroad trespasser injuries (0.63, 95% CI: 0.49, 0.75), motor vehicle non-traffic crashes (0.42, 95% CI: 0.28, 0.56), falls (0.37, 95% CI: 0.07, 0.83), fire injuries (0.34, 95% CI: 0.20, 0.51), drowning (0.31, 95% CI: 0.21, 0.42), and homicides (0.29) (36). Taylor et al. (2010) noted that intentional injuries (OR: 1.38, 95% CI: 1.22, 1.55) had a higher per-drink risk than unintentional injuries (OR: 1.32, 95% CI: 1.27, 1.36), with falls showing slightly overlapping risks (74).

The strong link of BAC and injury has a biological basis, and starts at low drinking levels. Eckardt and colleagues (1998) in their seminal review found a dose-response relationship between levels of BAC and reaction time and psychomotor coordination, with impairment resulting in injury starting at BACs around

0.04 to 0.05 g/DL on average (84). As there is genetic variability in the underlying processes, epidemiological studies found effects at lower levels of concentration.

Situations where alcohol consumption may lead to a disproportionate amount of harm

There are other circumstances when alcohol consumption may lead to a substantial amount of harm. These include people who:

- Are taking medications which may have a harmful interaction with alcohol (a list of medications which interact with alcohol can be found at: https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/harmful-interactions-mixing-alcohol-with-medicines).
- Are using illicit benzodiazepines, cannabis, opioids, methamphetamine, cocaine; the co-use and interaction of alcohol and other substances has been shown to cause additional harms (66, 85-88).
- Have a medical condition which can be exacerbated by alcohol consumption (i.e., liver disease, bipolar disorder, abnormal heart rhythm, diabetes mellitus, hypertension, or chronic pain, etc.) (89-93).
- Are under the legal drinking age of 21 (94).
- Plan to drive a vehicle or operate machinery (73-75, 95).
- Are pregnant or trying to become pregnant (96, 97).
  Are breast feeding (98).

Alcohol consumption during pregnancy

Alcohol consumption during pregnancy can result in a wide range of adverse health effects on the developing fetus, including cognitive, behavioral, emotional, and adaptive functioning deficits, as well as congenital anomalies, with the most prominent of these effects being fetal alcohol spectrum disorder (FASD). A previous systematic review by Popova et al. identified 428 comorbid conditions associated with individuals with FASD, spanning 18 of the 22 chapters of the ICD-10. The most prevalent conditions were congenital malformations, deformities, chromosomal abnormalities, and mental and behavioral disorders (96). Additionally, a systematic review and modeling study found that in 2012 the estimated prevalence of FASD in the United States was 15.2 (95% CI: 7.5, 25.3) per 100,000 people (97).

Alcohol consumption during breastfeeding

A systematic review by Haastrup et al. on alcohol use during breastfeeding found multiple effects of alcohol consumption on breastfeeding (98). Haastrup et al., identified eight studies that showed alcohol intake inhibits milk ejection reflex, causing a temporary decrease in milk yield. Twelve publications examined the pharmacokinetics of alcohol during lactation, finding alcohol passes freely into breast milk

in approximately the same concentrations as in maternal blood, and the concentration declines linearly at the same rate as in maternal blood. Once metabolized, the toxic metabolite acetaldehyde was not found to be excreted into breast milk. Eleven studies examined the effects of alcohol consumption on the nursing infant. Three studies demonstrated that children breastfed by females who had consumed alcohol prior to feeding (i.e., within 4 hours) ingested less milk than they would have otherwise. This may be due to a decrease in milk production as opposed to a dislike for the taste of the milk. The health impact of breastfeeding after consuming alcohol included changes in children's sleep patterns (including a reduction in the amount of active (REM) sleep). The review concluded that the long-term effects of alcohol in mother's milk on the infant were unknown; however, these may potentially include pseudo-Cushing syndrome and decreased psychomotor development.

Discussion

In the United States, males and females have a 1 in 1000 risk of dying from alcohol use if they consume more than 7 drinks per week. This risk increases to 1 in 100 if they consume more than 9 drinks per week. Males and females who consumed 1 drink per day had an increased risk of liver cirrhosis, esophageal cancer, oral cancer, and injuries, but a lower risk for ischemic stroke. In addition, females also had a higher risk for liver cancer and a lower risk for diabetes mellitus when they drank 1 drink per day. However, drinking patterns shape risk. Specifically, even infrequent high per-occasion drinking may eliminate the lower levels of risk for ischemic stroke.

The results of this study are applicable to the general population and do not represent the risk function for any specific individual. The overall effect of alcohol consumption on all-cause mortality is dependent upon the risk of diseases and injuries that are causally related to alcohol. These risks are affected by numerous factors, including smoking, diet, physical activity, obesity, hepatitis infection, and genetics (e.g., genetic variations in the Aldehyde dehydrogenase 2 (ALDH2) gene). While some of these variables were controlled for in the underlying systematic reviews, they also influence a person’s risk for diseases and injuries causally related to alcohol. Therefore, alcohol would have a greater impact on the health of people who smoke, have poor diets, engage in low physical activity, are obese, have hepatitis infection, or have a family history of specific diseases than it would other individuals. For example, while low amounts of alcohol may not have a noticeable impact on liver cirrhosis for people who have a low risk of developing liver cirrhosis, even low amounts of alcohol can lead to mortality among people with a hepatitis C infection (99).

Cutoffs used for alcohol and health studies

Studies on alcohol and health are often based on the risk of harms and what level of risk is "acceptable". However, acceptable risk levels may vary from person to person and be context-dependent (e.g., is there a beneficial tradeoff for exposure to a risk?). For environmental hazard regulations, an involuntary risk of 1 in 1,000,000 lifetime deaths is the standard definition of an acceptable threshold (100-103). Since societies tend to accept higher risks for voluntary behaviors than for involuntary exposures, some previous studies drew upon Starr's analysis (1969, p. 1237) (30, 100-105). Starr analyzed data on mortality from various activities, as well as the time and money spent on these activities, and found that the public is willing to accept risks from voluntary behaviors that are 1,000 times greater than the risks from involuntary behaviors. Combined with thresholds for the regulation of environmental hazards, this equates to a voluntary risk threshold of one death in 1,000 lifetimes. We note that Starr's work is dated and limited by several factors (106); the analyses focused on mortality rather than morbidity, negative experiences, or harming others (106). Furthermore, risk acceptability is based on multiple factors that differ between individuals and populations. Individuals interpret risk according to numerous factors: perceived benefit, immediacy of the effect, knowledge about the risk to the exposed person, certainty of the scientific information regarding the risk, control over risk, newness of the risk, if the risk is catastrophic, and the severity of the consequences (107). However, Australia, and the United Kingdom have used an alcohol-attributable lifetime mortality risk of 1 per 100 people for determining the threshold for acceptable risk (30, 104). Although this level of risk is substantial and seems incompatible with public health objectives, this may reflect society being more willing to accept a higher risk of death associated with alcohol consumption compared to other voluntary activities (100). We report thresholds of risk not because we view any as acceptable per se, but they help put risk into perspective and to facilitate benchmarking.

Limitations

This study did not identify any systematic reviews on the impact of alcohol consumption on HIV/AIDS, other sexually transmitted diseases, cervical cancer, or depression. Accordingly, the current review does not quantify the impact of alcohol on these diseases. Furthermore, this study was limited to diseases and injuries where a causal link between alcohol consumption and disease/injury occurrence has been established. As more research is performed, conditions where there was previously thought to be a causal link with alcohol consumption may be found to be non-causal (such as gastric cancer (108)). Furthermore, conditions may be designated as causal as enough scientific evidence accumulates on the effects of alcohol consumption and health.

In addition, the relationships between alcohol and health in this report are informed primarily by observational studies. The limitations of this literature are considerable and need to be acknowledged; in general, the literature may under-estimate alcohol-related risk. People who drink are often compared to those who do not drink, and ideally to those who have never or only very rarely consumed alcohol. However, many of these non-drinkers are in fact former drinkers who quit drinking due to poor health (due to alcohol use or other reasons); as such they are misclassified and "contaminate" the non-drinking reference group (109). In addition, non-drinkers tend to have other risk factors for ill health that are unrelated to alcohol; this is difficult to account for statistically. Finally, most cohort studies that are used to assess relationships between alcohol and disease were not designed to study alcohol consumption and enroll participants several decades after most persons in the United States begin drinking. Because of this, persons who have died or became disabled from alcohol-related problems in young and middle adulthood are not available to be enrolled in studies.

The cohort and case-control studies underlying the meta-analyses used to model the lifetime risk of alcohol-attributable deaths have several limitations. First, chronic alcohol use is assessed through cross-sectional self-reports, which can introduce biases. Additionally, the use of a single baseline measurement followed by long-term follow-up leads to regression dilution bias. As the time interval between assessments increases, the misestimation of the association becomes more pronounced (110). Self-reported alcohol use is also subject to recall and social desirability bias, which can result in underreporting of alcohol consumption (111). To address potential underestimation of alcohol consumption in cohort studies when modeling the lifetime risk of alcohol-attributable deaths, we assumed that 10% of alcohol consumed by cohort participants was not captured in these studies.

Cohort studies typically include participants who are more likely to return for follow-up compared to the general population. Consequently, these studies often consist of middle-class, middle-aged participants from similar cultural backgrounds (112, 113). As a result, the RRs derived from these studies may have limited generalizability to other groups defined by factors such as sex, age, socio-economic status, and other modifiers (112, 113).

Both the amount of alcohol consumed and the patterns of consumption influence risk. The lifetime risk curves for diseases directly take into account the amount of alcohol consumed and indirectly take into consideration the patterns of drinking, (i.e., the underlying risk functions used take into consideration the average drinking patterns of the underlying cohorts). However, it should be noted that as these cohorts are from numerous countries and are typically designed for ease of follow-up and are disease free at baseline, their drinking patterns may not be representative of the general United States population, with people who

consume alcohol in these cohorts possibly being less likely to engage in binge drinking compared to the general population.

As the harms caused by beer, wine, spirits, and other alcoholic beverages are based mainly on ethanol content, regardless of the form in which the ethanol is consumed, we only modeled the impact of ethanol consumption on health. However, for unintentional injury there is evidence of a higher risk due to the consumption of spirits as there is a higher BAC curve due to the potential for the consumption of a larger amount of ethanol over a shorter period of time when compared to beer and wine (29). Furthermore, although not modeled as part of the lifetime risk of an alcohol-attributable death, alcohol poisonings are caused predominately by the consumption of spirits (114).

Additionally, it should be noted that the antioxidative and anti-carcinogenic properties of resveratrol have received attention; however, it has been estimated that for every cancer prevented by resveratrol in red wine, the ethanol contained in red wine causes 100,000 cancer cases (115). Therefore, the health benefits of resveratrol were not modeled as the effects of resveratrol on cancer prevention are negligible.

Relevance to underage alcohol consumption

The findings of this study have direct implications for the burden of underage drinking in the United States. In 2023, 27.9% of 12 to 20 year olds consumed alcohol in the past year, and 8.6% binge drank in the past month (116). Underage youth (i.e., people below the legal drinking age) were a key population that this report identified as having a higher risk for alcohol-attributable harms. The immediate consequences of underage drinking tend to manifest as alcohol-attributable injuries, in part because underage youth tend to consume larger volumes of alcohol per drinking occasion than adults do (117). On average, 4,096 underage youth died from excessive alcohol use each year between 2020 and 2021, and 96% of these deaths (3,931) were from injuries (118). While rates of underage drinking are declining in the U.S. (119), rates of alcohol-attributable deaths increased among those younger than 20 years old from 2016 to 2020 (120). Underage alcohol-attributable deaths have a profound public health impact due to the high YPLL per death compared to adults. When averaging data for 2020 and 2021, underage alcohol-attributable deaths resulted in 240,414 YPLL in the U.S. (118).

The consequences of underage drinking can also develop as youth age. The age at which youth begin to drink alcohol is a key determinant of their adult drinking patterns. Early initiation of alcohol use, particularly before age 14, is associated with increased risk of meeting criteria for an alcohol use disorder later in life even after accounting for family history (121). More broadly, underage youths' drinking

patterns tend to persist into adulthood; youth who drink heavily before they reach the legal drinking age tend to consume alcohol regularly when they are adults (122, 123). This report showed that such regular consumption, even at levels of one drink per day, are associated with a broad array of potential health consequences, including elevated risk of liver cirrhosis; breast, esophageal, and oral cancers; and unintentional injuries. Drinking patterns that persist over the life course shape cumulative exposure to alcohol, which may be particularly important in shaping the risk for some chronic harms, such as cancer (124). The report noted a lowered risk of ischemic stroke (males and females) and diabetes (females) among those who average one alcoholic drink per day. Yet, young people who start drinking alcohol at an earlier age are more likely to binge drink at least weekly as adults (125) – a pattern that, as shown in this study, renders non-significant such associations in which alcohol consumption lowered the risk for health conditions.

Comparison to studies which use all-cause mortality studies

The use of all-cause mortality studies to examine population estimates about alcohol and health is problematic (34). Studies on all-cause mortality include deaths from conditions that have no causal relationship with alcohol, thereby increasing the risk of confounding and reducing the specificity of the findings (i.e., that associations are due to a causal relationship with alcohol).

