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Effect of Alcohol Consumption on the Development of Depression, Anxiety and Suicidal Ideation: Update of a Systematic Review

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About this Document

This document was produced by Cochrane Canada for the Canadian Centre on Substance Use and Addiction. It was prepared for Cochrane Canada by Dr. Nancy Santesso and Matthew Melo.

Summary of Findings

Key Messages

- The literature assessing the link between alcohol consumption and the development of depression, anxiety and suicidal ideation continues to grow. This literature will be important to consider when updating the Low-Risk Alcohol Drinking Guidelines in Canada.
- In adults, daily quantity of alcohol intake has little to no influence on the odds of developing depression over 4–10 years, and it is likely that the frequency of alcohol intake does not either. Currently, the evidence for the influence of alcohol consumption on the onset of anxiety is uncertain, but it suggests that there is little to no influence, even with heavy episodic or binge drinking greater than once a month. However, past heavy episodic or binge drinking may be associated with a moderately greater odds of suicidal ideation.
- In adolescents, it is likely that higher levels or greater frequency of alcohol consumption has little to no influence on the development of depression or anxiety. However, greater frequency or heavy episodic or binge drinking may be associated with an increased odds of suicidal ideation. Initiating drinking before age 13 may also be associated with an increase in suicidal ideation, but not with anxiety.
- Longitudinal studies assessing the development of anxiety and suicidal ideation over time are needed to increase our certainty. Based on this update, studies should address the evidence associating greater frequency and heavy episodic drinking with the onset of suicidal ideation in both adults and adolescents, and in adolescents initiating alcohol consumption before age 13.

Introduction

In 2011, the Canadian Centre on Substance Use and Addiction (CCSA) published the first Low Risk Alcohol Drinking Guidelines (LRDGs).(Butt et al., 2011) The LRDGs provide people living in Canada with advice for safe drinking to reduce short-term and long-term health risks, including physical and mental illnesses. The LRDGs provide recommendations for the amount and frequency of alcohol intake per day and per week, and about the initiation of drinking in youth to reduce health risks. CCSA is leading the update of these guidelines in collaboration with representatives from other organizations in Canada (including Health Canada), scientists and knowledge mobilization specialists. The process involves broad consultation with key stakeholders and a review of the latest evidence about alcohol. Since the guidelines are being developed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) –ADOLOPMENT (Adaptation, Adoption, De Novo Development) process, evidence that was synthesized to inform other guidelines may be used to adopt, adapt or develop new recommendations for the update (Schünemann et al., 2017). The report is intended for members of the Low-Risk Alcohol Drinking Guidelines (LRDG) Scientific Expert Panels and those interested in understanding the detailed process followed in developing the new guidelines, such as policy makers, healthcare professionals and alcohol scientists.

In November 2018, a comprehensive systematic review of the evidence for the association between alcohol consumption and mental health outcomes was published to support the update of the National Health and Medical Research Council alcohol guidelines for people in Australia (Newton et al., 2018). This review addressed the association of patterns and levels of alcohol consumption with a variety of mental health disorders in studies and documents published up to May 2018.

Evidence for whether different amounts or frequencies of alcohol intake influence the risk of depression, anxiety and suicidal ideation was sought. The authors included longitudinal studies measuring alcohol intake at one point in time and mental health at a later point in time to determine the risk of future events, and when these studies were not available, they included cross-sectional studies. However, the authors cautioned that results from cross-sectional studies could only provide evidence of the concurrent prevalence of specific alcohol intake and mental health illness, and the risk of future events could not be determined. The review also attempted to provide evidence about future risks of mental health illness in different populations, such as in males and females, or in youth and adults. At the time of publication, however, there was little evidence to make conclusions about the risks in different populations.

Given the potential for publications since May 2018, an update of this review is warranted to inform the new LRDGs for people living in Canada.

Methods

Objective and Criteria

This is a rapid update of the systematic literature review on the association between alcohol consumption and the onset of mental health disorders that was published in 2018 (Newton et al., 2018). This update does not address all of the mental health disorders included in the 2018 review. While most of the inclusion and exclusion criteria were similar to the 2018 review (Appendix A), there were some changes. Changes from the 2018 review for this review included:

1. Addressing the association of alcohol consumption on the development of depression, anxiety and suicidal ideation;
2. Including longitudinal studies with a time element for depression and anxiety;
3. Including longitudinal studies and cross-sectional studies for suicidal ideation if no information was available from longitudinal studies; and
4. When possible, separating the evidence by subgroups for adults (including young adults, adults and older adults) and adolescents; and for males and females.

Our search for new studies has been particularly for longitudinal studies and studies conducted in Canada. In addition, we also hoped to find studies that analyzed data from Indigenous populations but were not successful.

Inclusion Criteria

To be included in this update, a study must:

1. Take as its focus people in the general population with physical or mental health conditions, or people with a family history of alcohol dependence;
2. Measure levels of alcohol intake, including any frequency or quantity and any patterns of intake (e.g., binge or heavy drinking);
3. Report the association of alcohol intake with anxiety, suicidal thoughts or depression:
    i. For depression or anxiety or suicidal ideation, it can be either a) alcohol levels measured at baseline, and anxiety or depression or suicidal ideation measured at least six months later; or b) anxiety or depression or suicidal ideation measured at baseline but alcohol levels in the past history measured;
    ii. For suicidal ideation, in addition to a) or b) include c) suicidal ideation and levels of alcohol reported for the same period of time; and
4. The study must be in English or French.

Exclusion Criteria

The following criteria were applied to determine to exclude a study from this update:

1. The study population has a specific clinical health condition only (e.g., cancer) or includes only people with alcohol use disorder;

2. A study reports whether mental health conditions (anxiety, depression, suicidal thoughts, disorders) lead to alcohol intake; or
3. A study reports the outcome of depression or anxiety for the same period as alcohol intake.

Search and Screening for Studies

Key electronic databases, trial registries, websites and other reference articles were searched for the 2018 review up to May and September 2018 using tailored search strategies for each source. For this rapid update, we conducted a comprehensive search of the key databases (Medline, Embase and PsycInfo) up to December 2021 using similar terms to the 2018 review search strategy (see Appendix B for the detailed search strategy), but we did not search grey literature or trial registries. Screening forms were pilot tested and revised by two investigators. To complete this rapid update, one investigator screened the titles and abstracts of all the studies, and another investigator screened 30% of the studies. Two investigators screened the full text of the potentially relevant articles. We used the Covidence web-based software platform (https://www.covidence.org/) to manage the screening.

Data Collection and Synthesis

For each study, one investigator extracted data into an Excel spreadsheet and another investigator verified the data. Disagreements were resolved by discussion. Key data collected included the population (including subgroups such as sex, age, or existing mental or physical illness), the pattern or level of alcohol intake and measurement, outcomes including depression, anxiety or suicidal ideation and measures, effects such as adjusted and unadjusted odds ratio and confidence intervals and time periods, and risk of bias information. When studies included analyses at multiple time points, we used data from the most recent time point.

Across studies there were differences in the categories of alcohol intake. In the 2018 review, the amount of alcohol consumed per day reported in studies was converted to grams of alcohol intake and then to categories of intake according to the LRDGs. We used the following categories: none (0 g/day), low (≤ 20 g/day for women and ≤ 30 g/day for men), moderate (30–40 g/day for women and 30–50 g/day for men), and high (≥ 40 g/day for women and ≥ 50 g/day for men). In articles where matching was not possible due to limited descriptions, the categories as provided by the authors were used.

We have synthesized the results across studies based on methods proposed by Cochrane for when meta-analyses are not possible (McKenzie & Brennan, 2022). We did not summarize results from each study so as not to emphasize one study over another based on unclear reasons. Instead, similar to the 2018 review, we present the relative risk, beta or correlation values from each study according to the amount or frequency of alcohol intake or both. We then interpreted the results by the direction of the effect and the size of the effect. We interpreted the probability of developing or the association of mental health conditions with alcohol intake using the Monson criteria suggested by Oleckno (Monson, 1980; Oleckno, 2002). If the calculated relative risk was between 1.1 and 1.5 it was considered weak or small; between 1.6 and 3.0 it was considered moderate; and 3.1 or higher it was considered strong or large. When the degree of correlation was provided, we interpreted 0.9–1.0 as very high correlation, 0.7–0.9 as high correlation, 0.5–0.7 as moderate correlation, 0.3–0.5 as low correlation, and less than 0.3 as little to no correlation. Note that these cut-offs refer to the risk estimate and not to the confidence intervals. The width of the confidence interval or a confidence interval that included the null effect informed whether an estimate was imprecise or

certain in the GRADE approach. If a confidence interval included a null effect or a result was not statistically significant, it was not interpreted as "no association" (Wasserstein & Lazar, 2016).

Risk of Bias Assessment

The 2018 review assessed the internal and external validity of the studies. For the studies found in this update, we used criteria identified for etiology or risk factor studies or both (Hayden et al., 2013). The key criteria used in this rapid update to inform internal validity were bias due to confounding; bias in selection of participants into the study (in particular, potential inclusion of people already with the outcome); bias in measurement of exposures or outcomes; and bias due to missing data. External validity was addressed in the GRADE approach when assessing the overall certainty of the evidence.

Assessment of Certainty of Evidence and GRADE Tables

We summarized the evidence for each mental health outcome (depression, anxiety and suicidal ideation) using GRADE. Where available, we included information by subgroup (age, sex and prior mental or physical illness). The certainty of the evidence was assessed using the GRADE approach for prognostic studies (Foroutan et al., 2020). The GRADE approach specifies that the ideal study design to inform questions about the probability of a health outcome is a cohort study, registry or database linkage study that compares the outcome between people with different characteristics (e.g., intakes of alcohol), and especially from one point in time to another. When these studies are used to answer questions about the probability of an outcome and there are no biases, that body of evidence can provide high certainty evidence for a conclusion about probability. However, if the studies are biased or there are other biases, then our certainty is reduced. In the GRADE approach, the following domains were used to rate down the certainty: study limitations (risk of bias), indirectness, inconsistency, imprecision and publication bias. The following domains were used to rate up the certainty: large effect, dose response and opposing biases. The overall certainty of the evidence was rated as very low, low, moderate or high. The following categories of certainty of evidence are interpreted as described:

- **High certainty evidence:** We are very confident that the variation in risk associated with the prognostic factor (probability of future events in those with or without the prognostic factor) lies close to that of the estimate.
- **Moderate**-certainty **evidence:** We are moderately confident that the variation in risk associated with the prognostic factor (probability of future events in those with or without the prognostic factor) is likely to be close to the estimate, but there is a possibility that it is substantially different.
- **Low-certainty evidence:** Our certainty in the estimate is limited. The variation in risk associated with the prognostic factor (probability of future events in those with or without the prognostic factor) may be substantially different from the estimate.
- **Very low-certainty evidence:** We have very little certainty in the estimate. The variation in risk associated with the prognostic factor (probability of future events in those with or without the prognostic factor) is likely to be substantially different from the estimate.

We used informative statements to communicate the findings: high certainty evidence is communicated using words such as "will" or "is"; moderate-certainty evidence is communicated as "likely"; low certainty evidence is communicated as "may" have an effect; and very low certainty evidence is communicated by statements that we are very uncertain (Santesso et al., 2020).

