Technical report

Systematic literature review on the association between alcohol consumption and mental health disorders

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Contributions of authors

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Declarations of interest

The authors of this document have no financial or other perceived or real conflicts of interest pertaining to alcohol or the conditions assessed. The funding for this project was received from the Office of the NHMRC.

Changes from protocol to final report

Feedback was received from the Chair of the Alcohol Working Committee after the finalisation of the protocol. The inclusion criteria were therefore expanded to include acute outcomes of suicide attempts/ideation/successful suicide.

A large volume of prospective cohort studies were identified reporting on the association between alcohol and mental health. Cohort studies provide a time element, which can help distinguish between questions of whether alcohol consumption influences mental health outcomes, or whether those with mental health problems are more or less likely to consume alcohol. Studies without a time element such as cross-sectional surveys, were therefore excluded for the main outcomes, where there were prospective cohort studies (depression, anxiety, PTSD). However, for suicidal ideation/suicide attempts, large cross-sectional studies (over 1000 participants) were included if they controlled for levels of depression.

Contents

1 Scope and Purpose

1.1 Objective of the systematic review

The objective of the systematic review was to comprehensively search for, collate, analyse and synthesise the results of primary studies which reported on the association between various levels and/or patterns of alcohol consumption and the mental health outcomes of interest, focusing on studies published since January 2007[1].

The systematic review will then inform the revision of the *Australian Guidelines for Reducing the Health Risks from Drinking Alcohol 2009.* The aim is to reduce the mental health impact of alcohol consumption for people in Australia.

1.2 Health question covered by the systematic review

The systematic review addresses the following research question:

1. What is the **association** between various levels and/or patterns of **alcohol consumption** and **mental health disorders** (mood disorders[2] and anxiety disorders[3] are the main outcomes of interest) in the general population and various subgroups:
    - By age group
    - By sex and/or gender
    - People with existing physical and/or mental health conditions
    - People with a family history of alcohol dependence
    - People using licit and/or illicit drugs

The research question was developed using a Population, Exposure, Comparator and Outcome (PECO) framework. The review questions and outcomes were defined by ONHMRC and the AWC prior to the commencement of the evidence evaluation.

The PECO framework guiding the systematic review question is presented in Table 1.

[1] Consistent with the date that last literature searches were undertaken for the 2009 Alcohol Guidelines

[2] "Those disorders that have a disturbance in mood as their predominant feature" – MeSH Descriptor Data 2018, https://meshb.nlm.nih.gov/record/ui?ui=D019964

[3] "Persistent and disabling anxiety" – MeSH Descriptor Data 2018, https://meshb.nlm.nih.gov/record/ui?ui=D001008

Table 1 PECO criteria for the evaluation of association between alcohol consumption and mental health disorders

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 and comparator	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)[a]
Outcomes	Critical: Chronic mental health disorders (depression, anxiety, alcohol-related psychosis) Important: depressive symptoms, symptoms of anxiety, suicidal ideation/suicide attempts/completed suicide

[a] Reference groups may consist of occasional drinkers, lifetime abstainers or current abstainers, which may include former drinkers.

The age-based subgroups were classified based on the age at time of exposure to alcohol. There were very few studies which restricted recruitment to the elderly population (people aged ≥65 years), so an 'older adult' subgroup was assessed, which included studies which focused on adults with a lower age limit of 50 years.

The outcomes listed were amended from the draft systematic review protocol, on the basis of advice from the Alcohol Working Committee and the methodological reviewer.

1.3 Population to whom the guideline is meant to apply

The systematic review addresses the available evidence on the general public, including people of different age groups, sex/gender, people with different physical and/or mental health conditions, people with a family history of alcohol dependence, and people who use licit and/or illicit drugs.

The revised guidelines will be made available to the general public, government agencies, health organisations, health professionals and the alcohol industry. All of these groups of people could be considered target users of the guideline.

2 Stakeholder involvement

2.1 Group membership

2.1.1 Identification of key stakeholders and establishment of the Alcohol Working Committee

NHMRC established the Alcohol Working Committee (AWC) to oversee this work and guide the evaluation of the evidence on the health effects of alcohol consumption. They identified the topic of the association between alcohol and mental health as being a priority area for review. They provided guidance on the systematic review protocol and will comment on the evidence evaluation report, considering the outcomes of the evidence evaluation in order to update NHMRC's *Australian Guidelines for Reducing Health Risks from Drinking Alcohol 2009.* They will also consider comments received during consultation on the draft revised guidelines, and update the revised draft with consideration to comments from public consultation and expert review.