To assess causality of the relationship between a risk factor and a specific cause of death, representative samples are not necessary. However, for studies which measure the relationship between alcohol consumption and all-cause mortality, the task is not about causality, but about the relationship between alcohol use and mortality. The types of deaths included in all-cause mortality studies may not be representative of current causes of death in the United States because they are based on the distribution of death in the population or cohort that is studied. Indeed, many all-cause mortality studies combine cohort studies from numerous countries outside of the United States (126). For instance, participants in cohort studies often have a higher probability of cardiovascular deaths and a lower probability of liver cirrhosis and other “deaths of despair” compared to the general population (33). Additionally, cohorts for prospective studies are usually selected for ease of follow up (127), resulting in a bias favouring stable middle-class populations, which are unlikely to have the same characteristics as general populations. Even in the case where cohort studies are formulated based on population surveys, these samples are not representative of the general population, as they fail to attract sufficient participation numbers for certain groups, such as marginalised urban male youths, and exclude by design populations such as individuals experiencing homelessness and individuals who are institutionalized (128). The lack of representativeness can be easily assessed by comparing the coverage rate of surveys – they underestimate considerably the

level of drinking (e.g., (38, 128, 129)). As the composition of the outcome variable (mortality) changes in each underlying study and is not representative of mortality in the general population, the results of meta-analyses on all-cause mortality become arbitrary and change markedly based on the inclusion of studies, and even more so on the inclusion of countries from where the studies were conducted.

These two challenges in all-cause mortality studies prevent researchers from using them to validly conclude whether a given level of alcohol use causes alcohol-specific mortality risk for the United States 'population (34, 35). Therefore, it is necessary to estimate mortality risk based on cause-specific risks (i.e., specific risks from conditions causally related to alcohol), as was done in the present study, to inform public health prevention efforts because only these direct risks are preventable.

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Appendix

Methods

Table A1. Diseases and injuries included in the modeling study

Disease	ICD-10 codes
Communicable, maternal, neonatal, and nutritional diseases	A00-A00.9, A01.0-A14, A15-A28.9, A32-A39.9, A48.1-A48.2, A48.4-A48.5, A50-A58, A60-A60.9, A63-A63.8, A65-A65.0, A68-A70, A74, A74.8-A75.9, A77-A96.9, A98-A98.8, B00-B06.9, B10-B10.8, B15-B16.2, B17.0, B17.2, B19.1, B20-B27.9, B29.4, B33-B33.1, B33.3-B33.8, B34.2, B47-B48.8, B50-B53.8, B55.0, B56-B57.5, B60-B60.8, B63, B65-B67.9, B69-B72.0, B74.3-B75, B77-B77.9, B83-B83.8, B90-B91, B94.1, B95-B95.5, B97.2, B97.4-B97.6, C58-C58.0, D50.1-D50.8, D51-D52.0, D52.8-D53.9, D70.3, D89.3, E00-E02, E40-E46.9, E51-E61.9, E63-E64.0, E64.2-E64.9, F02.1, F02.4, F07.1, G00.0-G00.8, G03-G03.8, G04-G05.8, G14-G14.6, G21.3, H70-H70.9, I00, I02, I02.9, I98.0-I98.1, J00-J02.8, J03-J03.8, J04-J04.2, J05-J05.1, J06.0-J06.8, J09-J15.8, J16-J16.9, J20-J21.9, J36-J36.0, J91.0, K52.1-K52.3, K67.0-K67.8, K75.3, K76.3, K77.0, K93.0-K93.1, M03.1, M12.1, M49.0-M49.1, M73.0-M73.1, M89.6, N74.1, N96, N98-N98.9, O00-O07.9, O09-O16.9, O20-O26.9, O28-O36.9, O40-O48.1, O60-O77.9, O80-O92.7, O96-O98.6, O98.8-P04.2, P04.5-P05.9, P07-P15.9, P19-P22.9, P23.0-P23.4, P24-P29.9, P35-P37.2, P37.5-P39.9, P50-P61.9, P70-P70.1, P70.3-P72.9, P74-P78.9, P80-P81.9, P83-P84, P90-P92.9, P94-P94.9, P96, P96.3-P96.4, P96.8, R19.7, U04-U04.9, U06-U07.2, U82-U89, Z16-Z16.3
Tuberculosis	A10-A14, A15-A19.9, B90-B90.9, K67.3, K93.0, M49.0, N74.1, P37.0, U84.3
Pneumonia	B97.4-B97.6, J12.1, J13-J13.9, J14-J14.0, J15.3-J15.4, J15.6
Non-communicable diseases	A46-A46.0, A66-A67.9, B18-B18.9, B33.2, B86, C00-C13.9, C15-C22.8, C23-C25.9, C30-C34.9, C37-C38.8, C40-C41.9, C43-C45.9, C47-C54.9, C56-C57.8, C60-C63.8, C64-C67.9, C68.0-C68.8, C69.0-C69.8, C70-C73.9, C75-C75.8, C81-C82.9, C83.0-C83.8, C84-C85.0, C85.2-C85.8, C86-C86.6, C88-C91.0, C91.2-C91.3, C91.6, C92-C92.6, C93-C93.1, C93.3, C93.8, C94-C94.5, C94.7-C96.9, D00.1-D00.2, D01.0-D01.3, D02.0-D02.3, D03-D06.9, D07.0-D07.2, D07.4-D07.5, D09.0, D09.2-D09.3, D09.8, D10.0-D10.7, D11-D12.9, D13.0-D13.7, D14.0-D14.3, D15-D16.9, D22-D27.9, D28.0-D28.7, D29.0-D29.8, D30.0-D30.8, D31-D36, D36.1-D36.7, D37.1-D37.5, D38.0-D38.5, D39.1-D39.2, D39.8, D40.0-D40.8, D41.0-D41.8, D42-D43.9, D44.0-D44.8, D45-D47.9, D48.0-D48.6, D49.2-D49.4, D49.6, D55-D58.9, D59.1, D59.3, D59.5, D60-D61.9, D63.1, D64.0, D66-D67, D68.0-D69.4, D69.6-D69.8, D70-D70.0, D70.4-D75.8, D76-D77, D86-D86.9, D89-D89.2, E03-E03.1, E03.3-E06.3, E06.5-E07.1, E10-E11.9, E16.1-E16.9, E20-E23.0, E23.2-E24.1, E24.3-E27.2, E27.4-E34, E34.1-E34.8, E65-E66.0, E66.2-E68, E70-E85.2, E88-E88.2, E88.4-E88.9, F00-F02.0, F02.2-F02.3, F02.8-F03.9, F10-F16.9, F18-F18.9, F24, F50.0-F50.5, G10-G13.8, G20-G20.9, G23-G24, G24.1-G25.0, G25.2-G25.3, G25.5, G25.8-G26.0, G30-G31.9, G35-G37.9, G40-G41.9, G45-G46.8, G47.3, G61-G61.9, G62.1, G70-G72, G72.1-G73.7, G90-G90.9, G95-G95.9, H05.0-H05.1, I01-I01.9, I02.0, I05-I09.9, I11-I13.9, I20-I25.9, I27.0-I27.2, I28-I28.9, I30-I31.1, I31.8-I37.8, I38-I41.9, I42.1-I42.8, I43-I43.9, I47-I48.9, I51.0-I51.4, I60-I63.9, I65-I66.9, I67.0-I67.3, I67.5-I67.7, I68.0-I68.2, I69.0-I69.3, I70.2-I70.8, I71-I73.9, I77-I89.9, I98, I98.2, J30-J35.9, J37-J39.9, J41-J46.9, J60-J63.8, J66-J68.9, J70, J70.8-J70.9, J82, J84-J84.9, J91, J91.8-J92.9, K20-K20.9, K22-K22.6, K22.8-K29.9, K31-K31.8, K35-K38.9, K40-K42.9, K44-K46.9, K50-K52, K52.8-K52.9, K55-K62.6, K62.8-K62.9, K63.5, K64-K64.9, K66.8, K67, K68, K70-K70.3, K71.7, K73-K75, K75.1-K75.2, K75.4-K76.2, K76.4-K77, K77.8, K80-K83.9, K85-K86.9, K90-K90.9, K92.8, K93.8, L00-L05.9, L08-L08.9, L10-L14.0, L51-L51.9, L88-L89.9, L93-L93.2, L97-L98.4, M00-M03.0, M03.2-M03.6, M05-M09.8, M30-M36.8, M40-M43.1, M65-M65.0, M71.0-M71.1, M72.5-M72.6, M80-M82.8, M86.3-M86.4, M87-M87.0, M88-M89.0, M89.5, M89.7-M89.9, N00-N08.8, N10-N12.9, N13.6, N15-N16.8, N18-N18.9, N20-N23.0, N25-N28.1, N29-N30.3, N30.8-N32.0, N32.3-N32.4,

Disease	ICD-10 codes
	N34-N34.3, N36-N36.9, N39-N39.2, N41-N41.9, N44-N44.0, N45-N45.9, N49-N49.9, N60-N60.9, N72-N72.0, N75-N77.8, N80-N81.9, N83-N83.9, N84.0-N84.1, N87-N87.9, P04.3-P04.4, P70.2, P96.0-P96.1, Q00-Q07.9, Q10.4-Q18.9, Q20-Q28.9, Q30-Q36, Q37-Q45.9, Q50-Q87.8, Q89-Q89.8, Q90-Q93.9, Q95-Q99.8, R78.0-R78.5, R95-R95.9, X45-X45.9, X65-X65.9, Y15-Y15.9
Neoplasms	C00-C13.9, C15-C22.8, C23-C25.9, C30-C34.9, C37-C38.8, C40-C41.9, C43-C45.9, C47-C54.9, C56-C57.8, C60-C63.8, C64-C67.9, C68.0-C68.8, C69.0-C69.8, C70-C73.9, C75-C75.8, C81-C82.9, C83.0-C83.8, C84-C85.0, C85.2-C85.8, C86-C86.6, C88-C91.0, C91.2-C91.3, C91.6, C92-C92.6, C93-C93.1, C93.3, C93.8, C94-C94.5, C94.7-C96.9, K62.0-K62.1, K63.5, N60-N60.9, N84.0-N84.1, N87-N87.9
Oral cavity cancer*	C01-C08.9
Pharyngeal cancer (excluding nasopharynx)	C09-C10.9, C12-C13.9
Laryngeal cancer	C32-C32.9
Esophageal cancer	C15-C15.9
Colon and rectum cancer	C18-C21.9
Liver cancer	C22-C22.8
Female breast cancer	C50-C50.9
Cardiovascular diseases	B33.2, G45-G46.8, I01-I01.9, I02.0, I05-I09.9, I11-I11.9, I20-I25.9, I27.0, I27.2, I28-I28.9, I30-I31.1, I31.8-I37.8, I38-I41.9, I42.1-I42.8, I43-I43.9, I47-I48.9, I51.0-I51.4, I60-I63.9, I65-I66.9, I67.0-I67.3, I67.5-I67.6, I68.0-I68.2, I69.0-I69.3, I70.2-I70.8, I71-I73.9, I77-I83.9, I86-I89.0, I89.9, I98, K75.1
Ischemic heart disease	I20-I25.9
Ischemic stroke	G45-G46.8, I63-I63.9, I65-I66.9, I67.2-I67.3, I67.5-I67.6, I69.3
Intracerebral hemorrhage and subarachnoid hemorrhage	I60-I60.9, I61-I62, I62.1-I62.9, I67.0-I67.1, I68.1-I68.2, I69.0, I69.1-I69.2
Hypertensive heart disease	I11-I11.9
Atrial fibrillation and flutter	I48-I48.9
Alcoholic cardiomyopathy**	I42.6
Digestive diseases	B18-B18.9, I84-I85.9, I98.2, K20-K20.9, K22-K22.6, K22.8-K29.9, K31-K31.8, K35-K38.9, K40-K42.9, K44-K46.9, K50-K52, K52.8-K52.9, K55-K62, K62.2-K62.6, K62.8-K62.9, K64-K64.9, K66.8, K67, K68, K70-K70.3, K71.7, K73-K75, K75.2, K75.4-K76.2, K76.4-K77, K77.8, K80-K83.9, K85-K86.9, K90-K90.9, K92.8, K93.8, M09.1
Cirrhosis and other chronic liver diseases	B18-B18.9, I85-I85.9, I98.2, K70-K70.3, K71.7, K73-K75, K75.2, K75.4-K76.2, K76.4-K76.9, K77.8
Pancreatitis	K85-K86.9
Alcohol use disorders**	E24.4, F10-F10.9, G31.2, G62.1, G72.1, P04.3, Q86.0, R78.0, X45-X45.9, X65-X65.9, Y15-Y15.9
Diabetes mellitus	E10-E10.1, E10.3-E11.1, E11.3-E11.9, P70.2
Idiopathic epilepsy	G40-G41.9
Injuries	D52.1, D59.0, D59.2, D59.6, D69.5, D70.1-D70.2, D78-D78.8, E03.2, E06.4, E09-E09.9, E16.0, E23.1, E24.2, E27.3, E36-E36.8, E66.1, E88.3, E89-E89.9, G21.0-G21.1, G24.0, G25.1, G25.4, G25.6-G25.7, G72.0, G93.7, G97-G97.9, I95.2-I95.3, I97-I97.9, I98.9, J70.0-J70.5, J95-J95.9, K43-K43.9, K52.0, K62.7, K91-K91.9, K94-K95.8, L55-L55.9, L56.3, L56.8-L56.9, L58-L58.9, M87.1, N14-N14.4, N30.4, N65-N65.1, N99-N99.9, P93-P93.8, P96.2, P96.5, R50.2, U00-U03, V00-V86.9, V87.2-V87.3, V88.2-V88.3, V90-V98.8, W00-W46.2, W49-W62.9, W64-W70.9, W73-W75.9, W77-W81.9, W83-W94.9, W97.9, W99-X06.9, X08-X39.9, X47-X48.9, X50-X54.9, X57-X58.9, X60-X64.9, X66-X83.9, X85-Y08.9, Y35-Y84.9, Y87.0-Y87.1, Y88-Y88.3, Y89.0-Y89.1
Road injuries	V01-V04.9, V06-V80.9, V82-V82.9, V87.2-V87.3
Unintentional injuries	D52.1, D59.0, D59.2, D59.6, D69.5, D70.1-D70.2, D78-D78.8, E03.2, E06.4, E09-E09.9, E16.0, E23.1, E24.2, E27.3, E36-E36.8, E66.1, E88.3, E89-E89.9,