Results

Results of the Search

We screened 3,195 records from the search of the electronic databases by titles and abstracts. We retrieved the full text of 143 potentially relevant articles and identified 23 studies that met our criteria. These studies were added to the studies already identified by the 2018 review. The full flow of included studies is available in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram in Appendix C. The characteristics of the studies included in this update are available in Appendix D and the description of the studies from the 2018 review can be found in the technical report of the 2018 review (Newton et al., 2018).

The following results are reported by the risk or odds of developing an outcome: depression, anxiety and suicidal ideation. When possible, we separated the findings by the association of the quantity of alcohol consumption, frequency and heavy episodic or binge drinking, usually defined as consuming five standard drinks or more for men, or four standard drinks or more for women. For adolescents, we also included the association of the outcomes with age of initiation of drinking. For each outcome, we have summarized the association across studies and have not described the individual studies in the text, so as not to highlight one study over another. Instead, we summarize the results taking into consideration the risk of bias of the studies. After describing and synthesizing the studies, we provide a summary statement in bold of the association between the evidence and the outcome and identify the certainty of the evidence according to the GRADE approach. All tables in the results sections are colour coded to indicate the risk of bias assessment: studies that are shaded green are low risk, studies shaded yellow are moderate risk and studies shaded red are high risk.

Alcohol Consumption and Development of Depression

Adults

Quantity of Alcohol Consumption and Development of Depression

Thirty-three longitudinal studies assessed quantity of alcohol and the risk of developing depression over time in adults. Seven studies were found through the update of the 2018 review (Garcia-Esquinas et al., 2018; Gemes et al., 2019; Holmes et al., 2021; Keyes et al., 2020; Lee et al., 2018; Liang et al., 2021; Ruiz-Estigarribia et al., 2019). The studies included adults, young and older adults (14 were in older adults) with follow-up from 4–10 years in most studies (range from 1–28 years). Fifteen studies include participants from United States (U.S.), Australia or the United Kingdom (U.K.); only one study included participants in Canada (17,000). The results of 31 studies are described in Table 1. Two additional studies reported results that are in the text: Magnusson-Hansen 2017 followed 3,706 participants for six years and reported a beta 0.92 for adults with alcohol consumption at moderate or high levels; and Johnson 2013 reported a small increase in risk of depression in 384 women drinking six or more drinks per week and who had been drunk one or more times in the past year. Studies in Table 1 are organized by adults and older adults. Most studies reported the quantity of alcohol intake by different amounts of grams of alcohol consumed per day and the odds of depressive symptoms. In other studies, alcohol intake and depressive symptoms were measured using continuous scales and the association between these variables are reported as correlation or beta values.

When considering the association of increasing quantities of alcohol consumption and future development of depression within a study, most studies showed no association or increased odds.

When considering the effects across studies, most studies showed no association or odds of depressive symptoms with increasing amounts of alcohol intake per day, and in some studies a very small reduction. This lack of association was true when including only low risk of bias studies, but also true in moderate or high risk of bias studies. However, five out of the 31 studies found a small to moderate increase with amounts greater than current guidelines (greater than a "low intake"), but these were at moderate or high risk of bias. Findings were similar in studies where analyses were conducted for males and females.

There is little to no association of the quantity of alcohol intake and future development of depression over 4–10 years in adults and older adults. (High certainty evidence.)

Table 1: Quantity of alcohol consumption and development of depression

Study (country, number of participants, follow-up of depressive symptoms)	None 0 g/day	Low ≤ 20 (women) – ≤ 30 (men) g per day	Moderate 30-40-(women) and 30-50 (men) g per day	High ≥ 40 (women) and ≥ 50 (men) g per day
Adults	**None**	**Low**	**Moderate**	**High**
Holmes 2021 (Germany, *n* = 420; 1 year)	OR 0.47 (not stat sig)	*OR* =0.21 (stat sig)	ref	ref
Armeli 2015 (U.S., *n* = 522; 4 years)	-	Beta value indicated no effect for quantity and frequency of consumption		
Cabello 2017 (many countries, *n* = 7,908; 5-8 years)	ref	*OR* =0.93; 95% CI [0.57, 3.67]		-
Ruggles 2017 (U.S., *n* = 5,479 males; 6 years)	-	-	Males: *OR* =1.09	
Ruiz-Estigarribia 2019 (Spain, *n* = 14,908; median 10.4 years)	ref	HR = 1.08; 95% CI [0.93, 1.24]	-	-
Sui 2009 (U.S., *n* = 14,333; 12 years)		Males: *OR* =1.01; 95% CI [0.87, 1.18] Females: *OR* =1.00; 95% CI [0.75, 1.33]		
Bi Lee 2018 (Korea, *n* = 2,511 males, 4 years)	same	same	uOR = 0.98 to 1.00	uOR = 1.19 to 1.26 (stat sig)
Paljarvi 2009 (Finland, *n* = 15,926; 5 years)	ref	*OR* =1.11; 95% CI [1.01, 1.21]	*OR* =1.43; 95% CI [1.28, 1.60]	
Van Gool 2007 (Netherlands, *n* = 1,169; 6 years)	-	RR = 1.15; 95% CI [0.68, 1.96]	RR = 2.48; 95% CI [1.05, 5.69]	
Bulloch 2012 (Canada, *n* = 17,276 ≥12 years; 6 years)		HR = 0.9; 95% CI [0.7, 1.3]		
Gea 2012 (Spain, *n* = 13,619; 4–10 years)	ref	HR = 0.81; 95% CI [0.49, 0.86] Males: HR 0.76; 95% CI [0.45, 1.29] Females: HR 0.78; 95% CI [0.50, 1.21]	HR = 0.86; 95% CI [0.53, 1.39] Males: HR = 0.76; 95% CI [0.40, 1.47] Females: HR = 1.06; 95% CI [0.43, 2.63]	
Keyes 2019 (many countries, *n* = 57,296, ≥ 50 years; 10 years)	uOR = 1.75 (1.66,1.85)	uOR = 1.41; 95% CI [1.35,1.48]	ref	uOR = 1.19; 95% CI [1.11, 1.27]

Gemes 2019 (Sweden, *n* = 5087, 10-12 years)	RR = 1.60; 95% CI [1.27,2.01]	ref	RR = 1.05; 95% CI [0.83, 1.32]	RR = 1.77; 95% CI [1.13, 2.78]
Bell 2015 (U.K., *n* = 7,478; 28 years)	HR = 1.02 (0.89,1.16)	ref	HR = 0.86; 95% CI [0.53, 1.39]	
Onwuameze 2013 (U.S., *n* = 257 males; 3 years)	-	Males: RR = 0.94; 95% CI [0.79, 1.13]		
Otten 2018 (Netherlands, *n* = 594; 4 years)	ref	Beta values indicated no effect for quantity of consumption in males or females		
Mason 2008 (U.S., *n* = 429; 4 years)	-	Beta values indicated no effect for quantity of consumption		
Older adults	**None**	**Low**	**Moderate**	**High**
Weyerer 2013 (Germany, *n* = 2512 older adults; 3 years)	ref	HR = 0.84; 95% CI [0.62, 1.14]	HR = 1.18; 95% CI [0.79, 1.76]	
Bots 2008 (EU, *n* = 826 older men; 5 years)	ref	Males: *OR* =0.36; 95% CI [0.15, 0.90]	Males: *OR* =0.64; 95% CI [0.23, 1.80]	
Hiles 2015 (AUS, *n* = 1,410 older adults; 5 years)	ref	Males: *OR* =1.35; 95% CI [0.45, 4.08] Females: *OR* =0.70; 95% CI [0.33, 1.49]	Males: *OR* =0.83; 95% CI [0.20, 3.43] Females: *OR* =0.36; 95% CI [0.04, 3.43]	
Luppa 2012 (Germany, *n* = 860 older adults; 8 years)	ref		HR = 2.33; 95% CI [1.09, 4.96]	
Liang 2021 (China, England, U.S., *n* = 29,506 middle aged and older adults; median 8 years)	ref	Men: HR = 0.89; 95% CI [0.77, 1.04] Women: HR = 0.89; 95% CI [0.80, 0.98]	Men: HR = 0.94; 95% CI [0.63,1.38] Women: HR = 0.91; 95% CI [0.76, 1.08]	
Chang 2016 (U.S., *n* = 21,728 older adults; 10 years)	ref			Females: HR = 1.13; 95% CI [1.01, 1.26]
An 2015 (U.S., *n* = 24,759 older adults; 10 years)	ref	HR = 1.05; 95% CI [0.98, 1.13] Males: HR = 1.05; 95% CI [0.95, 1.17] Females: HR = 1.09; 95% CI [0.98, 1.20]		
Byers 2012 (U.S., *n* = 7240 older women; 12 years)	ref	Females: *OR* =0.99 (0.69, 1.43)		
Garcia-Esquinas 2018 (Spain, *n* = 1,200 older adults; 2.8 years)	ref	Same as mod	Prevalence rate ratio: 1.03; 95% CI [0.84, 1.26]	Prevalence rate ratio: 0.88; 95% CI [0.56, 1.36]
Lang 2007 (U.K., *n* = 7286 older adults; 3 years)	-	*z* = 0.02 (not stat sig) Males: *z* = 0 Females: *z* = 0		
Garcia-Esquinas 2018 (Spain, *n* = 3,971 older adults; 7.4 years)	ref	Prevalence rate ratio: 0.92; 95% CI [0.79, 1.06]	Prevalence rate ratio: 1.00; 95% CI [0.84, 1.20]	
Gea 2013 (Spain, *n* = 5,505 older adults; 7 years)	ref	HR 0.79; 95% CI [0.53,1.16] Males: HR 0.75; 95% CI [0.39, 1.43] Females: HR 0.61; 95% CI [0.30, 1.27]		

Tanaka 2011 (Japan, *n* = 9,201 older adults; 7 years)	ref	Males: *OR* =0.54; 95% CI [0.26, 1.13] Females: *OR* =0.67; 95% CI [0.37, 1.19]	Males: *OR* = 0.99; 95% CI [0.46, 2.11] Females: *OR* =0.39; 95% CI [0.05, 3.08]
Paulson 2018 (U.S., *n* = 3,177 older adults; 8 years)	ref	Beta value indicated a moderate increase (beta = 0.493)	
Tait 2012 (AUS, *n* = 39,104 older adults; 4 years)	Ref (up to 20 g/day)	Males: *OR* =0.99; 95% CI [0.82, 1.19] Females: *OR* =1.22; 95% CI [1.08, 1.38]	Males: *OR* =1.3; 95% CI [1.06, 1.59] Females: *OR* =1.54; 95% CI [1.22, 1.95]

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Frequency of Alcohol Consumption and Development of Depression

Nine longitudinal studies assessed the frequency of alcohol intake and the risk of developing depression over time. No new studies were found in the update of the review. Frequency was measured differently across studies. However, we estimated frequency as none, occasional (<1 drink per month), low (1–4 times per week) and high (≥ 4 times per week). The results of studies that included adults and young adults (six studies), and older adults (three studies) are shown in Table 2. Follow-up of participants covered a wide range: from two years to 28 years. Two studies included participants from Canada (Meng, 2017; Meng et al., 2017); and the other studies included participants from the U.S., the U.K., Norway, China and Taiwan. The study from Taiwan with 2,500 older adults was the only study at low risk of bias; and most of the other studies were at moderate risk of bias.