The AWC comprises experts in drug and alcohol research, epidemiology, biostatistics and modelling, addiction, mental health, clinical public health, fetal alcohol spectrum disorders, Aboriginal and Torres Strait Islander health and consumer advocacy.

Table 2 Alcohol Working Committee members

Member	Position
Professor Kate Conigrave (Chair)	Senior Staff Specialist and Professor of Addiction Medicine at Royal Prince Alfred Hospital and Sydney Medical School, the University of Sydney
Professor Emily Banks (Deputy Chair)	Researcher in chronic disease epidemiology at the Australian National University
Professor Tanya Chikritzhs	Professor at the National Drug Research Institute, Curtin University
Dr Rebecca Armstrong	Director of Public Health Insight, the University of Melbourne, and Joint Co-ordinating Editor, Cochrane Public Health
Dr Michael Livingston	Post-Doctoral Research Fellow at the Centre for Alcohol Policy Research, La Trobe University
Professor Dan Lubman	Director, Turning Point at Eastern Health, and Professor of Addiction Studies and Services at Monash University
Dr Colleen O'Leary	Research Associate at Curtin University, and Coordinator, Standards Monitoring at Western Australian Office of the Chief Psychiatrist
Professor Alison Ritter	Director at Drug Policy Modelling Program, and Deputy Director, National Drug and Alcohol Research Centre.
Professor Robert Ali	Director, Community Based Treatment Drug and Alcohol Service SA and Director, WHO Collaborating Centre
Professor Peter D'Abbs	Academic, Menzies School of Health Research
Dr Mark Harris	Professor of General Practice, Scientia Professor, and Executive Director at the Centre for Primary Health and Equity, the University of New South Wales
Ms Anne McKenzie AM	Head, Consumer and Community Health Research Network, the University of Western Australia
Mr Scott Wilson	Director of Aboriginal Drug and Alcohol Council, South Australia
Ms Nicole Hewlett	Project manager, Menzies School of Health Research

2.1.2 Systematic review authors

The systematic review on the association between alcohol and mental health was performed by Adelaide Health Technology Assessment. They were chosen for their expertise and track record in performing systematic reviews on mental health topics (depression and posttraumatic mental health) for NHMRC Evidence-based guidelines.

2.2 Target population preferences and views

The revised guidelines will be made available to the general public, government agencies, health organisations, health professionals and the alcohol industry for comment, in order to seek their views and preferences. They are considered the target users of the guideline.

3 Rigour of development

In order to answer the research question outlined in section 1.3, a systematic review of the literature was performed.

3.1 Strategy used to search for, identify and retrieve studies

3.1.1 Bibliographic databases

The peer reviewed literature was searched for studies that consider the association between mood or anxiety disorders and alcohol consumption. The search canvassed the following databases: PubMed (Medline and Pre-MEDLINE), Embase.com, the Cochrane Library (Cochrane Database of Systematic reviews and the Database of Abstracts of Reviews of Effects), CINAHL and PsycInfo.

The search strategy used contains the key elements of the research question, outlined in Section 2.1.1. Table 3 to Table 7 contain the search terms for this review. These included a combination of text words and MeSH/Emtree indexing terms, according to the database searched. The elements of the clinical question in each table were combined using 'AND' in these Boolean searches. An example of a search strategy in full is provided in Appendix A, page 27.

Table 3 Search terms for evidence to inform the systematic review questions (PubMed)

Element of clinical question	Pubmed/Medline search terms
Exposure	"Alcohol-Related Disorders"[MeSH] OR "Alcohol Drinking "[MeSH] OR "Alcohol Abstinence"[MeSH] OR "Alcoholic Beverages"[MeSH] OR "alcohol use"[Title/Abstract] OR alcoholic[Title/Abstract] OR (alcohol AND drink*)[Title/Abstract] OR "alcohol consumption"[Title/Abstract]
Outcomes/Population	"Mood Disorders"[MeSH] OR "Anxiety Disorders"[MeSH] OR anxious[Title/Abstract] OR worry[Title/Abstract] OR worried[Title/abstract] OR anxiety[Title/Abstract] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed[Title/Abstract] OR mood[Title/Abstract])
Limits	Publication date from 2007/01/01

MeSH = Medical Subject Heading, based on a Medline/PubMed platform

Table 4 Search terms for evidence to inform the systematic review questions (Cochrane Library)