Disease	ICD-10 codes
	G21.0-G21.1, G24.0, G25.1, G25.4, G25.6-G25.7, G72.0, G93.7, G97-G97.9, I95.2-I95.3, I97-I97.9, I98.9, J70.0-J70.5, J95-J95.9, K43-K43.9, K52.0, K62.7, K91-K91.9, K94-K95.8, L55-L55.9, L56.3, L56.8-L56.9, L58-L58.9, M87.1, N14-N14.4, N30.4, N65-N65.1, N99-N99.9, P93-P93.8, P96.2, P96.5, R50.2, W00-W46.2, W49-W62.9, W64-W70.9, W73-W75.9, W77-W81.9, W83-W94.9, W97.9, W99-X06.9, X08-X39.9, X47-X48.9, X50-X54.9, X57-X58.9, Y40-Y84.9, Y88-Y88.3
Falls	W00-W19.9
Drowning	W65-W70.9, W73-W74.9
Fire, heat, and hot substances	X00-X06.9, X08-X19.9
Poisonings (excluding alcohol)	X47-X48.9
Exposure to mechanical forces	W20-W38.9, W40-W43.9, W45.0-W45.2, W46-W46.2, W49-W52
Self-harm and interpersonal violence	U00-U03, X60-X64.9, X66-X83.9, X85-Y08.9, Y35-Y38.9, Y87.0-Y87.1, Y89.0-Y89.1
Self-harm	X60-X64.9, X66-X83.9, Y87.0
Interpersonal violence	X85-Y08.9, Y87.1

* YLD include lip cancer (C00)

** The impact of diseases 100% attributable to alcohol were not modeled when estimating the impact of alcohol consumption on lifetime mortality and morbidity. Includes poisonings due to alcohol

Systematic review of meta-analyses

Systematic search strategy

Table A2. Keyword search strategies for PubMed

Systematic Review	Key word category	Keywords
Guidance on alcohol and health		
	Study design	“Systematic review” OR “meta-analysis”
	Exposure	"alcohol" OR "ethanol"

Screening of articles

Titles and abstracts of articles were screened for inclusion by two independent reviewers and were retained for full text review if they were deemed to have relevant information. Articles were included if they met the inclusion criteria outlined in Table A2. Assessment of full-text articles that are deemed to have uncertain eligibility for inclusion in the study were conducted in duplicate and independently. Investigators discussed differences in data extraction to reach a consensus.

Table A3. Inclusion and exclusion criteria

Inclusion criteria	
1	Systematic review and meta-analysis
2	Study was published on January 1, 2010 or afterwards
3	Exposure of interest is average alcohol use
4	The study reports an odds ratio, risk ratio, relative risk, or hazards ratio
5	The confounders taken into account in the underlying observational studies are reported
Exclusion criteria	
1	Study was beverage specific (wine, beer or spirits only) and not focused on total alcohol use
2	Study was focused on patterns of alcohol use and not total alcohol use

Data extraction

Data were extracted (see Table A3) by two independent reviewers. In cases where there was not enough information presented in the article, corresponding authors were contacted.

Table A4. Data extraction

Extracted data	
1	General information: authors’ names, year of publication
2	Conflicts of interest
3	Funding sources
4	Study objective(s)
4	Systematic review registration
5	Inclusion criteria
6	Exclusion criteria
7	Definition of the outcome of interest

8	Definition of exposure of interest
9	Reference group used for the relative risk estimations
10	Databases searched
11	Search dates
12	Search terms
13	Total number of studies included in the quantitative synthesis
14	Data characteristics: number of cases, number of person years, attrition rates, estimates of effect and association (odds ratios, relative risks, hazards ratios) and their error (standard error or confidence intervals), and adjustment factors.
15	Alcohol exposure measurement: When standard drinks are the unit of measurement, standard conversion factors will be used to standardize alcohol consumption to grams per day of pure alcohol.
16	Methods used for the meta-analysis
17	Tests for publication bias
18	Tests for heterogeneity
19	Analyses will be performed, if possible, by sex, age, and race (i.e., Black, White, Hispanic, Pacific islander, Asian, Other)

Estimating the burden of disease in the United States in 2022 attributable to alcohol use - Formulas

The PAF for alcohol use is estimated based on a Levin-based method which combines data on alcohol exposure (the prevalence of lifetime abstainers (P_{LA}), prevalence of past year abstainers (i.e., previous drinkers) (P_{PD}), and prevalence of drinkers (P_D), with corresponding relative risk estimates (see Formula A1).

[Formula A1]

$$PAF = \frac{P_{LA} + P_{PD}RR_{PD} + \int_{0.037\ g/day}^{250\ g/day} P_D(x) \cdot RR_D(x)dx - 1}{P_{LA} + P_{PD}RR_{PD} + \int_{0.037\ g/day}^{250\ g/day} P_D(x) \cdot RR_D(x)dx}$$

The number of alcohol-attributable deaths (AA_Deaths) and alcohol-attributable years lived with disability (YLD) (AA_YLD) were estimated by applying the PAFs to corresponding deaths and YLD estimates by sex, age, and cause of death or morbidity. The risk of death for people who engaged in lifetime abstention (Risk_D_LA) for a given cause of death (c) and age (a) was estimated by subtracting the total number of alcohol-attributable deaths (AA_Deaths) from the total number of deaths, and dividing this number by the population (Pop in the formulas below) (See Formula A2). Similarly, the risk of disability for people who engaged in lifetime abstention (Risk_D_YLD) for a given cause of disability (c) and age (a) was estimated by subtracting the total number of alcohol-attributable YLD (AA_YLD) from the total number of YLD and dividing this number by the total population of the United States (See Formula A3).

[Formula A2]

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

[Formula A3]

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

Lifetime risks of alcohol-attributable mortality and morbidity - Formulas

The lifetime risks of experiencing alcohol-attributable mortality and morbidity were estimated based on a cause-specific approach. The lifetime risks of experiencing alcohol-attributable mortality and morbidity represent absolute risks. The first step in this approach was the estimation of age-, sex- and cause-specific alcohol-attributable mortality and morbidity risks. Cause-specific alcohol-attributable mortality risk (Risk_D_AA) for a given life year was estimated by multiplying Risk_D_LA by the corresponding relative risk given an age, sex, cause, and average daily alcohol consumption amount (see Formula A4). Cause-specific alcohol-attributable morbidity (measured in YLD) risk was estimated by multiplying Risk_YLD_LA by the corresponding relative risk given an age, sex, cause, and average daily alcohol consumption amount (see Formula A5).

[Formula A4]

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

[Formula A5]

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

Total alcohol-attributable mortality risk and morbidity risk for a given life year was estimated by summing all cause-specific alcohol-attributable mortality risk and morbidity risk for a given life year, respectively (see Formulas A6 to A12).

[Formula A6]

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

[Formula A7]

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

[Formula A8]

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

[Formula A9]

$$Lifetime\_R\_Death_{s,x} = \left[\sum_{a=0}^{n} Alive_{a,s,x} \cdot Risk\_D\_AA_{a,s,x}\right]$$

[Formula A10]

$$Lifetime\_R\_YLL_{s,x} = \left[\sum_{a=0}^{n} Alive_{a,s,x} \cdot Risk\_D\_AA_{a,s,x} \cdot YLL_{a,s}\right]$$

[Formula A11]

$$Lifetime\_R\_YLD_{s,x} = \left[\sum_{a=0}^{n} Alive_{a,s,x} \cdot Risk\_YLD\_AA_{a,s,x}\right]$$

[Formula A12]

$$Lifetime\_R\_DALYs_{s,x} = Lifetime\_R\_YLL_{s,x} + Lifetime\_R\_YLD_{s,x}$$

Results

Table A5. Systematic review study information

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
Communicable, maternal, neonatal, and nutritional diseases													
Tuberculosis	Simou et al., 2018 (52)	OVID, EMBSE, Web of Science	None	(1) comparative observational study designs (cohort/longitudinal, case-control, cross-sectional) (2) adults aged .18 years (3) alcohol consumption reported as an exposure (4) comparative/reference group of either no alcohol consumption or the lowest exposed category; and (5) TB reported as an outcome. Studies that provided only the abstract or which were reported as conference articles were also included.	Excluded studies related to latent tuberculous infection, multidrug-resistant TB, TB prevention, treatment adherence and hospital-acquired TB.	N	Y	PROSPERO (CRD42015029910)	2	2	PRISMA	Y	Newcastle-Ottawa Quality Scale
Pneumonia	Simou et al., 2018 (53)	Medline (via Ovid), Embase (via Ovid) and Web of Science	None	All comparative study designs (longitudinal, cohort, case–control and cross sectional) assessing the association between alcohol intake and the risk of CAP in generally representative adult populations (≥18 years)	Studies of selected populations such as people with HIV, hepatitis B or C virus infection, and those with hospital-acquired pneumonia	N	Y	PROSPERO (42015029910)	2	2	PRISMA	Y	Newcastle-Ottawa Scale
Non-communicable diseases													
Neoplasms													
Oral cavity and Pharyngeal cancer (excluding nasopharynx)	WCRFI, 2018 (54)	Medline	English	(1) Results from an epidemiologic study of one of the following types: Randomized controlled trial, Group randomized controlled trial (Community trial), Prospective cohort study, Nested case-control study, Case-cohort study, and Historical cohort study (2) Must have as outcome of interest, incidence of colorectal, colon or rectum cancers, or mortality for these cancers. (3) Have to present results on the relevant exposures (4) Published in English language	(1) Articles out of the research topic. (2) Studies focusing on pre-malignant colorectal conditions, for example colorectal adenomas (that will be the topic of a different review) (3) Articles that do not report measure of association between the exposure and the risk of colorectal, colon or rectum cancers (4) The measure of the relationship between exposure and outcome is only the mean difference of exposure (5) Articles that are supplement to the main manuscript (e.g. Authors' Reply). (6) Articles that published on-line as "Epub ahead of	N	Y	Protocol published prior to review being performed	2	2	NS	Y	Newcastle–Ottawa Quality Assessment Scale for cohort studies, CUP tools

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
					print" or "In Press". (7) Are not in English language								
Laryngeal cancer	WCRFI, 2018 (54)	Medline	English only	(1) Results from an epidemiologic study of one of the following types: Randomized controlled trial, Group randomized controlled trial (Community trial), Prospective cohort study, Nested case-control study, Case-cohort study, and Historical cohort study (2) Must have as outcome of interest, incidence of colorectal, colon or rectum cancers, or mortality for these cancers. (3) Have to present results on the relevant exposures (4) Published in English language	(1) Articles out of the research topic. (2) Studies focusing on pre-malignant colorectal conditions, for example colorectal adenomas (that will be the topic of a different review) (3) Articles that do not report measure of association between the exposure and the risk of colorectal, colon or rectum cancers (4) The measure of the relationship between exposure and outcome is only the mean difference of exposure (5) Articles that are supplement to the main manuscript (e.g. Authors' Reply). (6) Articles that published on-line as "Epub ahead of print" or "In Press". (7) Are not in English language	N	Y	Protocol published prior to review being performed	2	2	NS	Y	Newcastle–Ottawa Quality Assessment Scale for cohort studies, CUP tools
Esophageal cancer	WCRFI, 2018 (55)	Medline	English, Chinese, French, Italian, Spanish and Portuguese	(1) Must have as outcome of interest incidence or mortality of esophageal cancer; (2) Included in Medline from January 1st 2006 (3) Have to present results from an epidemiologic study in males and/or females of one of the following types: Randomized controlled trial, Group randomized controlled trial (Community trial), Prospective cohort study, Nested case-control study, Case-cohort study In individuals free of cancer at the moment of exposure assessment or intervention (except non melanoma skin cancer), Historical cohort study , In individuals free of cancer at the moment of exposure assessment or intervention (except non melanoma skin cancer)	(1) Cohort studies in which the only measure of the relationship between the relevant exposure and outcome is the mean difference of exposure (this is because the difference is not adjusted for main confounders) (2) Articles in foreign language that cannot be translated (members in the review team can read Chinese, French, Italian, Spanish and Portuguese).	N	Y	Protocol published prior to review being performed	2	2	CUP tools	Y	Newcastle – Ottawa Scale
Colon and rectum cancer	Jun et al., 2023 (56)	Embase, Cochrane Library,	English only	(1) Studies focusing on esophageal, stomach, liver,	(1) If multiple articles reported	N	not reported	NA	2	Not reported	PRISMA	Y	Newcastle – Ottawa