Most studies showed little to no association between the frequency of alcohol intake and future development of depression, and in fact the odds of depression from most studies were in the direction of a reduction in odds with increasing frequency of alcohol intake. There was one exception in a small study from Canada that showed a moderate positive association between occasional drinking (< 1 per month) and future development of depressive symptoms after 4 years, but this study was at moderate risk of bias.

There is likely little to no association between the frequency of alcohol consumption and the development of depression. (Moderate-certainty evidence due to risk of bias of the included studies.)

Table 2: Frequency of alcohol consumption and development of depression

Study (country, number of participants, follow-up of depressive symptoms)	None	Occasional < 1 per month	Low 1–4 times per month	Moderate 2–3 times per week	High ≥ 4 times per week
Tsai 2013 (Taiwan, *n* = 2,629 older adults; 2 years)	ref			*OR* =0.89; 95% CI [0.63, 1.26]	
Cheng 2016 (China, *n* = 10,858 older adults; 2 years)	ref	-	Males: *OR* =0.7; 95% CI [0.5, 0.9] Females: *OR* =1.3; 95% CI [0.5, 3.8]		
Cougle 2015 (U.S., *n* = 34 653 adults; 3 years)	ref		-	*OR* =0.88; 95% CI [0.83, 0.94]	
Meng 2017 (Canada, *n* = 877 adults; 4 years)	ref	RR 1.56; 95% CI [1.40, 1.75]	RR = 0.68; 95% CI [0.61, 0.76] Men: RR = 0.45; 95% CI [0.33, 0.62] Women: RR = 0.75; 95% CI [0.66, 0.85]		
Augestad 2008 (Norway, *n* = 6,661; 3-12 years)	ref	Males: HR 0.75 Females: 1.17	Males: 0.62 Females: 1.18	Males:0.47 to 0.59 Females: 0.72 to 1.02	
Meng 2017 (Canada, *n* =12,227 adults; 16 years)	ref		HR = 0.88; 95% CI [0.78, 1.00] Men: HR = 0.79; 95% CI [0.64, 0.98] Women: HR = 0.92; 95% CI [0.80, 1.05]		
Bell 2015 (U.K., *n* =7,478; 28 years)	HR 1.24	HR 0.97	ref	HR 1.17	
Cheng 2016 (China, *n* =17,708 older adults; 2 years)	ref	-	*OR* =0.6; 95% CI [0.5, 0.7]	*OR* =1.2; 95% CI [0.8, 1.7] compared to less than daily	
Mason 2008 (U.S., *n* =429; 4 years)	-	Beta values indicated no effect for quantity or frequency of consumption			

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Heavy Episodic or Binge Drinking and Development of Depression

Twelve longitudinal studies assessed the risk of developing depression in adults who reported binge drinking or heavy episodic drinking. One new study was found in the update of the review (Ruiz-Estigarribia et al., 2019). One study included older adults (Chou et al., 2011) and one large study included approximately 17,000 participants from Canada. The low risk of bias studies had similar definitions of heavy episodic or binge drinking (e.g., from ≥ 4–5 drinks per occasion over the past week to 12 months), but the length of follow-up of these studies ranged from 1 to 12 years (see Table 3).

The larger studies at low risk of bias found little to no association of heavy episodic or binge drinking with the odds of developing depressive symptoms in the future. However, there is some inconsistency as there were smaller studies also at low risk of bias that found a moderate to large association. The length of follow-up also did not appear to explain the differences.

There is likely little to no association of heavy episodic or binge drinking with the development of depression in the future (Moderate-certainty evidence due to some inconsistency.)

Table 3: Heavy episodic or binge drinking and development of depression

Study (country, number of participants, follow-up of depressive symptoms)	None	Binge or heavy drinking (≥ 4–5 drinks per occasion)
Zhang 2017 (Germany, *n* = 196; 1 year)	ref	"High risk drinker": *OR* = 1.73
Chou 2011 (U.S., *n* = 13,442 older adults; 3 years)	ref (non-HED)	*HED <1 month* Males: *OR* = 1.27; 95% CI [0.56, 2.86] Females: *OR* = 0.89; 95% CI [0.52, 1.51 *HED >1 month* Males: *OR* = 0.94; 95% CI [0.44, 2.03] Females: *OR* = 0.79; 95% CI [0.40, 1.55]
Cabello 2017 (many countries, *n* = 7,908; 5-8 years)	ref	*OR* =1.59; 95% CI [0.67, 3.75]
Sullivan 2011 (U.S., *n* = 2 446 adults; 6 years)	ref	*OR* =2.14; 95% CI [1.49, 3.07]
Ruiz-Estigarribia 2019 (Spain, *n* = 14,908; median 10.4 years)	ref	HR = 0.95; 95% CI [0.81, 1.12]
Gustafson 2012 (U.S., *n* = 3,194; up to 12 years)	ref	Correlation coefficient indicated no effect (-0.045)
Piasecki 2017 (U.S., *n* = 986; 1 year)	ref	Correlation coefficient indicated no effect (-0.02)
Paljarvi 2009 (Finland, *n* = 15,926; 5 years)	ref	Frequency of intoxication OR ranged from 1.14 to 1.49
Bulloch 2012 (Canada, *n* = 17,276; ≥ 12 years; 6 years)	-	HR = 1.1 (0.9,1.3)
Sloan 2011 (U.S., *n* = 7,386; ~20 years)	ref	Difference in propensity scores 3.7 (with occasional HED) and -1.0 (with other drinkers) representing little to no difference
Bell 2015 (U.K., *n* = 7,478; 28 years)	2–3 drinks/session	HR = 0.81; 95% CI [0.49, 0.86]
Mason 2008 (U.S., *n* = 429; 4 years)	ref	Beta values indicate no effect for heavy episodic drinking

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Adolescents

Quantity, Frequency and Heavy or Binge Drinking and Development of Depression

Nineteen longitudinal studies assessed different quantities and frequencies of alcohol consumption (including heavy or binge drinking) on the future development of depression. No new studies were found in the update of the review. All studies included in this update were longitudinal studies assessing alcohol intake and development of depression or depressive symptoms at a later time point; cross-sectional studies were not included. Table 4 provides a summary of the results from the included studies measuring quantity and frequency of alcohol intake on development of depressive symptoms and Table 5 provides results for studies measuring heavy or binge drinking on development of depressive symptoms.

Quantity and frequency of alcohol intake: Thirteen studies all from the 2018 review reported the association of the quantity or frequency of alcohol intake on the development of depression in future. Most of the studies analyzed data collected from the U.S., with some from the U.K. One study analyzed data from Canada (Hooshmand et al., 2012) and another data from Finland (Patwardhan et al., 2017). Depressive symptoms (rather than diagnosis or episode of depression) were typically measured after three years, but there is one study from Finland reporting the development of depressive symptoms after 12 years (Patwardhan et al., 2017). Most studies calculated the correlation or beta values for the association of alcohol intake and depressive symptoms using continuous scales. Only one study quantified the odds of depressive symptoms given different amounts of alcohol intake or frequency (Edwards et al., 2014). We therefore have interpreted the magnitude of the associations in Table 4 in most studies using the beta and correlation values.

Almost all studies reported little to no association with the quantity or frequency of alcohol intake with future development of depression over one to 12 years. These studies were at low to high risk of bias and included over 16,000 participants. Two studies with approximately 8,000 participants in total and both at moderate or high risk of bias reported small to moderate increased odds of depressive symptoms or episodes after on to three years of occasional and weekly alcohol consumption.

Heavy or binge drinking: Nine studies measured the association of heavy or binge drinking with future depressive symptoms in approximately 25,000 participants (see Table 5). Heavy or binge drinking was defined consistently across studies as ≥ 3 or 5 drinks per occasion or drinking to intoxication. Follow-up of depressive symptoms ranged from one to 13 years, which was measured in the largest study of over 12,000 adolescents (Wilkinson et al., 2016).

Most studies found little to no association of heavy or binge drinking with the development of depressive symptoms. The results of these studies were consistent with the largest study with over 12,000 participants, which was at low risk of bias (Wilkinson et al., 2016). Two studies found a small association, but both were at high risk of bias.

There is likely little to no association of the frequency or quantity of alcohol consumption, including heavy or binge drinking, and the development of depressive symptoms in adolescents. (Moderate-certainty evidence due to risk of bias.)

Table 4: Frequency or quantity of alcohol consumption and development of depression

Study (country, number of participants, follow-up of depressive symptoms)	Measure of alcohol intake	Results	Association of alcohol intake with development of depression
Hooshmand 2012 (Canada, *n* = 4,000; up to 3 years)	Quantity	Correlation values ranged from 0.04 to 0.14	Little to none
Parrish 2016 (Mexico, *n* = 620; 2 years)	Frequency	Beta value 0.04	Little to none
Hooshmand 2012 (Canada, *n* = 4,000; up to 3 years)	Frequency	Correlation values ranged from 0.09 to 0.17	Little to none
Danzo 2017 (U.S., *n* = 593 families, up to 3 years)	Quantity and frequency	Correlation coefficients ranged from 0.02 to 0.30; values were lower in males	Little to none
Edwards 2014 (U.K., *n* = 7,100, adolescents; 1-3 years)	Medium frequency (occasional compared to none)	Males: *OR* =2.25 (stat sig) Females: *OR* =1.63 (stat sig)	Moderate increases
Edwards 2014 (U.K., *n* = 7,100, adolescents; 1-3 years)	High frequency (weekly compared to none)	Males: *OR* =2.54 (stat sig) Females: *OR* =1.93 (stat sig)	Moderate increases
Fleming 2008 (U.S., *n* = 885; up to 3 years)	Frequency	Correlation values ranged from 0.05 to 0.23; values were lower in males	Little to none
McCarty 2012 (U.S., *n* = 512; 3 years)	Any consumption versus none	Beta values ranged from 0.02 to 0.17	Little to none
Wymbs 2014 (U.S., *n* = 521; 4 years)	Frequency	Beta values ranged from 0.02 to 0.18; no consistent difference in values between males and females	Little to none
Mason 2008 (U.S., *n* = 429; 2–6 years)	Quantity	Beta values ranged from 0.10 to 0.21	Little to none
Mason 2008 (U.S., *n* = 429; 2–6 years)	Frequency	Beta values ranged from 0.08 to 0.22	Little to none
Scholes-Balog 2015 (AUS, *n* = 927; 3 years)	Frequency	Beta values ranged from -0.051 to 0.049	Little to none
Mackie 2011 (U.K., *n* = 393; 1 year)	Quantity and frequency	Correlation values ranged from 0.08 to 0.20	Little to none
Mason 2011 (U.S., *n* = 151; 2 years)	Quantity and frequency	Beta values ranged from 0.24 to 0.27	Little to none
Patwardham 2017 (Finland, *n* = 6,963; 12 years)	Quantity and frequency	Beta value was 0.10	Little to none
Skogen 2016 (Norway, *n* =1,095; 1–3 years)	Weekly drinking versus less than weekly	Differences in beta coefficients ranged from 0.26 to 0.13	Small increase

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Table 5: Heavy or binge drinking and development of depression in adolescents

Study (country, number of participants, follow-up of depressive symptoms)	None	Heavy or binge drinking (≥3 or ≥5 drinks per occasion, or drinking to intoxication)	Association of alcohol intake with development of depression
Gustafson 2012 (U.S., *n* = 3,194; up to 12 years)	ref	Correlation coefficients ranged from 0.03 to 0.07	Little to none
Wilkinson 2007 (U.S., *n* = 12,107; 13 years)	ref	Beta values at 0.01 and -0.01	None
Cisler 2012 (U.S., *n* = 2,511; 1 year)	ref	Beta values ranged from 0.01 to 0.06	Little to none
Pesola 2015 (U.K., *n* = 1,883; 2 years)	ref	Small negative correlation, statistically significant for both males and females	Little to none
Needham 2007 (U.S., *n* = 10,828; 6 years)	ref	Very small negative correlation, statistically significant for females	None
Skogen 2016 (Norway, *n* = 1,095; 1-3 years)	ref	Beta values ranged from 0.27-0.32	Small
Mason 2011 (U.S., *n* = 151; 2 years)	ref	Beta values ranged from 0.24 to 0.27	Small
Chan 2013 (AUS, *n* = 969; 3 years)	ref	Beta values ranged from 0.08 to 0.15	Little to none
Mason 2008 (U.S., *n* = 429; 2-6 years)	ref	Beta values ranged from 0.13 to 0.14	Little to none

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Alcohol Consumption and Development of Anxiety

We found 10 longitudinal studies measuring the odds of developing anxiety in future with different levels of alcohol consumption and therefore did not include cross-sectional studies assessing the association of anxiety with alcohol consumption measured at the same time point. We found four studies for this update (Carvalho et al., 2018; Knox et al., 2019; Mustonen et al., 2021; Newton-Howes et al., 2019) and included six studies from the 2018 review. Studies did not clearly report the quantity or frequency of alcohol intake, therefore we categorized alcohol consumption into levels: none, low, moderate and high. Moderate level of intake was similar to a score of 3–7 in women and 4–7 in men on an AUDIT-C (Alcohol Use Disorders Identification Test) questionnaire (Babor et al., 2001; Richards et al., 2020).