Element of clinical question	Cochrane search terms
Exposure	"Alcohol-Related Disorders"(MeSH) OR "Alcohol Drinking "(MeSH) OR "Alcohol Abstinence"(MeSH) OR "Alcoholic Beverages"(MeSH) OR "alcohol use"(Title Abstract Keywords) OR alcoholic(Title Abstract Keywords) OR (alcohol AND drink")(Title Abstract Keywords) OR "alcohol consumption"(Title Abstract Keywords)
Outcomes/Population	"Mood Disorders"(MeSH) OR "Anxiety Disorders"(MeSH) OR anxious(Title Abstract Keywords) OR worry(Title Abstract Keywords) OR worried(Title Abstract Keywords) OR anxiety(Title Abstract Keywords) OR depression(Title Abstract Keywords) OR depressive(Title Abstract Keywords) OR depressed(Title Abstract Keywords) OR mood(Title Abstract Keywords)
Limits	Publication date from 2007/01/01

MeSH = Medical Subject Heading, based on a Medline/PubMed platform

Table 5 Search terms for evidence to inform the systematic review questions (Embase.com PICO search)

Element of clinical question	Embase search terms
Exposure	alcohol consumption/exp + 5 synonyms or alcohol disorder:ti,ab or drinking behaviour/exp + 7 synonyms or alcoholism/exp + 26 synonyms
Outcomes/Population	mood disorder/exp + 8 synonyms or anxiety disorder/exp + 2 synonyms or depression/exp + 13 synonyms
Limits	Years 2007 – 2018 Publication type: article, review, letter, article in press, chapter, erratum Language: English

Table 6 Search terms for evidence to inform the systematic review questions (CINAHL)

Element of clinical question	CINAHL search terms
Exposure	(MM "Alcohol-Related Disorders") OR (MM "Alcohol Drinking") OR (MM "Alcoholic Beverages") OR (MM "Alcoholics") OR (MM "Alcoholism") OR (Alcohol Abuse") OR (MM "Alcohol Drinking in College") OR TI alcohol consumption OR AB alcohol consumption OR TI (alcohol AND drink) OR AB (alcohol AND drink)OR TI (alcohol AND abstinence) OR AB (alcohol AND abstinence) OR TI alcohol use OR AB alcohol use OR TI alcoholic OR AB alcoholic
Outcomes/Population	(MM "Affective Disorders") OR (MM "Anxiety Disorders") OR (MM "Depression") OR TI anxious OR AB anxious OR TI worry OR AB worry OR TI worried OR AB worried OR TI anxiety OR AB anxiety OR TI depression OR AB depression OR TI depressive OR AB depressive OR TI depressed OR AB depressed OR TI mood OR AB mood
Limits	Publication date from 2007/01/01

Table 7 Search terms for evidence to inform the systematic review questions (PsycInfo)

Element of clinical question	Search terms
Exposure	alcohol abuse/ or alcohol drinking patterns/ or alcoholism/ or binge drinking/ or underage drinking/ or drinking behaviour/ or alcoholic beverages/
Outcomes/Population	depression/ or anxiety/ or emotional states/ or distress/ or (anxious or worry or worried or anxiety or depression or depressive or depressed or mood).ti or (anxious or worry or worried or anxiety or depression or depressive or depressed or mood).ab
Limits	Publication date from 2007/01/01

3.1.2 Other sources

Relevant papers had their reference lists pearled for other studies potentially missed in the searches. The ONHMRC and the AWC were also requested to forward any articles they know of which address the study selection criteria.

3.1.2.1 Trial registers and discussion of trials identified (from either registers or bibliographic databases)

Trials registers were searched, in case there were studies which reported on the relationship between alcohol consumption and mental health outcomes, in those undergoing treatment for mood disorders.

Table 8 Trial registers searched

Trial registry	No. of potentially relevant trials	No. included in evidence report
Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au/)	188	0
ClinicalTrials.gov (clinicaltrials.gov)	198	0
Trials Register of Promoting Health Interventions (TRoPHI) (http://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=12)	0	0
WHO International Clinical Trials Registry Platform (http://www.who.int/ictrp/search/en/)	661	0
ISRCTN registry (International Standard Registered Clinical/soCial sTudy Number) (http://www.isrctn.com/search?q=)	91	0

The potentially relevant trials identified could be grouped into several different categories:

- Interventions aimed at prevention of uptake of alcohol;
- Interventions aimed at treatment depression or anxiety; or
- Interventions aimed at treating alcohol use disorder (with or without comorbid depression or anxiety).

The studies which focused the prevention of alcohol uptake, assessed outcomes based on the intervention group, rather than exposure to alcohol consumption, so did not provide useful information on the impact of alcohol on mental health outcomes.