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
		PubMed, Scopus, and Web of Science		pancreatic, colorectal, larynx, lung, thyroid, breast, and prostate cancers (2) Original cohort studies (excluding abstracts, letters, reviews, and meta-analyses) (3) studies reporting quantitative findings regarding the relationship between alcohol consumption and the risk of cancer as hazard ratios (HRs), relative risks (RRs), or odds ratios (ORs) for alcohol drinkers compared to non-drinkers or occasional drinkers (4) Studies providing the standard error or confidence interval (CI) of the risk estimate or sufficient data for their calculation; and (5) studies with the full text accessible.	results from the same study, the most recent or complete article was included. (2) Studies that evaluated specific types of alcoholic beverages only were excluded to avoid potential confounding.								quality assessment scale
Liver cancer	WCRFI, 2015 (57)	Medline	None	Have to present results on an exposure/intervention relevant to the review (1) Must have as outcome of interest incidence or mortality of liver cancer (histological type not specified) or hepatocellular carcinoma. (2) Have to present results from an epidemiologic Study in males and/or females of one of the following types: (3) Randomized controlled trial (4) Group randomized controlled trial (Community trial) (5) Prospective cohort study (6) Nested case-control study (7) Case-cohort study (8) Historical cohort study	Cohort studies in which the only measure of the relationship between the relevant exposure and outcome is the mean difference of exposure (this is because the difference is not adjusted for main confounders).	N	Y	Protocol published prior to review being performed	2	2	Continuous update project	Y	Newcastle – Ottawa quality assessment scale
Female breast cancer	Sohi et al., 2024 (46)	PubMed and Embase	None	(1) The study was a prospective cohort study or reanalyzed data from individual prospective cohort studies. (2) The exposure was alcohol consumption. (3) The outcome was breast cancer incidence (4) The study reported alcohol and breast cancer risk ratio(s), relative risk(s), incident rate ratio(s), or hazards ratio(s), with their corresponding error estimates or confidence intervals	The results were beverage specific only (i.e., wine, beer, or spirits only). Preprints and other unpublished articles that had not undergone peer review were excluded from the systematic review	N	Y	PROSPERO (CRD42023431730)	2	2	PRISMA	Y	Newcastle – Ottawa quality assessment scale
Cardiovascular diseases													
Ischemic heart disease	Zhao et al., 2017 (58)	PubMed and Web of Science	English only	Included studies were original cohort studies published in English, with mortality from CHD outcomes and at least three levels of alcohol consumption quantified for human subjects of all ages.	NS	N	N	NA	NS	NS	PRISMA	N	-

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
Ischemic stroke	Larsson et al., 2016 (59)	PubMed	None	(1) Prospective studies that reported relative risks (RR) with 95 % confidence intervals (CI) for quantitative categories of alcohol consumption in relation to non- fatal or fatal ischemic stroke, intracerebral hemorrhage, or subarachnoid hemorrhage. (2) Participants were free of stroke and ischemic heart disease at baseline.	Studies that only reported data on total stroke (ischemic and hemorrhagic strokes combined) or total hemorrhagic stroke were not eligible.	N	N	NA	2	NS	MOOSE	Y	Newcastle–Ottawa Scale
Intracerebral hemorrhage and subarachnoid hemorrhage	Zhang et al., 2014 (60)	PubMed, EMBASE, and the Cochrane Library	None	(1) The study had a prospective design (prospective cohort or prospective nested case–control study). (2) The study investigated the association between alcohol intake and the risk of total stroke, hemorrhagic stroke, ischemic stroke, or stroke mortality. (3) The authors reported effect estimates (risk ratio [RR], hazard ratio [HR], or odds ratio [OR]) and 95% confidence intervals (CIs) for comparisons of different categories versus low alcohol intake.	All case–control studies because various confounding factors could bias the results.	N	N	NA	2	2	PRISMA	Y	Newcastle–Ottawa Scale
Hypertensive heart disease	Cecchini et al., 2024 (61)	PubMed and Embase	English only	(1) had employed a prospective cohort or cohort-nested case-control design, (2) had assessed both alcohol intake at baseline and incidence of hypertension during the follow-up, (3) included participants aged more than 18 years who were apparently healthy and without evidence of diseases or disorders such as cardiovascular disease or diabetes at the beginning of the study, (4) compared the risk of incident hypertension at two or more levels of alcohol exposure, (5) reported relative risk estimates as rate ratios (RRs), hazard ratios (HRs), or odds ratios (ORs), and provided a 95% confidence interval (CI) (6) was written in English	Studies in which alcohol intake was expressed only as a continuous variable, thus providing risk estimates based on 1-unit increments in exposure based on a linear model because such studies are not suitable for the assessment of departure from linearity. We did not also consider studies based on binge alcohol drinking.	N	Y	PROSPERO (no. CRD42022314389)	3	3	PRISMA	Y	ROBINS-E
Atrial fibrillation and flutter	Jiang et al., 2022 (62)	PubMed, Embase, Cochrane	English only	(1) Prospective design (2) At least three types of alcohol consumption were reported, (3) numbers of participants and cases in each type of alcohol consumption were reported, (4) the adjusted relative risk (RR) and the corresponding 95% confidence interval (CI) of incident AF in each type of	NS	N	N	-	NS	NS	MOOSE	Y	Newcastle-Ottawa scale

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
				alcohol consumption were reported.									
Digestive diseases													
Cirrhosis and other chronic liver diseases	Llamosas-Falcon et al., 2022 (49)	PubMed/Medline, Embase	Not stated	(1) Studies included were articles with a longitudinal or case-control design. (2) The exposure variable was the quantity of alcohol use. (3) The outcome was LC morbidity (incidence of LC or decompensated LC) and mortality (ICD-8 and ICD-9 codes 571 and ICD-10 codes K70, K73, K74).	Studies were excluded if they were not published as full reports, they used a cross sectional design, there was not enough data to compute the relative risk related to alcohol use or presented their results with both sexes combined.	N	Y	PROSPERO: CRD42022299680.	2	2	PRISMA	Y	Cochrane Risk-of-Bias Tool for Non-Randomized Studies (ROBINS-I)
Pancreatitis	Samokhvalov et al., 2015 (63)	Medline, Embase, and Web of Science	None	The following inclusion criteria were used: (1) case-control or cohort studies that reported on the relationship between alcohol consumption and the risk of T2DM (2) studies that reported the quantity of alcohol use as the exposure variable with at least two categories compared with a third reference category (e.g., lifetime abstainers or current abstainers), as it has been previously reported that the association between alcohol consumption and T2DM is nonlinear (3) the outcome was risk of T2DM (diagnosis defined by the American Diabetes Association guidelines [17] or ICD-10 code E11, ICD-8, and ICD-9 code 250), including incident and/or mortality cases (4) the method of assessing T2DM was either by an objective assessment (e.g., laboratory findings or medical records) or self-report, and (5) studies that reported odds ratios, relative risks (RR), or hazard ratios (HR) and their 95% CI or information allowing us to compute them.	Studies were excluded if they were not published as full reports, if they did not have enough data to compute quantitative results, if alcohol consumption could not be converted into grams per day, or if the outcome was type 1, autoimmune, or gestational diabetes, insulin resistance, prediabetes, or specific complications (e.g., diabetic retinopathy or neuropathy).	Y	N	-	Not specified.	Assessments of full-text articles with uncertain eligibility and data abstraction were conducted independently by AVS and MR.	PRISMA	Y	Custom list of quality criteria
Diabetes mellitus	Llamosas-Falcón et al., 2023(64)	PubMed/Medline, Embase	NS	(1) Studies included were articles with a longitudinal or case-control design. (2) The exposure variable was the quantity of alcohol use. (3) The outcome was LC morbidity (incidence of LC or decompensated LC) and mortality (ICD-8 and ICD-9 codes 571 and ICD-10 codes K70, K73, K74).	Studies were excluded if they were not published as full reports, they used a cross sectional design, there was not enough data to compute the relative risk related to alcohol use or	N	Y	PROSPERO (CRD42022340247)	2	extracted by 1 author and verified by 3 authors	PRISMA	Y	Newcastle-Ottawa quality assessment scale

Disease	Study selected	Databases searched	Language restrictions	Inclusion criteria	Exclusion criteria	COI (Y/N)	SR Registration (Y/N)	SR Registration Info	# of Reviewers Screening Studies	# of Reviewing Extracting Studies	SR tool used (e.g. PRISMA, MOOSE)	RoB Reported (Y/N)	Quality assessment
					presented their results with both sexes combined.								
Epilepsy	Woo et al., 2022 (65)	Embase and MEDLINE databases	None	Cohort or case-control studies that reported the risk of epilepsy morbidity or unprovoked seizures associated with alcohol consumption.	Studies were excluded if the main outcome was a provoked seizure or if the study population included patients who had previously been diagnosed with epilepsy. Papers with duplicate databases or inclusion errors were excluded.	N	Y	PROSPERO (Registration number: CRD42021241960)	2	2	PRISMA	Y	Newcastle – Ottawa quality assessment scale

Table A6. Relative risks for different levels of alcohol consumption by disease

Cause of death	Sex	Drinks per week			Drinks per day		
		1	2	3	1	2	3
Communicable, maternal, neonatal, and nutritional diseases							
Tuberculosis	Both	1.02 (1.01, 1.02)	1.03 (1.03, 1.03)	1.05 (1.04, 1.05)	1.11 (1.09, 1.12)	1.24 (1.19, 1.26)	1.37 (1.31, 1.41)
Pneumonia	Both	1.01 (1.01, 1.01)	1.02 (1.02, 1.02)	1.03 (1.02, 1.04)	1.07 (1.06, 1.08)	1.15 (1.11, 1.17)	1.24 (1.18, 1.27)
HIV/AIDS	-	-	-	-	-	-	-
Other sexually transmitted diseases	-	-	-	-	-	-	-
Non-communicable diseases							
Neoplasms							
Oral cavity	Both	1.03 (1.02, 1.04)	1.06 (1.04, 1.08)	1.09 (1.05, 1.13)	1.22 (1.13, 1.32)	1.48 (1.27, 1.75)	1.80 (1.44, 2.31)
Pharyngeal cancer (excluding nasopharynx)	Males	1.02 (1.01, 1.04)	1.04 (1.01, 1.08)	1.06 (1.02, 1.12)	1.16 (1.04, 1.31)	1.34 (1.09, 1.71)	1.55 (1.13, 2.23)
	Females	1.05 (1.00, 1.10)	1.09 (1.00, 1.20)	1.14 (0.99, 1.32)	1.37 (0.99, 1.90)	1.87 (0.97, 3.60)	2.55 (0.96, 6.83)
Laryngeal cancer	Males	1.02 (1.01, 1.02)	1.04 (1.02, 1.05)	1.05 (1.03, 1.07)	1.13 (1.07, 1.17)	1.27 (1.15, 1.37)	1.44 (1.23, 1.61)
	Females	1.04 (1.01, 1.08)	1.08 (1.01, 1.16)	1.13 (1.02, 1.25)	1.32 (1.04, 1.68)	1.75 (1.09, 2.83)	2.31 (1.13, 4.76)
Esophageal cancer	Males	1.06 (1.04, 1.08)	1.12 (1.08, 1.17)	1.19 (1.13, 1.26)	1.51 (1.32, 1.71)	2.27 (1.75, 2.94)	3.42 (2.31, 5.04)
	Females	1.05 (1.03, 1.06)	1.09 (1.05, 1.13)	1.14 (1.08, 1.21)	1.37 (1.20, 1.55)	1.87 (1.44, 2.41)	2.55 (1.73, 3.75)
Colon and rectum cancer	Males	1.16 (1.04, 1.28)	1.16 (1.04, 1.28)	1.16 (1.04, 1.28)	1.14 (1.09, 1.20)	1.29 (1.23, 1.34)	1.29 (1.23, 1.34)
	Females	1.00 (0.97, 1.04)	1.00 (0.97, 1.04)	1.00 (0.97, 1.04)	1.01 (0.78, 1.30)	1.07 (1.00, 1.14)	1.07 (1.00, 1.14)
Liver cancer	Males	1.01 (1.00, 1.01)	1.01 (1.00, 1.02)	1.02 (1.01, 1.03)	1.04 (1.01, 1.07)	1.09 (1.03, 1.15)	1.13 (1.04, 1.23)
	Females	1.04 (1.01, 1.06)	1.07 (1.02, 1.13)	1.11 (1.02, 1.20)	1.28 (1.06, 1.52)	1.63 (1.12, 2.32)	2.08 (1.18, 3.53)
Breast cancer							
Premenopausal	Females	1.01 (1.00, 1.01)	1.02 (1.00, 1.03)	1.02 (1.01, 1.04)	1.06 (1.01, 1.10)	1.12 (1.03, 1.21)	1.18 (1.04, 1.33)
Postmenopausal	Females	1.02 (1.02, 1.03)	1.05 (1.04, 1.05)	1.07 (1.06, 1.08)	1.17 (1.14, 1.20)	1.37 (1.31, 1.44)	1.61 (1.49, 1.73)
Cervical cancer	Females	-	-	-	-	-	-
Cardiovascular diseases							
Ischemic heart disease	Both	0.87 (0.71, 1.06)	0.87 (0.71, 1.06)	0.87 (0.71, 1.06)	0.87 (0.71, 1.06)	0.92 (0.75, 1.14)	0.92 (0.75, 1.14)
Ischemic stroke	Both	0.90 (0.85, 0.95)	0.90 (0.85, 0.95)	0.90 (0.85, 0.95)	0.92 (0.87, 0.97)	1.08 (1.01, 1.15)	1.08 (1.01, 1.15)
Intracerebral hemorrhage and subarachnoid hemorrhage	Both	0.96 (0.74, 1.24)	0.96 (0.74, 1.24)	0.96 (0.74, 1.24)	0.96 (0.74, 1.24)	1.21 (0.85, 1.73)	1.29 (0.98, 1.71)
Hypertensive heart disease	Males	1.03 (1.02, 1.03)	1.06 (1.04, 1.09)	1.08 (1.05, 1.10)	1.18 (1.13, 1.24)	1.34 (1.26, 1.42)	1.44 (1.34, 1.55)