Adults

Level of Alcohol Intake and Development of Anxiety

There are two longitudinal studies that assessed the development of anxiety in people with different levels of alcohol intake (Carvalho et al., 2018; Knox et al., 2019) (Table 6). Carvalho assessed intake in 6,095 adults aged ≥ 50 years old in Ireland after two years and was at low risk of bias (Carvalho et al., 2018). It found that the odds were either similar or slightly reduced with higher levels of alcohol intake compared to low levels. The Knox et al. study (at moderate risk of bias) measured consumption of different levels of alcohol over a three-year period in approximately 22,000 people in

the U.S., some of whom increased or decreased their intake and others who did not change their intake. The data for people who did not change their intake was used to calculate the odds of developing anxiety after three years (Knox et al., 2019). This study found odds ratios close to no association for moderate to high risk drinking levels, but more than doubling the odds at very high-risk levels. Overall, the results are inconsistent between the studies.

The evidence is very uncertain about the influence of different levels of alcohol consumption on the odds of developing anxiety in future: it may be similar whether drinking at moderate to high risk levels but greater when drinking at very high-risk levels. (Very low certainty evidence due to risk of bias, imprecision and inconsistency.)

Table 6: Levels of alcohol consumption and development of anxiety

Study (country, number of participants, follow-up)	Low risk	Moderate risk	High risk	Very high risk
Carvalho 2018 (Ireland, *n* = 6,095, older adults; 2 years)	ref (non-drinker)	*OR* =0.82; 95% CI [0.54, 1.24] Males: *OR* =0.61; 95% CI [0.28, 1.37] Females: *OR* =0.90; 95% CI [0.55, 1.47]	*OR* =0.95; 95% CI [0.54, 1.66] Males: *OR* =0.71; 95% CI [0.30, 1.68] Females: *OR* =1.18; 95% CI [0.59, 2.34]	
Knox 2019 (U.S., *n* = 22,005; 3 years)	ref	uOR= 0.94; 95% CI [0.65, 1.35]	uOR= 1.13; 95% CI [0.63, 2.05]	uOR= 2.5; 95% CI [1.73, 3.62]

Risk of bias assessment: green = low risk; yellow = moderate risk

Heavy Episodic Drinking and Development of Anxiety

Two longitudinal studies assessed the risk of developing anxiety in heavy versus non-heavy drinkers (Carvalho et al., 2018; Chou et al., 2011) (Table 7). Both studies sampled older adults: one in the U.S. after three years (Chou et al., 2011) and the other in Ireland after two years (Carvalho et al., 2018). The estimates from both studies show different direction of associations within and across the studies for the odds of developing anxiety with greater frequency of heavy episodic drinking, but confidence intervals are wide and overlap across studies. Considering the estimates and overlapping confidence intervals, the evidence may suggest that there is little to no association.

There may be little to no difference in the odds of developing anxiety with no heavy episodic or binge drinking and monthly or more frequent episodes in adults. (Low certainty evidence due to inconsistency and imprecision.)

Table 7: Heavy episodic drinking and development of anxiety

Study (country, number of participants)	Non-HED drinker	Less than monthly	Monthly or more
Chou 2011 (U.S., males *n* = 5,461; females *n* = 7,981)	ref	Males: *OR* =2.25; 95% CI [0.87, 5.8] Females *OR* =1.28; 95% CI [0.58, 2.82]	Males: *OR* =0.88; 95% CI [0.32, 2.42] Females: *OR* =0.50; 95% CI [0.18, 1.39]
Carvalho 2018 (Ireland, *n* = 6,095)	ref (non-drinker)	*OR* =0.73; 95% CI [0.48, 1.11] Males: *OR* =0.53; 95% CI [0.25, 1.13] Females: *OR* =0.82; 95% CI [0.51, 1.33]	*OR* =1.71; 95% CI [0.90,3.27] Males: *OR* =1.23; 95% CI [0.45,3.35] Females: *OR* =2.22; 95% CI [1.01,4.86]

Risk of bias assessment: green = low risk

Adolescents

Levels of Alcohol Consumption and Development of Anxiety

Five longitudinal studies assessed the development of anxiety over time with different levels of alcohol consumption in adolescents. No new studies were found with the update of the review. Studies included adolescents from the U.S., the U.K. and Finland and followed the development of anxiety over one to three years, with the exception of one study that measured anxiety after 13 years (Cerdá et al., 2013). The studies measured levels of alcohol consumption using quantity or frequency of consumption or a combination of both measures; measured anxiety at different follow-up periods; and also reported association as a continuum of intake or categorically. We therefore considered the direction of the effect and the magnitude to synthesize the results, as well as the risk of bias of the studies (Table 8). Two studies were at low risk of bias, but the sample sizes were small at approximately 500 participants in each (Cerdá et al., 2013; Parrish et al., 2016).

Based on the included studies, at low risk of bias there was little to no association with increasing alcohol consumption and development of anxiety over time. Although, the number of people in the low risk of bias studies is small, the results were similar in the moderate and high risk of bias studies that included approximately 10,000 adolescents.

There is likely little to no association of the frequency or level of alcohol consumption with the development of anxiety in adolescents. (Moderate-certainty evidence due to risk of bias.)

Table 8: Levels of alcohol consumption and development of anxiety

Study (country, number of participants, follow-up)	Measure of alcohol intake	Results	Association of alcohol intake with development of anxiety
Parrish 2016 (U.S., *n* = 620 14 year olds; 2 years)	Frequency	Unadjusted association was not statistically significant and represent little to no effect (beta = 0.02)	None
Cerdá 2016 (U.S., *n* = 503 boys, ages 13–19; 13 years)	Frequency (number of occasions of drinking in past year)	Did not statistically significantly increase anxiety	Little to none
Cerdá 2016 (U.S., *n* = 503 boys, ages 13–19; 13 years)	Quantity (average number of drinks per occasion in past year)	Statistically significantly increased anxiety For each additional increase to the average number of drinks per occasion, anxiety T-score increased by a small amount: 0.12, 95%CI [0.05, 0.19]	Little to none
Fröjd 2011 (Finland, *n* = 2,070 15–16 year olds; 2 years)	Drinking ≥ once/week compared to less	*OR* =1.3; 95% CI [0.6, 2.8]	Little to none
Fröjd 2011 (Finland, *n* = 2,070 15–16 year olds; 2 years)	Drunk at least once a week compared to less	*OR* =0.8; 95% CI [0.2, 3.6]	Little to none
Edwards 2014 (U.K., *n* = 7100, 1–3 years)	Medium frequency (occasional compared to none)	Males: uOR = 1.13; 95% CI [0.65, 1.95] Females: *OR* =1.19; 95% CI [0.80, 1.76]	Little to none
Edwards 2014 (U.K., *n* = 7,100, 1–3 years)	High frequency (weekly compared to none)	Males: uOR = 1.20; 95% CI [0.55, 2.62] Females: *OR* =1.41; 95% CI [0.84, 2.36]	Little to none
Mackie 2011 (U.K., *n* = 809, up to 18 months)	Quantity and frequency	No statistically significant directional effects; degree of correlation over time was none to low	Little to none

Risk of bias assessment: green = low risk; yellow = moderate risk; red = high risk

Age at Initiation

There are two longitudinal studies that report the development of anxiety disorder by age of initiation of alcohol consumption in adolescents: two of the studies assessed age at first alcohol intoxication (Mustonen et al., 2021; Newton-Howes et al., 2019); and one study also assessed age at first drink (Newton-Howes et al., 2019). Both studies are at moderate risk of bias and together include about 2,500 adolescents (Table 9). The results represent little to no association in the odds of developing anxiety based on age of initiation of drinking.

Drinking initiated before age 13 may not be associated with the onset of anxiety. (Low certainty evidence due to risk of bias and imprecision.)

Table 9: Association of development of anxiety and age at initiation of drinking

Study (country, number of participants)	Never (≥ 18 years)	Never (≥ 16 years)	Late teen (15–16 years)	Middle teen (13–14 years)	Pre-teen (≤ 12 years)
Age at first intoxication					
Mustonen 2021 (Finland, *n* = 1,492)	-	ref	HR = 0.91; 95% CI [0.62, 1.34]	HR = 1.08; 95% CI [0.81, 1.45]	HR = 1.39; 95% CI [0.84, 2.30]
Newton-Howes 2019 (New Zealand, *n* = 962)	ref	*OR* = 1.01; 95% CI [0.91, 1.13]			
Age at first drink					
Newton-Howes 2019 (New Zealand, *n* = 962)	ref	*OR* = 1.16; 95% CI [0.86, 1.57]			

Risk of bias assessment: yellow = moderate risk

Alcohol Consumption and Association with or Development of Suicidal Ideation

Eight cohort studies assessed the association of alcohol consumption and suicidal ideation in adults and young adults. Six studies were from the update (Kim et al., 2021; Kim & Lee, 2018; Kim & Burlaka, 2018; Kittel et al., 2019; Parker et al., 2019; Richards et al., 2020) and two studies were from the 2018 review (Glasheen et al., 2015; Herberman Mash et al., 2016). We did not find longitudinal studies measuring the odds of having suicidal ideations in the future. Instead, the studies are cross-sectional and only measure the association at one point in time. Due to the small numbers of studies and the differences in the categorization of quantity or frequency across studies, we have combined the quantity and frequency of alcohol intake into categorical levels: none, low, moderate and high. Moderate level of intake was similar to a score of 3–7 in women and 4–7 in men on AUDIT-C questionnaire (Babor et al., 2001; Richards et al., 2020).

Quantity and Frequency of Alcohol Intake and Suicidal Ideation

Seven cross-sectional studies assessed the association of levels of alcohol consumption with suicidal ideation at one point in time.(Glasheen et al., 2015; Herberman Mash et al., 2016; Kim et al., 2021; Kim & Lee, 2018; Kim & Burlaka, 2018; Kittel et al., 2019; Parker et al., 2019; Richards et al., 2020). Six of the studies included participants from U.S. and one included participants from Korea (Table 10). These studies typically compared higher levels of intake to different reference levels (none or low level) and calculated the odds of suicidal ideation. One study did not report associations using an odds ratio (Kim & Burlaka, 2018). This study reported that alcohol dependence and abuse was positively associated with suicidal ideation (beta 0.30 in males and beta 0.47 in females). All studies were at least at moderate risk of bias to answer the question about whether increasing levels of intake lead to future increases in suicidal ideation. The rationale for this risk of bias is that cross-sectional studies can only confirm association at the same point in time.

The large studies at moderate risk of bias found little to no association, while the smaller studies at moderate or high risk of bias found a small or weak association between suicidal ideation and higher levels of alcohol consumption. There also appeared to be no differences in the association between males and females.

Greater levels of alcohol consumption may not be associated with greater future suicidal ideation in adults. (Low certainty evidence due to risk of bias and inconsistency.)

Table 10: Association of level of alcohol consumption with suicidal ideation

Study (country, number of participants)	None	Low level	Moderate level (AUDIT-C score 3-7 in women and 4-7 in men)		High level	
Kim 2018 (U.S., *n* = 13,069)	ref	Males: *OR* =1.10; 95% CI [0.79, 1.52] Females: *OR* =1.21; 95% CI [0.91, 1.63]	Males: *OR* =1.44; 95% CI [0.91, 2.28] Females: *OR* =1.03; 95% CI [0.51, 2.09]		Males: *OR* =1.54; 95% CI [1.05, 2.24] Females: *OR* =0.63; 95% CI [0.22, 1.8]	
Kittel 2019 (U.S., *n* = 269,078)	ref	Males: *OR* =1.01; 95% CI [0.94, 1.30] Females: *OR* =1.07; 95% CI [0.95, 1.21]	Males: *OR* =1.02; 95% CI [0.86, 1.21] Females: *OR* =1.08; 95% CI [0.94, 1.23]	Males: *OR* =0.83; 95% CI [0.70,0.97] Females: *OR* =1.07; 95% CI [0.91-1.25]	Males: *OR* = 0.87; 95% CI [0.71, 1.08] Females: *OR* =1.00; 95% CI [0.84, 1.18]	Males: *OR* =0.97; 95% CI [0.75, 1.24] Females: *OR* =1.17; 95% CI [0.82, 1.59]
Herberman Mash 2016 (U.S., *n* = 3,813)	ref		*OR* = 1.05 (0.67, 1.65)			
Parker 2019 (U.S., *n* = 3,239)	ref				*OR* = 2.02; 95% CI [1.13, 3.64]	
Kim 2021 (Korea, *n* = 5,982)	ref		*OR* = 1.24; 95% CI [1.04, 1.48]		*OR* = 1.77; 95% CI [1.43, 2.17]	
Richards 2020 (U.S., *n* = 44,106)	ref	uOR 0.83 (0.79, 0.88)	uOR = 0.89; 95% CI [0.84, 0.94]		uOR = 1.84; 95% CI [1.67, 2.03]	

Risk of bias assessment: yellow = moderate risk; red = high risk

Heavy Episodic Drinking and Suicidal Ideation

Two cross-sectional studies from the U.S. assessed heavy episodic drinking with suicidal ideation using estimates that were unadjusted for other variables (Glasheen et al., 2015; Richards et al., 2020). Both found a small to moderate increase in suicidal ideation with heavy episodic drinking monthly or more compared to never or less than monthly but were at high risk of bias (Table 11). The difference in association between males and females was small.

In adults, there may be a small to moderate association between heavy episodic or binge drinking and the onset of suicidal ideation. (Low certainty evidence due to risk of bias.)

Table 11: Association of heavy episodic drinking with suicidal ideation

Study (country, number of participants)	Never	Less than monthly	Monthly or more
Glasheen 2015 (U.S., *n* = 136,500)	ref		Males: uOR = 1.63; 95% CI [1.43, 1.85] Females: uOR = 1.94, 95% CI [1.74, 2.16]
Richards 2020 (U.S., *n* = 44,106)	ref	uOR = 1.19 [1.13, 1.26]	uOR = 1.63; 95% CI [1.53, 1.74]

Risk of bias assessment: red = high risk

Adolescents

Seven cross-sectional studies reported on the association between alcohol consumption and suicidal ideation in adolescents. Three studies were from the update of the review (Ahuja et al., 2021; Cheng, 2019; Lee et al., 2021) and four studies were from the 2018 review (Kim & Kim, 2010; Peltzer & Pengpid, 2015; Schilling et al., 2009; Souza et al., 2010). Studies reported analyses from populations greater than 1,000 people.

Age at Initiation

Six cross-sectional studies reported on the age at initiation of drinking in adolescents or alcohol consumption and association with suicidal ideation in adolescents. Three studies were from the update (Ahuja et al., 2021; Cheng, 2019; Lee et al., 2021) and three studies were from the 2018 review (Peltzer & Pengpid, 2015; Schilling et al., 2009; Souza et al., 2010). One study was not included due to errors in reporting. Three studies took place in the U.S., two in Korea and one in Kiribati, Samoa, Solomon Islands and Vanuatu (Table 12). All studies were at moderate risk of bias to answer whether younger age at initiation leads to increased suicidal ideation in future.

Within studies, there was a greater association with suicidal ideation when initiating drinking in the pre-teen years versus middle or later teen years. However, the magnitude of the odds across studies when starting pre-teen was inconsistent and ranged from a larger (three times greater) odds to a small increase in odds (1.39 times greater). Some studies provided data by male and female but found similar odds of suicidal ideation in those groups (Kim & Kim, 2010; Peltzer & Pengpid, 2015).

There may be a moderate association between the onset of suicidal ideation and drinking initiated before age 13. (Low certainty evidence due to risk of bias and inconsistency.)

Table 12: Association of suicidal ideation and age at initiation of drinking

Study (country, number of participants)	Non-initiator	Late teen	Middle teen	Pre-teen
Cheng 2019 (U.S., *n* = 15,029)	ref	-		*OR* = 1.55 (stat sig)
Ahuja 2021 (U.S., *n* = 13,867)	ref	*OR* = 2.11; 95% CI [1.46, 3.04] threshold ≥ 15		*OR* =3 .64 (2.51, 5.28) threshold ≤ 14
Kim 2010 (Korea, *n* = 71,404)	ref	Males: *OR* = 1.11; 95% CI [1.01, 1.22] Females: *OR* = 1.21; 95% CI [1.12, 1.30]		Males: *OR* = 1.28; 95% CI [1.16, 1.41] Females: *OR* = 1.45; 95% CI [1.33, 1.59]
Lee 2021 (Korea, *n* = 57,303)	-	ref	*OR* = 1.139 (stat sig)	*OR* = 1.388 (stat sig)
Peltzer 2015 (Pacific countries, *n* = 6,540)	ref	*OR* = 1.95; 95% CI [1.32 ,2.89] Males: *OR* = 1.88; 95% CI [1.14, 3.10] Females: *OR* = 2.12; 95% CI [1.34, 3.34]		*OR* = 3.39; 95% CI [2.44, 4.71] Males: *OR* = 3.37; 95% CI [2.16, 5.27] Females: *OR* = 3.12; 95% CI [1.95, 4.90]

Risk of bias assessment: yellow = moderate risk

Frequency of Alcohol Consumption in Last Month

Three cross-sectional studies reported on the association between the level of alcohol consumption and suicidal ideation in adolescents (Cheng, 2019; Lee et al., 2021; Souza et al., 2010). The frequency was measured over the last month and in most studies measured no intake versus intake greater than once (Table 13). The studies were from various countries: one each from the U.S., Korea and Brazil, and all were at moderate risk of bias to answer whether higher alcohol consumption leads to increased suicidal ideation in future. Evidence from one study found that the number of times did not increase the odds of suicidal ideation incrementally (Lee et al., 2021). Across the studies, there was a moderate to large increase in odds of suicidal ideation when adolescents had a past history of drinking alcohol at least once in the past month.

In adolescents, consuming alcohol at least once in the past versus never having consumed may be associated with a moderately greater odds of suicidal ideation. (Low certainty evidence due to risk of bias.)

Table 13: Number of times of alcohol intake in past month and association with suicidal ideation

Study (country, number of participants)	No alcohol	Alcohol in past month	Daily
Cheng 2019 (U.S., *n* = 15,029)	ref	*OR* = 1.67 (stat sig) (at least once)	-
Lee 2021 (Korea, *n* = 57,303)	ref	*OR* = 3.908 (1–2/mo) to 4.454 (20–29/mo) (stat sig)	*OR* = 4.515 (stat sig)
Souza 2010 (Brazil, *n* = 1,039)	ref	*OR* = 1.64; 95% CI [1.04, 2.58] (at least once)	-

Risk of bias assessment: yellow = moderate risk

Amount of Alcohol Consumption and Suicidal Ideation

Only one cross-sectional study at moderate risk of bias assessed the amount of alcohol consumption and the association with suicidal ideation. This study included 57,303 adolescents from Korea and found that increasing amounts of alcohol (e.g., from one bottle to eight bottles of beer in the past month) compared to none was not associated with suicidal ideation: OR ranging from 0.93 to 1.0 (Lee et al., 2021).

In adolescents, the consumption of any alcohol in the past may have little to no influence on the development of suicidal ideation, but the evidence is very uncertain. (Very low certainty evidence due to risk of bias and imprecision.)

Heavy Episodic Drinking and Suicidal Ideation

Four cross-sectional studies assessed the association of suicidal ideation with heavy episodic drinking: two included participants from the U.S. (Cheng, 2019; Schilling et al., 2009), one included participants from Korea (Lee et al., 2021), and another included participants from Brazil (Souza et al., 2010). All studies were at moderate risk of bias since past heavy episodic drinking was measured at the same time that suicidal ideation was measured (Table 14). Three of four cross-sectional studies found that at least one episode of heavy episodic in the past month slightly increased the odds of having suicidal ideation (or attempts) (Cheng, 2019; Lee et al., 2021; Schilling et al., 2009) and one found a moderate increase (Souza et al., 2010). Within one study, the more episodes appeared to increase the odds, although the odds represented a moderate increase across all episode frequencies.

In adolescents, past heavy episodic or binge drinking may be associated with a slight increase in the risk of suicidal ideation. (Low certainty evidence due to risk of bias.)