		Females	1.00 (0.97, 1.03)	1.00 (0.93, 1.09)	1.01 (0.91, 1.11)	1.03 (0.85, 1.26)	1.23 (0.95, 1.59)	1.54 (1.02, 2.34)
	Atrial fibrillation and flutter	Males	1.01 (1.01, 1.02)	1.03 (1.02, 1.04)	1.04 (1.02, 1.05)	1.09 (1.06, 1.13)	1.20 (1.12, 1.28)	1.31 (1.19, 1.44)
		Females	1.01 (0.99, 1.02)	1.02 (0.99, 1.04)	1.02 (0.98, 1.07)	1.06 (0.95, 1.17)	1.12 (0.91, 1.36)	1.19 (0.87, 1.58)
	Digestive diseases							
	Cirrhosis and other chronic liver diseases	Males	1.04 (1.02, 1.07)	1.09 (1.04, 1.15)	1.14 (1.06, 1.23)	1.37 (1.18, 1.62)	2.10 (1.68, 2.65)	3.58 (2.90, 4.48)
		Females	1.13 (1.07, 1.19)	1.27 (1.15, 1.41)	1.43 (1.24, 1.67)	2.33 (1.74, 3.17)	5.38 (3.81, 7.73)	10.67 (7.78, 14.63)
	Pancreatitis	Both	1.01 (1.00, 1.02)	1.02 (1.00, 1.04)	1.03 (1.01, 1.05)	1.07 (1.01, 1.13)	1.14 (1.02, 1.27)	1.22 (1.04, 1.44)
	Diabetes mellitus	Males	1.00 (1.00, 1.00)	1.00 (1.00, 1.01)	1.01 (1.00, 1.01)	1.02 (1.00, 1.03)	1.03 (1.00, 1.07)	1.05 (0.99, 1.10)
		Females	0.93 (0.91, 0.94)	0.86 (0.82, 0.89)	0.80 (0.75, 0.84)	0.70 (0.65, 0.75)	0.74 (0.67, 0.81)	0.79 (0.69, 0.90)
	Epilepsy	Both	1.02 (1.01, 1.03)	1.04 (1.02, 1.06)	1.06 (1.02, 1.09)	1.13 (1.06, 1.21)	1.29 (1.12, 1.48)	1.46 (1.18, 1.79)
	Depression	-	-	-	-	-	-	-
Injuries								
	Unintentional injuries							
	Road injuries	Males	1.03 (1.02, 1.03)	1.05 (1.05, 1.07)	1.08 (1.07, 1.10)	1.20 (1.17, 1.25)	1.43 (1.36, 1.56)	1.71 (1.59, 1.94)
		Females	1.03 (1.02, 1.04)	1.05 (1.04, 1.07)	1.08 (1.07, 1.11)	1.20 (1.16, 1.28)	1.45 (1.34, 1.63)	1.74 (1.56, 2.09)
	Poisonings (other than alcohol)	Both	1.02 (1.01, 1.03)	1.04 (1.03, 1.07)	1.07 (1.04, 1.10)	1.17 (1.10, 1.25)	1.36 (1.20, 1.56)	1.58 (1.32, 1.94)
	Other unintentional injuries (excluding poisonings)	Both	1.04 (1.01, 1.08)	1.08 (1.01, 1.17)	1.12 (1.02, 1.27)	1.29 (1.04, 1.74)	1.68 (1.08, 3.04)	2.17 (1.12, 5.29)
	Intentional injuries							
	Self-harm	Males	1.02 (1.01, 1.02)	1.04 (1.03, 1.04)	1.05 (1.05, 1.07)	1.13 (1.11, 1.16)	1.28 (1.23, 1.35)	1.44 (1.37, 1.57)
		Females	1.03 (1.02, 1.03)	1.05 (1.04, 1.07)	1.08 (1.06, 1.11)	1.20 (1.15, 1.27)	1.43 (1.33, 1.61)	1.71 (1.54, 2.04)
	Interpersonal violence	Males	1.01 (1.01, 1.02)	1.03 (1.03, 1.04)	1.04 (1.04, 1.06)	1.11 (1.09, 1.14)	1.23 (1.19, 1.29)	1.36 (1.30, 1.47)
		Females	1.02 (1.01, 1.02)	1.04 (1.03, 1.05)	1.06 (1.04, 1.08)	1.14 (1.11, 1.19)	1.29 (1.22, 1.41)	1.47 (1.36, 1.67)

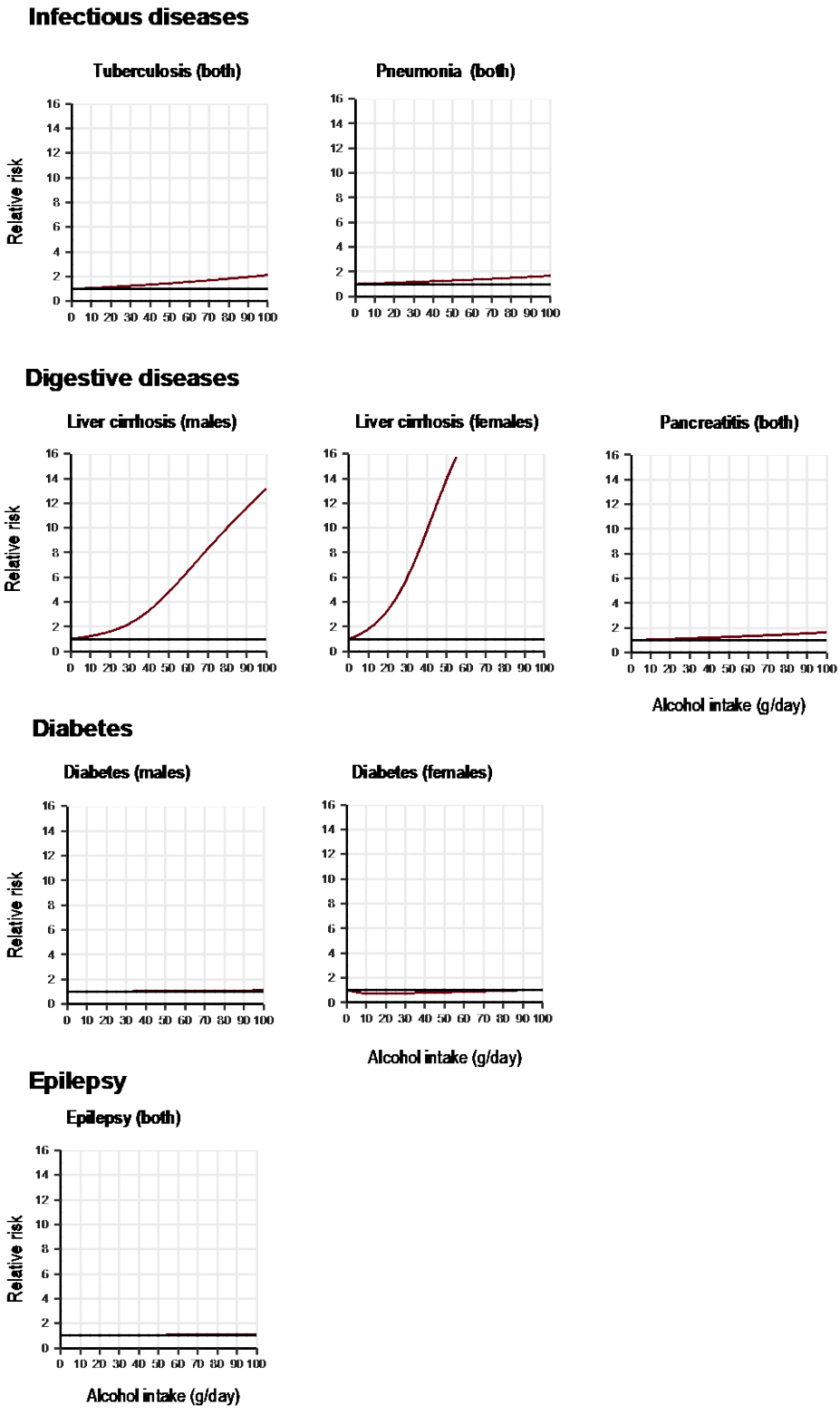

Figure A1. Relative risk functions for alcohol intake and infectious diseases, digestive diseases, diabetes and epilepsy

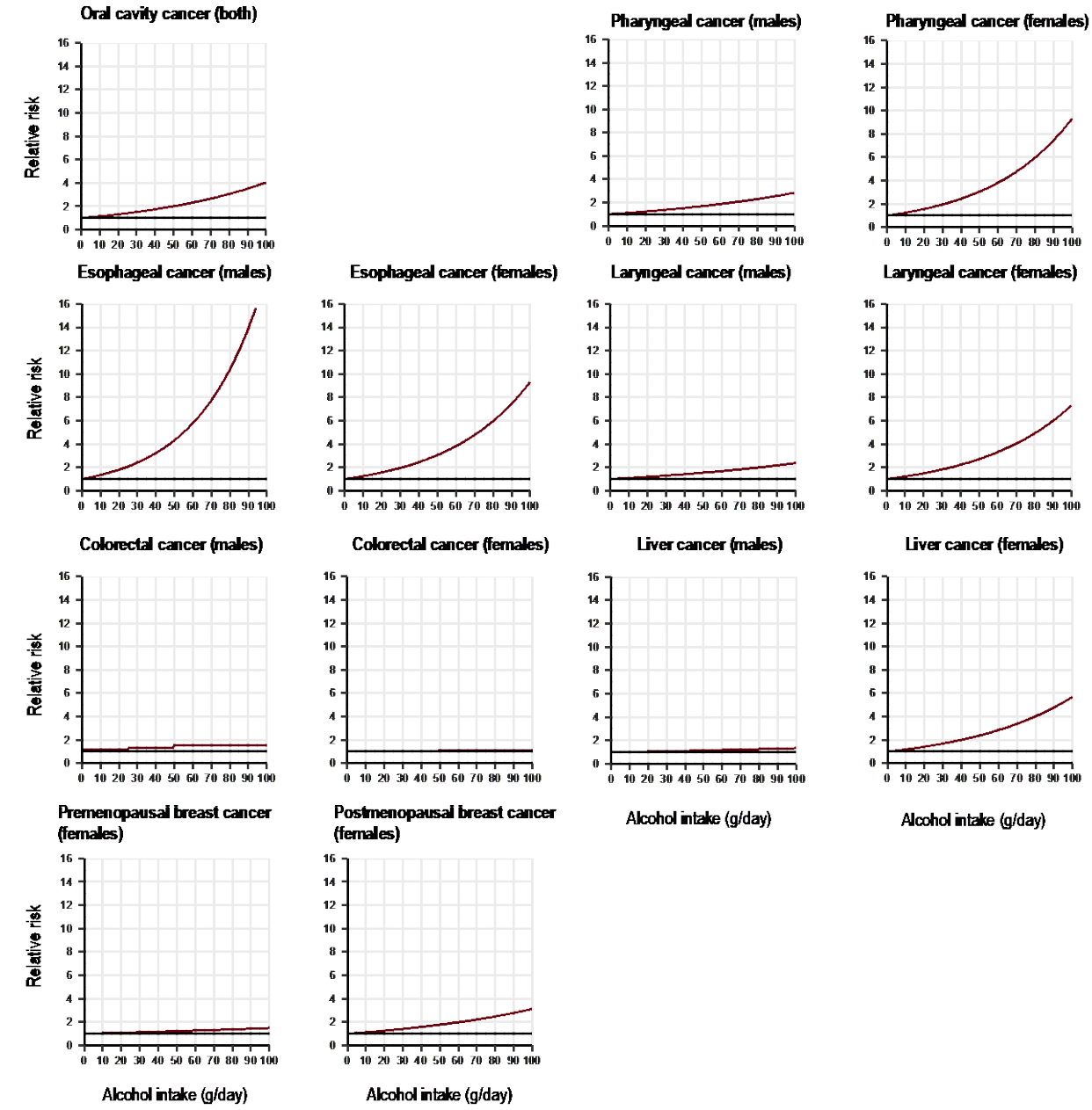

Figure A2. Relative risk functions for alcohol intake and cancer

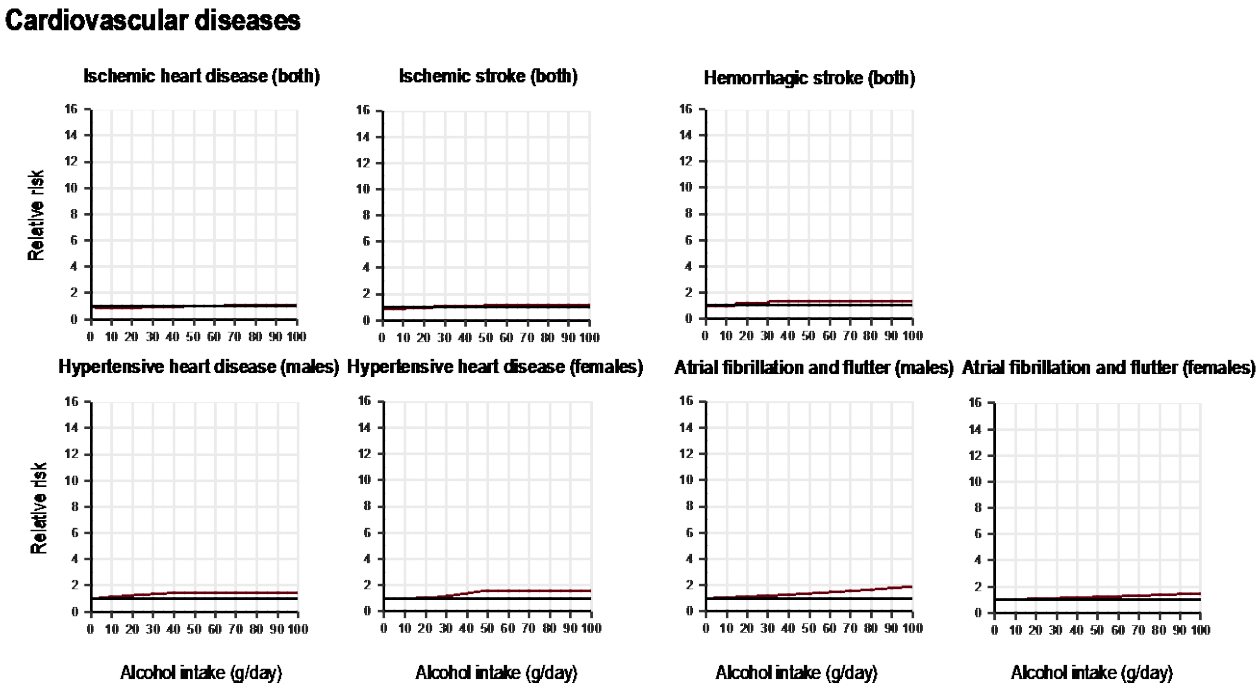

Figure A3. Relative risk functions for alcohol intake and cardiovascular disease

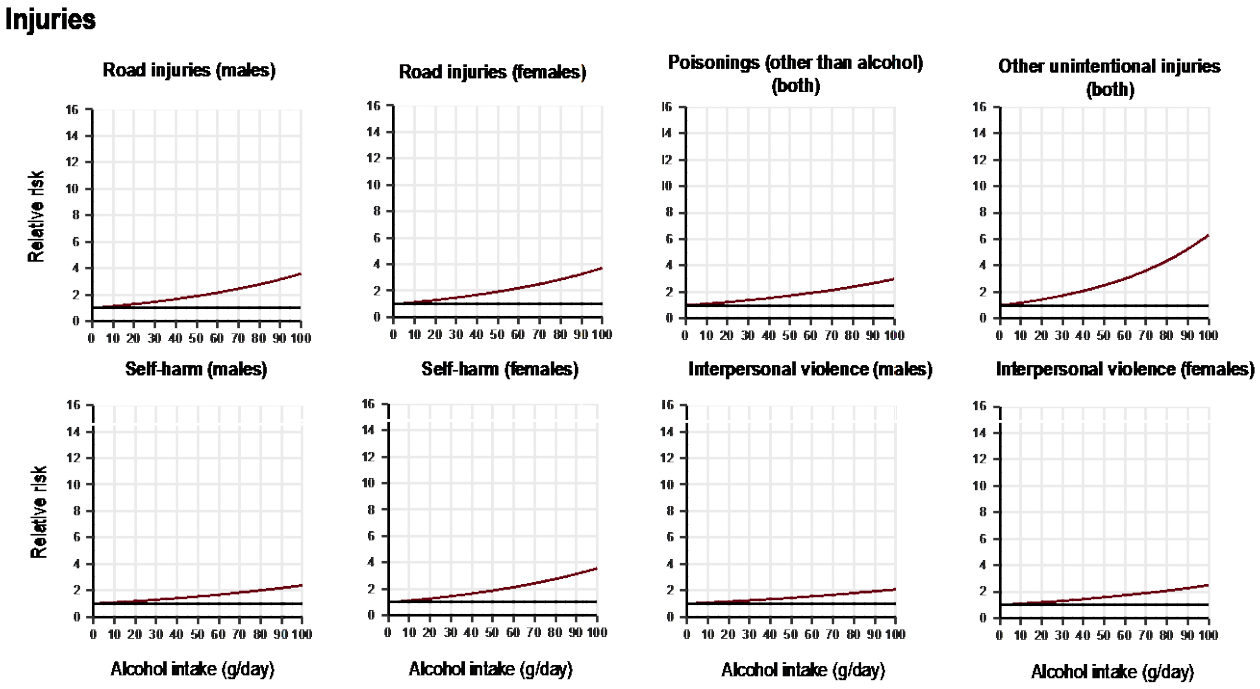

Figure A4. Relative risk functions for alcohol intake and injury

Table A7. Lifetime risk of an alcohol-attributable death by cause and sex

Sex	Age (years)	Drinks per week					
		1	2	3	7	14	21
Males	15 to 19	0.05 (0.04, 0.06)	0.10 (0.09, 0.13)	0.16 (0.13, 0.19)	0.38 (0.32, 0.47)	0.82 (0.68, 1.04)	1.33 (1.08, 1.71)
	20 to 24	0.08 (0.06, 0.10)	0.17 (0.13, 0.21)	0.25 (0.20, 0.32)	0.62 (0.50, 0.79)	1.35 (1.07, 1.75)	2.18 (1.71, 2.88)
	25 to 29	0.10 (0.06, 0.13)	0.21 (0.15, 0.28)	0.32 (0.24, 0.42)	0.80 (0.61, 1.05)	1.75 (1.34, 2.34)	2.84 (2.15, 3.87)
	30 to 39	0.17 (0.00, 0.34)	0.44 (0.23, 0.65)	0.70 (0.44, 1.00)	1.83 (1.30, 2.50)	4.18 (3.10, 5.78)	6.88 (5.09, 9.65)
	40 to 49	-0.10 (-0.77, 0.56)	0.19 (-0.49, 0.84)	0.48 (-0.22, 1.18)	1.71 (0.86, 2.62)	4.61 (3.27, 6.30)	7.75 (5.81, 10.58)
	50 to 59	-0.82 (-2.82, 1.10)	-0.47 (-2.47, 1.42)	-0.12 (-2.13, 1.79)	1.36 (-0.71, 3.31)	5.46 (3.14, 8.14)	9.52 (6.75, 12.94)
	60 to 69	-2.13 (-6.37, 1.86)	-1.72 (-5.95, 2.23)	-1.30 (-5.57, 2.61)	0.46 (-3.83, 4.46)	6.12 (1.87, 10.85)	11.12 (6.55, 16.37)
	70 plus	-13.66 (-36.71, 7.46)	-12.37 (-35.56, 8.44)	-11.06 (-34.26, 9.41)	-5.47 (-28.59, 14.57)	15.04 (-6.71, 35.66)	27.30 (5.58, 48.33)
	Total	-16.30 (-46.57, 11.41)	-13.46 (-43.99, 13.80)	-10.56 (-40.92, 16.42)	1.70 (-28.77, 29.08)	39.34 (9.65, 69.62)	68.92 (37.51, 101.23)
Females	15 to 19	0.02 (0.02, 0.03)	0.04 (0.03, 0.06)	0.06 (0.05, 0.09)	0.16 (0.13, 0.21)	0.35 (0.27, 0.48)	0.58 (0.44, 0.81)
	20 to 24	0.03 (0.02, 0.04)	0.06 (0.05, 0.08)	0.09 (0.07, 0.13)	0.24 (0.18, 0.32)	0.53 (0.40, 0.72)	0.87 (0.65, 1.22)
	25 to 29	0.03 (0.02, 0.05)	0.08 (0.05, 0.11)	0.12 (0.09, 0.16)	0.31 (0.23, 0.42)	0.71 (0.54, 0.99)	1.21 (0.91, 1.72)
	30 to 39	0.07 (0.00, 0.14)	0.18 (0.10, 0.28)	0.30 (0.19, 0.44)	0.85 (0.61, 1.18)	2.17 (1.65, 2.98)	3.91 (3.01, 5.42)
	40 to 49	-0.05 (-0.29, 0.21)	0.09 (-0.16, 0.38)	0.25 (-0.02, 0.56)	0.99 (0.58, 1.52)	3.08 (2.36, 4.17)	5.87 (4.66, 7.93)
	50 to 59	-0.34 (-1.02, 0.41)	-0.12 (-0.80, 0.66)	0.12 (-0.58, 0.93)	1.32 (0.46, 2.39)	5.02 (3.78, 6.77)	9.92 (7.96, 12.76)
	60 to 69	-1.08 (-2.70, 0.69)	-0.80 (-2.43, 1.00)	-0.49 (-2.09, 1.31)	1.16 (-0.57, 3.25)	6.72 (4.48, 9.55)	13.79 (10.87, 17.66)
	70 plus	-13.48 (-30.26, 4.23)	-12.47 (-29.19, 5.30)	-11.34 (-28.08, 6.52)	-4.87 (-22.22, 13.88)	21.95 (3.61, 40.93)	46.28 (25.55, 65.84)
	Total	-14.79 (-34.02, 5.57)	-12.93 (-32.42, 8.00)	-10.88 (-30.25, 10.57)	0.15 (-19.37, 21.90)	40.53 (18.49, 63.28)	82.43 (57.78, 108.45)

Table A8. Lifetime risk of an alcohol-attributable death by cause and alcohol consumption per 1000 people