Table 14: Heavy episodic drinking and association with suicidal ideation

Study (country, number of participants)	None	1–2/month	3–4/month	≥ 5/month
Cheng 2019 (U.S., *n* = 15,029)	ref	*OR* = 1.21 (stat sig)	-	-
Lee 2021 (Korea, *n* = 57,303)	ref	*OR* = 1.233 (stat sig)	*OR* = 2.133	*OR* = 3.228 (stat sig)
Souza 2010 (Brazil, *n* = 1,039)	ref	*OR* = 1.94; 95% CI [0.86, 4.36] (at least once)	-	-
Schilling 2009 (U.S., *n* = 31,953) (suicidal attempts only)	ref	*OR* = 1.22; 95% CI [1.06, 1.42]	-	-

Risk of bias assessment: yellow = moderate risk

Discussion and Conclusions

Results and Overall Certainty of the Evidence

With this rapid update, we added 24 new studies to the evidence found in the 2018 review. We added both longitudinal and cross-sectional studies to inform the association with and development of depression, anxiety and suicidal ideation depending on alcohol consumption in a general population. Most of the new studies were added to the body of evidence for the association of alcohol consumption and suicidal ideation; however, these studies were cross-sectional and not longitudinal. Although there were few new studies to inform depression and anxiety, we attempted to synthesize the results differently than the 2018 review. The previous review provided textual descriptions of each individual study and the results of a study could be emphasized simply by the amount of text it takes to describe it. Instead, we counted the number of studies according to the direction and the magnitude of the effect to determine an overall effect and considered studies at lower risk of bias. We also applied the GRADE approach specifically to assess prognosis (i.e., the risk of future mental health illness) in groups of people identified by a specific prognostic factor (i.e., alcohol consumption). Thus, when longitudinal studies contributed data to the evidence base, we assessed the certainty as high, and then rated down the certainty of the evidence based on the GRADE domains (e.g., risk of bias, indirectness, inconsistency, imprecision and publication bias) or rated up the certainty based on other domains (e.g., large effect, dose response or opposing biases). We then used the GRADE approach to make informative conclusions, while taking into consideration the certainty of the evidence.

Based on this method of synthesis the following conclusions can be made. There is high certainty evidence that there is no association between the quantity of alcohol intake and the development of depression in adults after four to 10 years, and moderate-certainty evidence that there is no association with the frequency of alcohol consumption. In adolescents, it is also likely that higher levels or greater frequency of alcohol consumption, including heavy episodic or binge drinking, is not associated with the onset of depression (moderate-certainty evidence).

To date, there are still few longitudinal studies following adults to assess the development of anxiety. We are still very uncertain about the association of low or high levels of alcohol consumption, including heavy episodic or binge drinking, with the odds of developing anxiety (very low certainty evidence). For adolescents, it is likely that greater levels or frequency of alcohol intake has no influence on the odds of developing anxiety later in life (moderate-certainty evidence), and there may be no influence on anxiety over time if drinking is initiated before age 13 (low certainty evidence).

There are no longitudinal studies assessing the risk of developing suicidal ideation and alcohol consumption. We have therefore based our conclusions on evidence from cross-sectional studies and are less certain about this evidence since the direction of effect over time is unknown. In adults, greater levels of alcohol consumption may not influence the onset of suicidal ideation, but heavy episodic or binge drinking may be moderately associated with an increase in the odds of suicidal ideation in future (low certainty evidence). In adolescents, there may also be a moderate association with the odds of increased suicidal ideation with more frequent alcohol consumption, including heavy episodic or binge drinking (low certainty evidence). Initiating drinking before age 13 may be moderately associated with suicidal ideation in the future, but not associated with anxiety.

The certainty that we have in these conclusions is based on the risk of bias across the studies that informed the evidence as well as other factors such as the number of people in the studies, the population characteristics and settings, consistency of the results and publication bias, which are

the GRADE domains. For some conclusions, the evidence was rated as high or moderate-certainty, which signifies that the association or lack of association we found "is true" or "is likely true." Since most evidence came from very large real-world studies and databases in a general population (including over 10,000 people) that showed consistent results, we did not rate down for imprecision or inconsistency for most outcomes.

We also did not rate down the certainty when studies at low risk of bias contributed to the evidence, but the assessment of low risk of bias is debatable. Depending on the weight placed on the potential for specific risks of bias, some studies could have been judged at a higher risk of bias than the risk of bias we determined. One potential risk is due to "sick quitters" (Shaper et al., 1988). It is posited that if people consuming alcohol are compared to people "who do not currently drink," then the association with a poor outcome may be attenuated because the latter group may have been drinking before but then quit due to poor outcomes. This bias would thereby equalize the number of poor outcomes between groups and then show smaller or no association with alcohol consumption. In this review, we did not consider this potential risk of bias as reason to rate down the certainty of the evidence.

In contrast, we did more heavily weight the risk of bias related to the presence of an outcome (e.g., depression, anxiety or suicidal ideation) at baseline: studies where the outcome was present, or it was unclear were considered at higher risk of bias. Our risk of bias assessment may differ from some readers, and so in some instances the conclusions may be less certain conclusions. Nevertheless, the magnitude of the effect would not change, only the certainty in that magnitude would change. For example, high certainty that there is "little to no influence" of alcohol consumption on the risk of the onset of depression may become moderate-certainty that there is "little to no influence"; it would not change to "there is an influence," since the magnitude of the associations across studies is still "little to none."

Limitations of the Review

The 2018 review found over 15,000 citations and included over 40 studies. In this rapid update, we performed a less comprehensive search than the 2018 review. Although we did not search trial registries or websites for grey literature, we searched the major databases for articles published between 2018 and December 2021. In this review, we focused on longitudinal studies when available except for suicidal ideation for which the 2018 review only found cross-sectional studies. Similarly, we did not find longitudinal studies assessing suicidal ideation. However, there is still not a large body of evidence from longitudinal studies that assess the development of anxiety and in retrospect an additional search for cross-sectional studies may have been useful to inform that topic. With this update, we had hoped to be able to pool together results across studies using statistical analysis, but as with the 2018 review, thresholds and definitions for alcohol quantity or frequency vary across studies and therefore a statistical analysis could not be performed. In addition, studies often do not report results in a format that can be easily pooled, for example, by providing odds ratios with standard errors or confidence intervals.

We also found that many studies did not report results that could be easily interpreted. Today, as researchers, we understand that concluding that there is no effect or association based on a p-value statistic is not appropriate and not helpful to decision makers, but unfortunately studies, even ones recently published and included in this update, provide little data that can be used to make healthcare decisions. In some studies, we were able to interpret a beta or B coefficient exponentiated as an odds ratio, but in other studies it was not clear if this would be possible to do and therefore results were reported according to the author. In the 2018 review, the GRADE approach was used, but in

many incidences a synthesized result was not provided and therefore GRADE was often applied to a single study. In this update, we attempted to synthesize the results from most studies using rigorous methods based on the direction of the effect and the size of effect. We described the size of effect using common rules of thumb for no, small or weak, moderate, and large or strong associations. We then applied the GRADE approach to assess the certainty of the body of evidence. In so doing, decision makers can use the synthesized results in this updated review to inform recommendations.

Implications for the Update of the Low-Risk Alcohol Drinking Guidelines

When using the GRADE approach to assess the certainty of a result from a synthesis of evidence, certainty is rated as very low, low, moderate or high. When making recommendations, evidence that is moderate or high certainty can lead to stronger recommendations especially when all other factors, such as patient values and preferences, resources, equity considerations, acceptability and feasibility also point to similar conclusions. In this rapid update, we found moderate and high certainty evidence in little to no effect of alcohol consumption on developing depression in the future. But we are less certain about the results we found for anxiety and even less certain about the results for suicidal ideation in future. The evidence we have suggests that there are little to no effects of alcohol consumption on developing anxiety, but there may be important future increases in suicidal ideation with alcohol consumption, especially with heavy episodic or binge drinking. Although we are less certain in the latter, recommendations will likely need to address the potential for this greater risk. Unfortunately, because there is less evidence for anxiety and suicidal ideation, we were not able to define specific levels or frequencies of consumption that could be recommended. We also did not have enough evidence to determine if there were subgroup differences, for example, in males versus females or in key populations such as Indigenous populations. The results we found did not specifically include people with clinical mental health disorders and assess the association of alcohol to outcomes in that population. The evidence we did find, however, can be directly applicable to the general population.

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Appendix A: Inclusion Criteria from 2018 Review

Element	Criteria
Population	The general population If evidence is identified, the following specific subpopulations will be examined: Sex Elderly (people ≥ 65 years) Youth (people < 18 years and between 18–25 years) People with existing mental and physical illnesses People with existing alcohol dependence People with strong family history of alcohol dependence People on medicines or other drugs (prescribed and illicit) including interactions
Exposure	Varying levels of alcohol consumption in a single episode or drinking occasion and/or patterns of alcohol consumption over time
Comparator	Reference level and/or pattern of alcohol consumption (including no alcohol consumption) Reference groups may consist of occasional drinkers, lifetime abstainers or current abstainers, which may include former drinkers
Outcomes	Critical: Chronic mental health disorders (depression, anxiety, alcohol-related psychosis) Important: Depressive symptoms, symptoms of anxiety, suicidal ideation, suicide attempts, completed suicide

Appendix B: Search Strategy

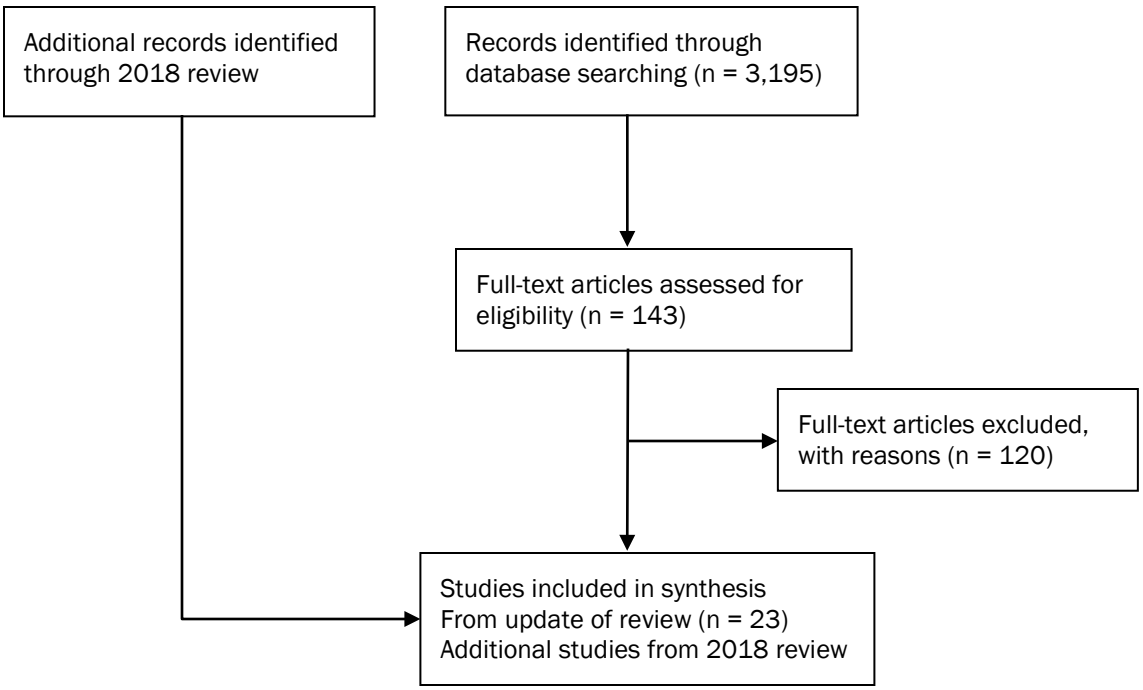
Updated search from Newton et al. 2018 from January 2018 to December 2021

Database:

Embase <1996 to 2021 December 17>; APA PsycInfo <1987 to November Week 5 2021>; Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <2017 to December 17, 2021>