Sex	Cause	Drinks per week					
		1	2	3	7	14	21
Males	Communicable diseases	0.0 (0.0, 0.0)	0.1 (0.0, 0.1)	0.1 (0.1, 0.1)	0.2 (0.2, 0.2)	0.4 (0.3, 0.4)	0.6 (0.5, 0.6)
	Neoplasms	2.5 (0.7, 4.2)	2.8 (0.8, 4.6)	3.0 (1.0, 5.0)	3.9 (2.3, 5.5)	8.4 (5.7, 10.9)	11.4 (7.6, 15.3)
	Diabetes mellitus	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.1 (0.0, 0.3)	0.3 (0.0, 0.6)	0.4 (0.0, 0.8)
	Cirrhosis and other chronic liver diseases	0.3 (0.1, 0.4)	0.6 (0.3, 0.9)	0.9 (0.4, 1.3)	2.2 (1.2, 3.5)	6.0 (3.9, 9.0)	13.4 (10.1, 18.0)
	Pancreatitis	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.2 (0.1, 0.2)	0.2 (0.1, 0.3)
	Epilepsy	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.1 (0.1, 0.1)	0.2 (0.1, 0.3)	0.3 (0.2, 0.5)
	Cardiovascular diseases	-20.7 (-54.2, 10.5)	-20.1 (-53.6, 11.1)	-19.5 (-53.1, 11.8)	-16.7 (-50.6, 14.9)	-1.1 (-33.5, 34.1)	2.3 (-28.9, 35.9)
	Road injuries	0.2 (0.2, 0.3)	0.5 (0.4, 0.6)	0.8 (0.7, 0.9)	1.8 (1.6, 2.3)	4.0 (3.4, 5.0)	6.4 (5.4, 8.3)
	Unintentional injuries	1.0 (0.4, 1.3)	2.0 (0.8, 2.7)	3.1 (1.2, 4.0)	7.5 (2.9, 10.1)	16.1 (6.0, 22.5)	26.2 (9.2, 38.4)
	Intentional injuries	0.3 (0.3, 0.4)	0.7 (0.6, 0.8)	1.0 (0.8, 1.2)	2.4 (2.0, 3.0)	5.0 (4.2, 6.4)	7.8 (6.6, 10.1)
	Total	-16.3 (-46.6, 11.4)	-13.5 (-44.0, 13.8)	-10.6 (-40.9, 16.4)	1.7 (-28.8, 29.1)	39.3 (9.6, 69.6)	68.9 (37.5, 101.2)
Females	Communicable diseases	0.0 (0.0, 0.0)	0.1 (0.0, 0.1)	0.1 (0.1, 0.1)	0.2 (0.2, 0.2)	0.4 (0.3, 0.5)	0.6 (0.5, 0.7)
	Neoplasms	0.7 (0.0, 1.4)	1.4 (0.5, 2.3)	2.2 (1.0, 3.3)	5.5 (0.0, 11.3)	12.4 (7.4, 17.8)	19.2 (11.4, 28.9)
	Diabetes mellitus	-0.6 (-0.8, -0.5)	-1.2 (-1.5, -0.9)	-1.6 (-2.1, -1.3)	-2.6 (-3.2, -2.1)	-2.3 (-2.9, -1.8)	-1.8 (-2.6, -1.1)
	Cirrhosis and other chronic liver diseases	0.5 (0.4, 0.7)	1.1 (0.7, 1.6)	1.7 (1.2, 2.5)	5.1 (3.4, 7.6)	15.9 (11.7, 22.6)	34.4 (26.5, 46.0)
	Pancreatitis	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)
	Epilepsy	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)	0.3 (0.2, 0.5)
	Cardiovascular diseases	-16.4 (-38.9, 8.8)	-16.2 (-39.5, 9.7)	-16.1 (-40.2, 10.6)	-15.0 (-41.7, 14.6)	-0.7 (-31.0, 33.6)	6.1 (-24.2, 40.8)
	Road injuries	0.1 (0.1, 0.2)	0.2 (0.2, 0.3)	0.4 (0.3, 0.5)	0.9 (0.7, 1.2)	1.9 (1.5, 2.7)	3.1 (2.4, 4.5)
	Unintentional injuries	0.6 (0.2, 0.8)	1.3 (0.4, 1.6)	2.0 (0.6, 2.5)	4.9 (1.5, 6.3)	10.5 (3.1, 14.1)	17.0 (4.7, 24.2)
	Intentional injuries	0.1 (0.1, 0.2)	0.3 (0.2, 0.3)	0.4 (0.3, 0.5)	0.9 (0.7, 1.3)	2.0 (1.5, 2.8)	3.2 (2.5, 4.6)
	Total	-14.8 (-34.0, 5.6)	-12.9 (-32.4, 8.0)	-10.9 (-30.3, 10.6)	0.1 (-19.4, 21.9)	40.5 (18.5, 63.3)	82.4 (57.8, 108.5)

Table A9. Lifetime risk of an alcohol attributable PYLL lost by cause and alcohol consumption per 1000 people

Sex	Cause	Drinks per week					
		1	2	3	7	14	21
Males	Communicable diseases	0.3 (0.3, 0.4)	0.6 (0.5, 0.7)	0.9 (0.8, 1.1)	2.2 (1.9, 2.6)	4.5 (3.8, 5.2)	6.9 (5.8, 8.0)
	Neoplasms	33.2 (8.9, 55.9)	36.6 (10.8, 60.7)	40.2 (12.8, 65.6)	51.9 (30.4, 72.2)	110.7 (75.9, 143.9)	150.5 (100.7, 200.7)
	Diabetes mellitus	0.3 (0.0, 0.5)	0.5 (-0.1, 1.1)	0.8 (-0.1, 1.6)	1.8 (-0.2, 3.7)	3.6 (-0.4, 7.3)	5.3 (-0.6, 10.9)
	Cirrhosis and other chronic liver diseases	5.1 (2.7, 7.9)	10.4 (5.4, 16.3)	16.0 (8.2, 25.1)	41.5 (22.1, 66.1)	113.8 (73.3, 170.8)	253.8 (193.2, 342.8)
	Pancreatitis	0.2 (0.1, 0.3)	0.4 (0.1, 0.7)	0.6 (0.2, 1.1)	1.4 (0.6, 2.3)	2.8 (1.5, 4.2)	4.4 (2.8, 6.2)
	Epilepsy	0.3 (0.2, 0.4)	0.6 (0.4, 0.9)	1.0 (0.5, 1.3)	2.3 (1.3, 3.2)	4.9 (2.6, 7.0)	7.8 (3.9, 11.5)
	Cardiovascular diseases	-214.0 (-563.3, 116.6)	-207.6 (-558.1, 124.2)	-201.0 (-552.8, 131.9)	-171.8 (-528.2, 166.0)	-7.3 (-354.0, 376.9)	30.9 (-303.9, 400.9)
	Road injuries	7.8 (6.7, 9.6)	15.7 (13.5, 19.4)	23.8 (20.5, 29.6)	58.0 (49.6, 72.9)	125.4 (106.1, 160.3)	203.7 (170.6, 265.7)
	Unintentional injuries	23.4 (11.7, 32.3)	47.3 (23.5, 65.6)	71.7 (35.4, 99.8)	174.7 (84.3, 247.7)	376.8 (174.6, 552.9)	611.4 (271.3, 935.4)
	Intentional injuries	11.0 (9.4, 13.8)	22.2 (18.9, 27.7)	33.5 (28.5, 42.0)	80.4 (68.2, 101.4)	168.6 (142.1, 215.6)	265.5 (222.3, 343.9)
	Total	-132.5 (-442.3, 158.0)	-73.2 (-383.9, 219.4)	-12.6 (-325.8, 278.0)	242.5 (-76.0, 536.6)	903.9 (532.9, 1326.9)	1540.2 (1079.8, 2093.2)
Females	Communicable diseases	0.4 (0.3, 0.4)	0.7 (0.6, 0.8)	1.1 (0.9, 1.3)	2.6 (2.1, 3.0)	5.2 (4.3, 6.2)	7.9 (6.5, 9.4)
	Neoplasms	9.7 (-0.5, 18.8)	19.6 (6.3, 31.5)	29.7 (13.2, 44.5)	74.7 (1.3, 153.2)	170.3 (102.7, 242.7)	266.4 (159.8, 395.9)
	Diabetes mellitus	-7.5 (-9.9, -5.7)	-14.4 (-18.6, -11.0)	-20.4 (-26.1, -15.7)	-32.8 (-40.2, -26.9)	-29.4 (-36.7, -22.4)	-23.6 (-33.5, -14.0)
	Cirrhosis and other chronic liver diseases	9.9 (6.8, 13.9)	21.0 (14.2, 29.9)	33.3 (22.3, 48.1)	98.5 (66.0, 145.5)	306.9 (227.3, 436.3)	669.4 (517.0, 902.5)
	Pancreatitis	0.1 (0.0, 0.3)	0.3 (0.1, 0.5)	0.4 (0.1, 0.8)	1.0 (0.3, 1.7)	2.0 (1.0, 3.1)	3.1 (1.9, 4.5)
	Epilepsy	0.3 (0.2, 0.4)	0.6 (0.3, 0.9)	1.0 (0.5, 1.4)	2.3 (1.2, 3.4)	4.8 (2.4, 7.3)	7.6 (3.7, 11.8)
	Cardiovascular diseases	-148.7 (-367.0, 90.7)	-147.7 (-373.0, 98.1)	-146.8 (-378.8, 105.8)	-138.9 (-394.1, 139.5)	-7.4 (-299.3, 326.9)	57.1 (-231.8, 394.5)
	Road injuries	3.9 (3.1, 5.2)	7.9 (6.3, 10.6)	12.0 (9.5, 16.2)	29.4 (23.1, 40.2)	63.8 (49.3, 89.9)	103.9 (79.0, 151.1)
	Unintentional injuries	11.8 (5.6, 16.0)	23.9 (11.2, 32.6)	36.3 (16.9, 49.6)	88.6 (40.2, 123.5)	191.6 (83.2, 277.4)	310.8 (129.0, 471.5)
	Intentional injuries	4.6 (3.7, 6.2)	9.3 (7.4, 12.5)	14.2 (11.2, 19.0)	34.4 (27.1, 47.0)	74.2 (57.5, 103.8)	120.0 (91.5, 172.5)
	Total	-115.5 (-293.1, 76.4)	-78.8 (-255.0, 116.9)	-39.2 (-214.1, 162.9)	159.8 (-28.9, 386.1)	782.0 (533.5, 1083.1)	1522.5 (1203.5, 1954.0)

Table A10. Lifetime risk of an alcohol-attributable DALY lost by cause and alcohol consumption per 1000 people

Sex	Cause	Drinks per week					
		1	2	3	7	14	21
Males	Communicable diseases	0.3 (0.3, 0.4)	0.7 (0.6, 0.8)	1.0 (0.9, 1.2)	2.4 (2.0, 2.8)	4.9 (4.1, 5.6)	7.5 (6.2, 8.6)
	Neoplasms	37.6 (10.0, 63.4)	41.3 (12.1, 68.5)	45.1 (14.2, 73.7)	57.2 (33.6, 79.6)	121.8 (83.9, 157.7)	163.8 (110.1, 217.7)
	Diabetes mellitus	2.1 (-0.2, 4.2)	4.1 (-0.5, 8.4)	6.2 (-0.7, 12.6)	14.3 (-1.7, 29.4)	28.3 (-3.3, 58.1)	41.8 (-4.9, 86.7)
	Cirrhosis and other chronic liver diseases	5.2 (2.7, 8.1)	10.6 (5.5, 16.6)	16.3 (8.4, 25.6)	42.4 (22.5, 67.4)	116.2 (74.9, 174.3)	259.0 (197.2, 349.8)
	Pancreatitis	0.2 (0.1, 0.4)	0.5 (0.1, 0.8)	0.7 (0.2, 1.3)	1.7 (0.7, 2.8)	3.4 (1.8, 5.1)	5.3 (3.3, 7.4)
	Epilepsy	1.0 (0.5, 1.3)	2.0 (1.1, 2.7)	3.0 (1.6, 4.1)	7.3 (3.9, 10.0)	15.2 (7.9, 21.7)	23.9 (12.0, 35.5)
	Cardiovascular diseases	-239.8 (-621.1, 121.6)	-231.5 (-614.4, 131.5)	-223.0 (-607.7, 141.7)	-182.6 (-573.7, 189.2)	33.0 (-357.2, 464.5)	85.7 (-293.7, 504.4)
	Road injuries	11.1 (9.6, 13.7)	22.5 (19.4, 27.8)	34.1 (29.3, 42.3)	83.0 (71.1, 104.2)	178.9 (151.6, 228.2)	289.9 (243.2, 377.1)
	Unintentional injuries	34.1 (14.0, 45.0)	69.1 (28.1, 91.3)	104.9 (42.3, 139.3)	257.1 (100.5, 347.9)	558.9 (207.2, 785.9)	915.4 (320.1, 1355.3)
	Intentional injuries	11.6 (9.9, 14.5)	23.5 (20.0, 29.3)	35.4 (30.2, 44.4)	85.0 (72.1, 107.2)	178.2 (150.2, 227.8)	280.4 (234.8, 363.1)
	Total	-136.5 (-463.0, 160.7)	-57.3 (-386.8, 240.1)	23.7 (-307.3, 317.7)	367.8 (15.7, 677.1)	1238.8 (787.7, 1673.7)	2072.8 (1457.9, 2704.3)
Females	Communicable diseases	0.4 (0.3, 0.5)	0.8 (0.6, 0.9)	1.2 (1.0, 1.4)	2.7 (2.3, 3.2)	5.5 (4.6, 6.6)	8.4 (6.9, 10.1)
	Neoplasms	11.6 (0.2, 22.0)	23.4 (8.5, 36.8)	35.6 (17.0, 52.2)	89.0 (6.5, 177.6)	201.9 (127.1, 282.4)	315.2 (197.3, 457.7)
	Diabetes mellitus	-67.9 (-88.9, -51.3)	-129.8 (-168.2, -98.9)	-183.5 (-235.1, -141.3)	-295.3 (-363.3, -242.5)	-265.0 (-331.6, -202.2)	-213.3 (-302.8, -126.5)
	Cirrhosis and other chronic liver diseases	10.2 (7.0, 14.3)	21.5 (14.5, 30.7)	34.1 (22.8, 49.3)	100.9 (67.6, 149.1)	314.3 (232.7, 446.9)	685.5 (529.4, 924.0)
	Pancreatitis	0.2 (0.0, 0.4)	0.4 (0.1, 0.7)	0.6 (0.1, 1.1)	1.4 (0.5, 2.3)	2.8 (1.4, 4.2)	4.3 (2.6, 6.1)
	Epilepsy	1.1 (0.6, 1.6)	2.2 (1.1, 3.1)	3.3 (1.7, 4.8)	7.9 (4.1, 11.7)	16.6 (8.3, 25.2)	26.0 (12.6, 40.7)
	Cardiovascular diseases	-178.4 (-430.8, 96.0)	-176.5 (-438.0, 106.3)	-174.7 (-445.0, 116.7)	-158.9 (-460.2, 166.5)	27.8 (-331.1, 434.7)	105.4 (-256.7, 524.2)
	Road injuries	6.6 (5.3, 8.8)	13.3 (10.6, 17.9)	20.2 (16.0, 27.2)	49.3 (38.8, 67.5)	106.7 (82.5, 150.2)	173.1 (131.7, 251.0)
	Unintentional injuries	26.5 (8.7, 33.3)	53.8 (17.5, 67.8)	81.8 (26.4, 103.5)	201.6 (62.4, 260.6)	440.9 (127.5, 597.9)	723.8 (194.7, 1041.4)
	Intentional injuries	5.2 (4.1, 6.9)	10.5 (8.4, 14.1)	15.9 (12.7, 21.4)	38.8 (30.5, 52.8)	83.4 (64.6, 116.6)	134.6 (102.7, 193.3)
	Total	-184.6 (-376.1, 23.6)	-180.4 (-380.7, 32.1)	-165.5 (-373.8, 48.1)	37.4 (-216.7, 291.0)	934.8 (534.7, 1304.7)	1962.9 (1374.3, 2552.8)