1	(anxious or anxiety or depress* or suicid* or psychol* or psychopath* or psychiat*).ti.	890,369
2	((alcohol* adj2 (use* or drink* or consume or consumption or intake)) or (drink* or beer or wine or spirits)).ab.	429,114
3	1 and 2	17,962
4	(anxious or anxiety or depress* or suicid*).ab.	1,353,755
5	alcohol*.ti.	229,129
6	(drink* or substance use*).ti. and alcohol.hw,kf.	36,764
7	5 or 6	251,847
8	4 and 7	21,094
9	3 or 8	33,121
10	(associat* or correlat* or odds or risk or risks or regression or more likely or less likely).tw.	14,012,852
11	9 and 10	25,004
12	limit 11 to yr="2018 -Current"	8,858
13	conference abstract/ or conference*.pt. or case report/ or review.pt. or editorial.pt. or letter.pt.	11,704,901
14	12 not 13	7,511
15	(serum or mice or mouse or rodent* or MRI or gene or genes or genetic or receptor* or antigen*).mp.	10,675,488
16	14 not 15	6,665
17	limit 16 to yr="2018 - 2020"	4,623
18	remove duplicates from 17	2,155
19	limit 16 to yr="2021 -Current"	2,042
20	remove duplicates from 19	1,040
21	18 or 20	3,195

Appendix C: PRISMA Flow Diagram



Appendix D: Characteristics of Included Studies from Rapid Update

Study, country # of participants Database and Follow-up time	Measure of outcome (Note: text is often copied from the original document to maintain specific definitions)	Measure of alcohol consumption (Note: text is often copied from the original document to maintain specific definitions)	Bias due to confounding, selection, measurement of exposure or outcome, attrition
Garcia-Esquinas, 2018, Spain 1,200 seniors in Spain English Longitudinal Study of Ageing (ELSA) and Seniors-ENRICA cohorts, (Wave 1: 1998, 1991, or 2001), (Wave 2: 2002, 2003), Follow-up (2006-2007) 2.8 ENRICA and 7.4 (ELSA) year follow-up time	Depressive symptoms - Geriatric Depression Scale (GDS): Depressive symptoms were ascertained by a 10-item version of the GDS23. A higher score in the GDS indicates a greater level of depression. 2. Center for Epidemiologic Studies Depression Scale (CES-D): The ELSA study used the 8-item version of the CES-D)35. A higher score in the CES-D indicates a greater level of depression. 3. Self-reported depression: In the Seniors-ENRICA study this variable was defined as a positive answer to the question "Has a doctor ever told you that you have depression" or as being on antidepressant medication.	Quantity - Participants were classified as: (1) never drinkers (which also included occasional drinkers with average intake close to zero), (2) ex-drinkers (those who stopped drinking for at least 1 year prior to the interview), (3) moderate drinkers and 4) heavy drinkers. The threshold between moderate and heavy drinking at ≥40 g/day for men and ≥24 g/day for women.	Exclusion of participants with outcome not reported Attrition bias
Gemes, 2019, Sweden 5,087 middle age (mean age = 43) adults in Sweden PART study, first wave conducted 1998-2000, second wave: 2001-2003, third wave in 2010 12 years	Depressive symptoms - Major Depression Inventory (MDI) and DSM-IV diagnostic algorithm. The MDI contains 10 questions with answers on five-step Likert scales. If more than two answers were missing, the MDI value was considered to be missing; these observations were not included in the analyses.	Frequency and quantity - The amount and frequency of alcohol consumption was assessed by three questions with predefined response alternatives: 'Have you drank at least a glass of alcohol during the last 12 months?' ('yes', 'no'); 'How often do you drink alcohol?' ('monthly or less', '2–4 times a month', '2–3 times a week', '4 times a week or more') and 'How many "glasses" do you drink on a typical day when you drink alcohol?' ('1–2', '3–4', '5–6', '7–9', '10 or more').	Excluded participants with MDI scores greater than 26 at baseline Attrition bias
Bi Lee 2018, Korea 2511 males between the ages of 20 and 65 in Korea The data base utilized in this study was from the Korean Welfare Panel Study. This study began in 2006 and sampled 90% of the	Depressive symptoms - Centre for Epidemiological Studies Depression Scale (CES-D-11) Depression was assessed using the 11-item Centre for Epidemiological Studies Depression Scale (CES-D-11) (Radloff, 1977) with a 4-point Likert scale. Higher scores indicate higher levels of depression.	Frequency - AUDIT was used to measure problem drinking, which consisted of 10 items rated on a 5-point Likert scale developed by the World Health Organization (WHO). The total score ranges from 0 to 40 points and higher scores indicate higher levels of problem drinking. The standardized score of 'drinking with risk' from the AUDIT is more than 8 points.	Unadjusted analyses Exclusion of participants with outcome not reported

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population, excluding islands and special facilities. This study used data from 2011 – 2014, so four-year follow-up total.			
Liang 2021, China, England, and the U.S. 29,506 middle aged and older adults in China, England, and the U.S. The data were derived from three representative longitudinal cohorts in China, England, and the United States (U.S.): China Health and Retirement Longitudinal Study (CHARLS), the English Longitudinal Study of Ageing (ELSA), and the Health and Retirement Study (HRS). (1996 – 2014) Three Cohort studies CHARLS four-year follow-up. ELSA 2002- 2017. HRS 1996 - 2014	Depressive symptoms - CES-D was used in the ELSA and HRS, and the ten-item version of CES-D used in CHARLS. A score of 12 or higher was used to define depressive symptoms.	Quantity - The total consumption of alcohol was calculated by combining drinking frequency and volume per week. A standard drink was defined as 0.5 ounces (14 grams) of pure alcohol, corresponding to one 12-ounce (340-gram) beer, one 5-ounce (142-gram) glass of wine, or 1.5 ounces (43 grams) of distilled spirits. Participants were categorized as: never drinkers, ex-drinkers, current low-to-moderate drinkers (≤7drinks/week for women or ≤14 drinks/week for men), and heavy drinkers (>7 drinks/week for women or >14 drinks/week for men).	Participants with depression were excluded at baseline
Paulson 2018, U.S. 3,177 individuals over the age of 65 in the U.S. The Health and Retirement Study (HRS)—a cohort study on health and aging on adults	Depressive symptomatology - Ascertained with the abridged 8-item Center for Epidemiological Studies Depression (CES-D) measure from the HRS data. Participants answered “yes” or “no” to each item statement with respect to how they were feeling “much of the time” in the past week. Six of the statements were worded negatively (“felt depressed, felt that	Quantity - measured by average number of drinks per week, was collected via self-report. moderate drinking was characterized by 1–14 drinks per week. Respondents who reported 0 drinks per week were identified as abstinent.	outcome was present in people at baseline

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50+ which was conducted by the University of Michigan with support from the National Institute of Aging. (2006, 2008, 2010, 2012, 2014) No follow-up, just used data from each year mentioned above in the study	everything he/she did was an effort, sleep was restless, could not get going, felt lonely, and felt sad"), and two of the statements were worded positively ("enjoyed life and was happy"). Scores range on a scale from 0 to 8, with higher scores indicating higher levels of depression.		
Ruiz-Estigarrbia, 2019, Spain 14,908 university graduates in Spain The Seguimiento Universidad de Navarra (SUN) project was a prospective, cohort of Spanish university graduates which was used for this study. In this analysis data from 1999 – 2014 was used. Median of 10.4 follow-up years	Depression disorder - Incident cases of depression were defined as participants who were free of any previous history of depression at baseline, were not using any antidepressant treatment at baseline, and positively responded in any of the follow-up questionnaires to the question, "Have you ever been diagnosed with depression by a medical doctor?"; or reported habitual new use of antidepressant treatment in any of the follow-up questionnaires. Either of both criteria (medical diagnosis or onset of habitual antidepressants) was sufficient to be classified as a new case of depression.	Quantity - Alcohol consumption was recorded via this questionnaire and other items related to alcohol consumption were also collected in the baseline questionnaire. Moderate alcohol intake (women 0.1-5 g/d; men 0.1-10 g/d)	Participants with depression were excluded at baseline
Zhang 2018, Germany 1,482 females aged 18-25 in Germany Data came from the Dresden Predictor Study (DPS) which is a prospective study in Germany. (1997 – 1999) Follow-up time was approximately 17 months after baseline assessment (Ranged from 6-30 months)	Depression - DSM-IV Axis I disorders were assessed with the Diagnostiches Interview Beipsychischen Strungen. Participants also completed a battery of self-report questionnaires that provided detailed information about potential predictors of disorders and a comprehensive dimensional assessment of psychopathology. At baseline, the interview provided 7 days point and lifetime prevalence diagnoses. At follow-up, the interview provided 7 days point and period (i.e., from the interval between the two investigations) prevalence diagnoses.	Frequency - Alcohol consumption was assessed with a questionnaire that included questions assessing participants' drinking pattern in the last week and last 12 months, respectively. Questions about the consumption of beer, wine, and spirits were converted into a variable called "risk level alcohol consumption," reflecting levels of alcohol consumption in grams per day. Three categories were created for risk level: 1 = low-risk drinking (up to 20 g alcohol/ day); 2 = medium-risk drinking (20–40 g alcohol/day); 3 = high-risk drinking (over 40 g alcohol/day).	Not excluded at baseline, separated into those with or without incidence of MDD

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Holmes 2021 420 adults aged 18+ in Germany Collected data via PHQ-9 to assess depressive symptoms and TLFB for alcohol use. Follow-up occurred every 6 months for a maximum of 26 months	Depressive symptoms - Measured by the PHQ-9 during the screening and follow-up visits. The scores for each question ranged from 0 to 3 and were summed to provide an overall score ranging from 0 to 27. Higher scores indicated greater depressive symptoms.	Quantity Alcohol use was categorized as none, moderate, and high intake. None was defined as no alcohol intake within the past month. Moderate intake was defined as greater than zero and no more than one standard drink on any day in the past 30 days for women and greater than zero and no more than two standard drinks on any day in the past 30 days for men. High intake was defined as consuming greater than one standard drink on any day in the past 30 days for women and consuming greater than two standard drinks on any day for men in the past 30 days.	Depression was present at baseline
Keyes 2019, 19 countries 57,296 individuals aged 50 or over in 19 different counties Longitudinal data collected between 2004 and 2014 from 19 different countries from five ongoing cohort studies of individuals aged 50+ In this study countries began follow-up 3.47 years after baseline on average	Depressive symptoms - The sum of depressive symptoms was calculated, and a cut-off of ≥3 depressive symptoms for the 8-item CES-D scale (HRS), and ≥4 for both the 10-indicator CES-D scale (CHARLS and KLOSA) and the 12-indicator EURO-D scale (SHARE). Whenever a participant's sum score of self-reported depressive symptoms fell above these cut-offs, a depressive episode is recorded.	Quantity - Heavy drinkers using harmonized measures of frequency, quantity, drinks per day, and binge drinking. Drinks were converted to standard sizes and ethanol contents as well, and converting frequency of drinking into days per week. Heavy drinking combined regular heavy drinking and single episodes of binge drinking; moderate drinking was defined as drinking 1 or more days per week, with drinks per day ≤3 for men or ≤2 for women, and no binge drinking (>4 for men or >3 for women) in a single day. Heavy drinking was defined as >3 drinks per day on drinking days for men or >4 in a single day, and women have >2 drinks per day on drinking days or any instance of >3 in a single day.	Unadjusted analyses Only included people who did not have depression at baseline
Grazioli 2018, Switzerland 4,617 young men aged 19-20 who completed both waves of C-SURF (mean age = 19.95) Army-based cohort study on Substance Use Risk Factors (C-SURF), enrolment between 2010 and 2012 and follow-up	Suicide - Participants were asked to indicate how often they had attempted suicide in the past year on a Likert scale ranging from 1 to 5, where 1 = never, and 5 = 10 times or more often. Answers were dichotomized to yield a 1-year report of at least one suicide attempt, with 0 = no suicide attempt, 1 = at least one suicide attempt.	Quantity - The average number of drinking days and the number of standard drinks (i.e., a standard drink = 10 gr of ethanol) consumed per drinking day over the past 12 months were measured at baseline and at follow-up. The average number of drinks per week (total drinks per week) over the past 12 months at baseline and follow-up were computed by multiplying the number of drinking days by the number of drinks per drinking day.	Participants with history of suicidal attempt included at baseline