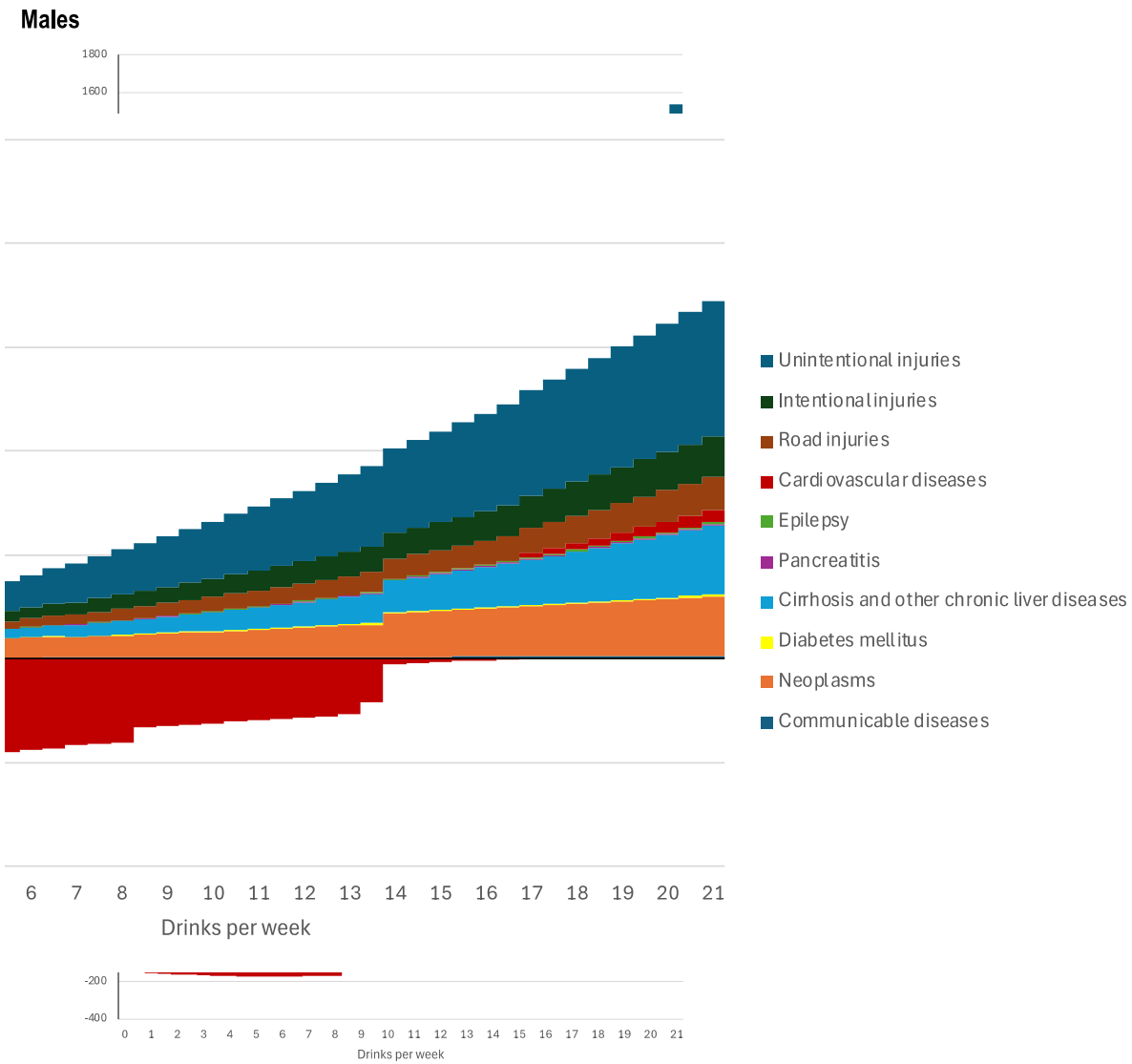

Figure A5. Lifetime risk of an alcohol-attributable PYLL by sex and cause

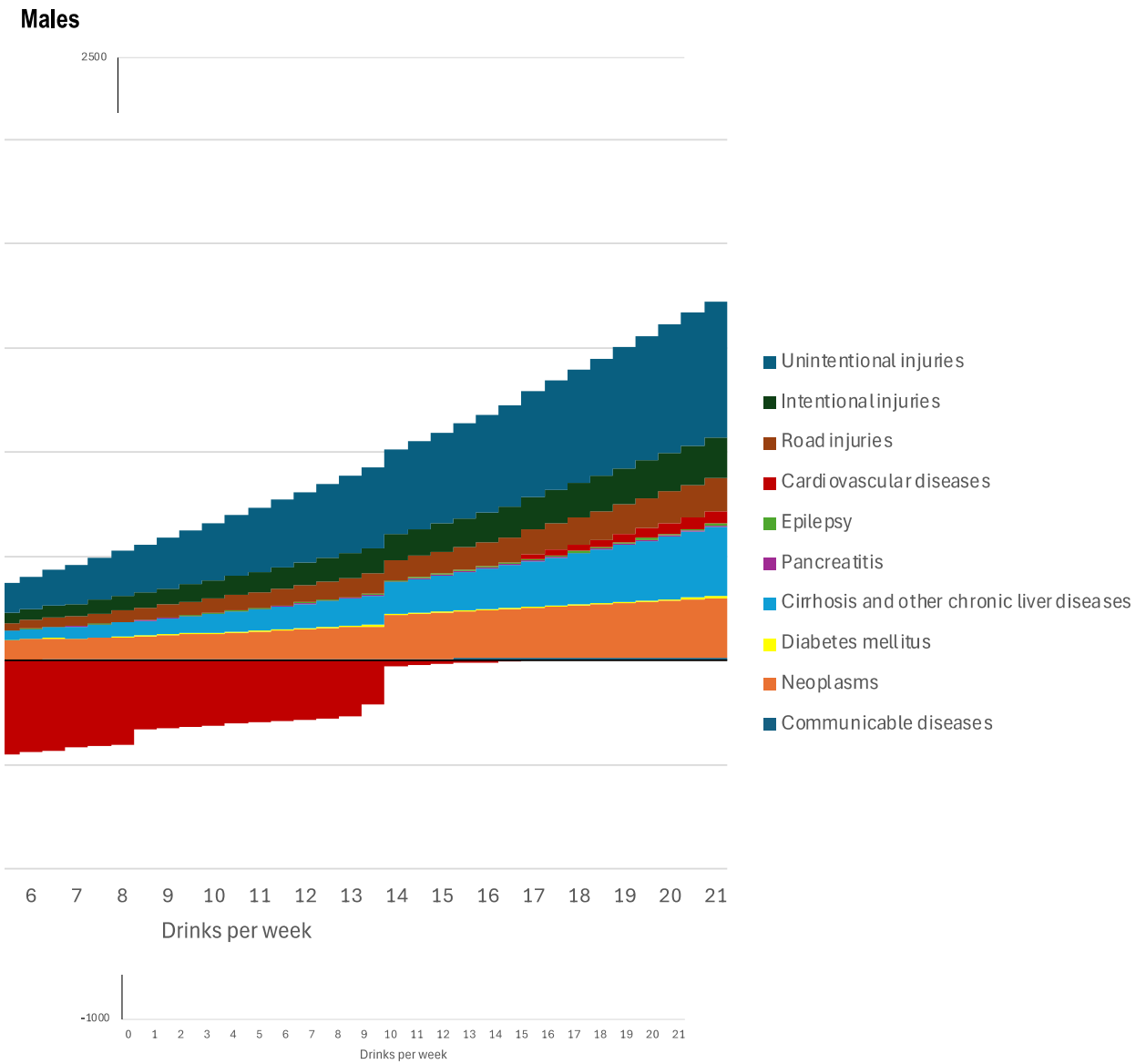

Figure A6. Lifetime risk of an alcohol-attributable DALY lost by sex and cause

Table A11. Lifetime risk of an alcohol-attributable cancer by sex, cancer site, and alcohol consumption per 1000 people

Sex	Cause	Drinks per week					
		1	2	3	7	14	21
Males	Lip and oral cavity cancer	0.23 (0.16, 0.28)	0.46 (0.33, 0.56)	0.70 (0.50, 0.85)	1.70 (1.18, 2.12)	3.65 (2.44, 4.68)	5.89 (3.79, 7.76)
	Other pharynx cancer	0.04 (0.01, 0.05)	0.07 (0.01, 0.10)	0.11 (0.02, 0.16)	0.26 (0.05, 0.39)	0.55 (0.10, 0.85)	0.86 (0.15, 1.42)
	Larynx cancer	0.06 (0.04, 0.07)	0.12 (0.08, 0.15)	0.18 (0.12, 0.22)	0.42 (0.27, 0.54)	0.86 (0.55, 1.13)	1.34 (0.84, 1.79)
	Esophageal cancer	0.14 (0.08, 0.19)	0.28 (0.17, 0.39)	0.43 (0.26, 0.60)	1.11 (0.70, 1.54)	2.64 (1.74, 3.60)	4.78 (3.31, 6.52)
	Colon and rectum cancer	5.06 (1.20, 8.69)	5.05 (1.20, 8.67)	5.04 (1.19, 8.65)	4.37 (2.69, 6.05)	8.82 (7.16, 10.48)	8.62 (7.00, 10.24)
	Liver cancer	0.05 (0.02, 0.08)	0.10 (0.04, 0.16)	0.15 (0.06, 0.24)	0.36 (0.13, 0.57)	0.71 (0.27, 1.16)	1.06 (0.39, 1.75)
	Breast cancer	-	-	-	-	-	-
	Total	**5.56 (1.66, 9.20)**	**6.08 (2.13, 9.69)**	**6.60 (2.72, 10.21)**	**8.22 (6.54, 10.12)**	**17.23 (14.74, 19.83)**	**22.56 (19.02, 26.33)**
Females	Lip and oral cavity cancer	0.13 (0.08, 0.18)	0.27 (0.16, 0.36)	0.40 (0.25, 0.54)	0.98 (0.59, 1.35)	2.11 (1.22, 3.01)	3.39 (1.89, 5.00)
	Other pharynx cancer	0.02 (0.00, 0.03)	0.04 (0.00, 0.05)	0.06 (0.00, 0.08)	0.14 (0.00, 0.22)	0.32 (0.00, 0.57)	0.54 (0.00, 1.15)
	Larynx cancer	0.03 (0.01, 0.05)	0.07 (0.01, 0.11)	0.11 (0.02, 0.16)	0.27 (0.04, 0.43)	0.60 (0.08, 1.07)	1.01 (0.12, 2.05)
	Esophageal cancer	0.07 (0.05, 0.09)	0.14 (0.09, 0.18)	0.21 (0.14, 0.28)	0.53 (0.34, 0.74)	1.21 (0.73, 1.80)	2.06 (1.15, 3.31)
	Colon and rectum cancer	0.00 (-1.22, 1.14)	0.00 (-1.21, 1.14)	0.00 (-1.21, 1.14)	0.34 (-8.08, 10.02)	2.35 (0.19, 4.87)	2.29 (0.19, 4.74)
	Liver cancer	0.11 (0.03, 0.16)	0.21 (0.07, 0.33)	0.33 (0.10, 0.50)	0.80 (0.23, 1.28)	1.76 (0.47, 3.09)	2.89 (0.71, 5.73)
	Breast cancer	2.23 (1.94, 2.56)	4.50 (3.91, 5.17)	6.81 (5.90, 7.84)	16.45 (14.19, 19.03)	34.68 (29.68, 40.60)	54.68 (46.28, 64.55)
	Total	**2.59 (1.36, 3.78)**	**5.23 (3.88, 6.57)**	**7.92 (6.41, 9.47)**	**19.52 (10.61, 29.80)**	**43.03 (37.22, 49.72)**	**66.87 (57.51, 77.52)**