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in 2012 and 2014 15-month follow-up from baseline			
Richards (2020), U.S. 44,106 individuals who had completed suicide Data was drawn from the electronic health record (EHR), insurance claims, health system enrolment, and state death certificate data from Kaiser Permanente Washington, a large health care system. No follow-up	Suicide attempt—within 90 days of the index visit were ascertained from state death certificate of death and EHR diagnostic codes. Suicide deaths and non-fatal attempts were combined due to the small number of deaths.	Frequency - Levels of alcohol consumption were measured categorically based on gender-specific AUDIT-C cut-points of the total score Frequency of heavy drinking episodes was measured categorically based on responses to the third AUDIT-C question, which asks how often patients consume six or more drinks on one occasion, with response options: “never,” “less than monthly,” monthly,” “weekly,” and “daily or almost daily”.	Unadjusted analyses A majority (71%) had MDD or anxiety in the past year, and all completed suicide by time of study
Ahuja 2021, U.S. 13,867 adults aged 18+ The Collaborative Psychiatric Epidemiology Survey (CPES) was used from 2001-2003 No follow-up	Suicidal behaviours including lifetime suicidal ideation and lifetime suicide attempt. Participants were asked: Have you seriously thought about committing suicide?’, ‘Did you ever think about committing suicide’, ‘Have you seriously thought about committing suicide in the past 12 months’.	Age of initiation - based on participants being asked how old they were when they first ever drank an alcoholic beverage. Three variables <14 years old, greater than 15 years old, and no alcohol use (reference group).	Included at baseline
Kim 2018, U.S. 67,901 young adults aged 18-25 (*M* = 21.02) 2014 National Survey on Drug Use and Health (NSDUH) public use data, it is a series of surveys that measure the prevalence and correlates of drug use in the U.S. No follow-up	Suicidal ideation and attempt - Suicide ideation is purely cognitive in nature, while intent is an emotional to cognitive process. Suicide attempt incorporates a high likelihood of death and an intent to kill oneself. Suicide ideation was measured by asking if the respondent seriously thought about trying to kill him/herself at any time in the past year. Suicide attempt was measured by asking if the respondent tried to kill him/herself during the past year. The response categories for outcome variables were dichotomous: 1 = “Yes”; 2 = “No.”	Quantity - A respondent was defined as having abused alcohol if he/she met one or more of four abuse criteria in the past year (i.e., having physical danger caused by regular alcohol use; repeatedly having trouble with the law caused by alcohol use) and was determined not to be dependent upon alcohol. A respondent was defined as having alcohol dependence if he/she met three or more of seven dependence criteria in the past year (i.e., using alcohol more often than intended; inability to cut down or stop using alcohol). The response categories for AAD were dichotomous: 0 = “No”; 1 = “Yes.”	Included at baseline

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Kim 2021, Korea 5,982 employees who received a mental health screening, 18+ Surveyed from the Kangbuk Samsung Workplace Mental Health Institute from 2016 – 2019 No follow-up	Suicidal ideation and Attempt – Ideation was assessed by a self-reported questionnaire with the question "Did you think about suicide over the past one month?" and the answer was categorized as "Yes" or "No. Suicide attempts were assessed by the question: "Did you attempt suicide over the past one year?" and the answer was categorized as "Yes" or "No."	Alcohol frequency – The Alcohol Use Disorder Identification Test (AUDIT) was used. The scores were categorized as "low risk" (0–7), "medium-risk" (8–15), and "substantial- to severe-risk" (16 and above).	Included at baseline
Kittel 2019, U.S. 269,078 individuals aged 18+ Data from the National Survey on Drug Use and Health (NSDUH) from 2008 to 2014 was used No follow-up	Suicidal ideation and attempt – Ideation: participants were asked whether they had seriously thought about trying to kill themselves within the past 12 months. Attempt - participants were asked if they had tried to kill themselves within the past 12 months.	Frequency & binge drinking - Participants were asked the total number of days they used alcohol in the past year, which was then recoded into a categorical variable (None, 1–11 days, 12–49 days, 50–99 days, 100–299 days, and 300–365 days). For binge drinking, participants were asked on how many days in the past month they had five or more drinks on one occasion. This was recoded to a dichotomous variable.	Outcome present at baseline
Sohn 2020, Korea 16,277 adults 19+ National Health and Nutrition Examination Survey (2016-2017) No follow-up	Suicide attempt - determined by whether or not a suicide attempt was made in the last year.	Quantity - Amount of drinks consumed prior to suicide attempt.	Outcome present at baseline
Lee 2021, Korea 60,040 in 2018, and 57,303 in 2019 adolescents (mean age around 15 years old) Korean Youth Risk Behavior Web-based Survey, conducted in 2018 and 2019 No follow-up	Suicidal ideation – Assessed using one of the items regarding suicidal ideation and suicide attempts included in the Korea National Health and Nutrition Examination Survey: "Have you had a suicidal thought in the past year?" Subjects selected one of the following answers: "I have never had such thoughts," "I have sometimes had such thoughts," and "I almost always have such thoughts." The subjects who responded that they never had suicidal thoughts were classified as not having suicidal ideation, and those who responded that they sometimes or almost always have suicidal thoughts were classified as having suicidal ideation.	Age of initiation - Pre-teen (pre-school to 6th grade), middle teen (7th to 9th grade), and late teen (10th to 12th grade).	Outcome present at baseline

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Cheng 2019, U.S. Average response per year = 15,029 school students, mean age = around 16.1 Youth Risk Behavior Surveillance System (YRBSS) (2007 – 2015 in two-year increments, i.e., 2007, 2009 etc.) No follow-up	Suicide Attempt – Participants were asked: (1) Did you ever feel so sad or hopeless almost every day for two weeks or more in a row that you stopped doing some usual activities? [felt sad or hopeless]; (2) Did you ever seriously consider attempting suicide? [considered suicide]; (3) Did you make a plan about how you would attempt suicide? [planned suicide]; (4) How many times did you actually attempt suicide? [attempted suicide]; (5) If you attempted suicide, did any attempt result in an injury, poisoning, or overdose that had to be treated by a doctor or nurse? [suicide attempt treated by a physician or nurse].	Age of initiation - first drink before 13, 1+ drinks past month, five + drinks 1+ past month, had 1+ drinks at school 1+ month.	Outcome present at baseline
Kim 2018, U.S. 67,901 young adults aged 18 to 25 2014 NSDUH public use data No follow-up	Suicidal ideation - asked: have you every thought of wanting to die in the past year?	Frequency of alcohol use - have you been drinking for the last year, how often do you drink alcohol: None, <1, 2-3, or 4> times per week.	Outcome was present at baseline
Parker 2019, U.S. 3,239 college students Creating Campus Change study, cross-sectional survey that assessed alcohol use patterns and mental health outcomes (2014-2015) No follow-up	Suicidal Ideation and attempt – Participants were asked “In the past month did you think that you would be better off dead or wish you were dead,” and, “In the past month did you attempt suicide?” Item scores were summed to yield a total risk score and were categorized as no (0), low (1–5), moderate (6–9), or high (10+) suicide risk.	Frequency - The consumption items of the Alcohol Use Disorders Identification Test (AUDIT-C) was used to assess alcohol consumption, drinking behaviours, and alcohol-related problems. Responses were scored according to their frequency over the past month or on a typical day, with scores range from 0 to 12. A cut-off score of 4 or higher was used for men and a score of 3 or higher was used for women to indicate hazardous drinking or active alcohol use disorders requiring advice and brief counselling or evaluation and treatment (hazardous drinking or active alcohol use disorders = 1, below recommended drinking limits = 0).	Included at baseline
Knox 2019, U.S. 22,005 adults 18+ NSEARC target population survey (2001-2002) baseline, and then	Anxiety and depressive disorders combined - Depressive disorders were diagnosed when ≥2 weeks of persistent depressed mood or anhedonia occurred, accompanied by ≥5 of the 9 DSM-IV symptoms of major depression. Anxiety disorders	Quantity - Mean ethanol consumption (grams) per day in the prior 12 months.	Unadjusted Outcome present at baseline

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2004-2005 data came from face-to-face interviews Three-year follow-up	similarly followed DSM-IV criteria. Both were combined into a single variable, "depression and/or anxiety disorders," coded positive if any of the disorders were present in the prior 12 months.		
Carvalho 2018, Ireland 6,095 adults aged 50+ Irish Longitudinal Study on Aging (TILDA) (2009 – 2011) Two-year follow-up	Anxiety symptoms – Assessed with the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A). The scores of the seven items were summed to create a scale that ranged from 0 to 21, with higher scores indicating greater symptoms of anxiety.	Quantity - Self-reported information on quantity and frequency of alcohol use in the last 6 months was used to calculate the number of drinks consumed per day and week.	Outcome present at baseline
Mustonen 2021, Finland 1,492 adolescents 15–16 year olds followed until the age of 33 The Northern Finland Birth Cohort 1986 Follow-up time = 15–16 years	Anxiety disorder – classified by International Classification of Diseases (ICD) anxiety criteria if participants had persistent, and excessive worry for at least six months. Additionally, restlessness, tension, tachycardia, and dyspnea unattached to a clearly identifiable stimulus.	Age of initiation – Collected via self-report questionnaire. Participants were asked "At what age did you get drunk for the first time? – (at 11 or younger; at 12 years; at 13 years; at 14 years; at 15 years; at 16 years or never)". The options were pooled into four categories (1. Never; 2. at 15–16 years; 3. at 13–14 years; and 4. at 12 years or before). Participants who reported never having been intoxicated from alcohol were considered as the reference group.	Excluded if they had any mental disorder before the age of 16
Newton-Howes 2019, New Zealand 1,265 adults aged 18 to 35 Christchurch Health and Development Study (CHDS) 1977 Follow-up time = 18 years	Anxiety disorder - Cohort members completed the Composite International Diagnostic Interview (CIDI) at ages 18, 21, 25, 30, and 35 years to classify if they met DSM-IV criteria for anxiety disorder over the intervals 18–21 years, 21–25 years, 25–30 years, and 30–35 years. Anxiety disorders included generalized anxiety disorder, panic disorder, agoraphobia, social phobia, and specific phobia.	Age of initiation - Cohort members were asked questions about their experiences of drinking alcohol at ages 11, 12 and 13 years. One of these questions asked cohort members to report the age at which they recalled first drinking alcohol. From the age of 11 years, cohort members were also asked if they had drunk alcohol in the last year (with a yes/no response option). At each assessment at ages 14, 15, 16, and 18 years, cohort members were asked about their usual frequency of alcohol consumption in the previous 12 months using a six-point scale ranging from "never" to "almost every day".	Outcome at baseline not reported