There were 25 studies which focused on the treatment of depression or anxiety, and looked at the relationship between alcohol consumption and outcomes of treatment. In these studies, the alcohol is viewed either as a prognostic factor, or as a moderating or mediating factor influencing response to treatment for mood disorders. However, further advice was received from the ONHMRC[4] that these studies did not need to be included, as studies which addressed how alcohol affected response to treatment did not address the research question. The list of studies identified is available on request.

Interventions aimed at treating alcohol use disorder did not have an appropriate comparison group, as all participants were high consumers of alcohol.

3.1.2.2 Website searching

A search of the grey literature included searching the following websites (to be consistent with the 2017 Alcohol Guidelines) in September 2018:

- Register of Australian Drug and Alcohol Research (http://www.nada.org.au/nada-focus-areas/research/researchresources)
- Black Dog Institute (http://www.blackdoginstitute.org.au/)
- National Drug and Alcohol Research Centre (http://ndarc.med.unsw.edu.au/)
- National Drug Research Institute (http://ndri.curtin.edu.au/)
- Australian Centre for Addiction Research (http://www.acar.net.au/)
- National Institute of Health and Care Excellence (https://www.nice.org.uk/)
- Agency for Healthcare Research and Quality (http://www.ahrq.gov/)
- Centres for Disease Control and Prevention (https://www.cdc.gov/)
- World Health Organisation (http://www.who.int/en/)
- National Institute on Alcohol Abuse and Alcoholism (https://www.niaaa.nih.gov/)
- International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO/)
- Health evidence Canada (http://www.healthevidence.org/)
- U.S. Preventive Services Task Force (https://www.uspreventiveservicestaskforce.org/)
- Public Health England (https://www.gov.uk/government/organisations/public-health-england)
- Indigenous HealthInfoNet (http://www.healthinfonet.ecu.edu.au/)
- International Agency for Research on Cancer (https://www.iarc.fr/)
- World Cancer Research Fund (https://www.worldwidecancerresearch.org/)

PROSPERO listed the protocols of two potentially relevant systematic reviews; however, these reviews were categorised as still ongoing (as at September 2018):

- Hunt, V & Delgadillo, J *(In Progress)* 'A review of associations between alcohol use and depression severity'. University of Sheffield (United Kingdom). PROSPERO CRD 42018096548.
- Collaton et al. (*In Progress)* 'A systematic review and meta-analysis of alcohol use as a predictor of the course of depression'. Centre for Addiction and Mental Health (Canada); University of Queensland; National Drug and Alcohol Research Centre (Australia) and the Public Health Institute (Unites States of America). PROSPERO CRD 42017070138.

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[4] Advice provided via teleconference on the 27th August 2018.

The World Health Organization (linked to from both the Centers for Disease Control and Prevention and the World Health Organization) produced a report *'Global status report on alcohol and health 2014'*, which initially appeared relevant, discussing the link between alcohol and depression and anxiety. However, on further examination of the references cited by this report, the evidence underpinning the statements were related to the association between Alcohol Use Disorder and depression and anxiety, rather than levels of alcohol consumption. These studies would therefore not have met our inclusion criteria.

No relevant articles were identified from the other website searches.

3.2 The process for selecting and screening studies

The inclusion/exclusion criteria were formulated based on the PECO (Population, Exposure, Comparator, Outcome) criteria used to define the research question. The PECO for selecting studies for appraisal are shown in Table 1, page 7.

In general, studies were excluded if they:

- Did not address the research questions;
- Did not provide information on the pre-specified exposure (alcohol use, i.e. studies which discussed substance use, without providing separate results for alcohol use, were excluded. Likewise, studies where the independent variable was an alcohol use disorder, without details of alcohol consumption, were also excluded);
- Did not address one of the pre-specified outcomes and/or provided inadequate data on these outcomes;
- Appeared to assess the influence of mental health on alcohol consumption (i.e. examining the association in the opposite direction);
- Did not have the appropriate study design, i.e. case reports or case series without a comparison (reference) alcohol consumption group, or cross-sectional studies;
- Were written in languages other than English;
- Focused on type of alcoholic beverage only, for example, beer or wine only; or
- Were only available in abstract form (*i.e.* conference abstract).

The research question of interest was whether alcohol affects mental health outcomes, rather than whether mental health status influences alcohol consumption. Studies without a time element (i.e. surveys or cross-sectional studies) are unable to determine the direction of effect. Preference was therefore given to higher level evidence with a time element (prospective cohort studies, all or none studies, retrospective cohort studies or case-control studies). Cross-sectional studies were therefore excluded.

Determination of eligibility of articles was performed in duplicate by two reviewers. Title and abstracts were screened in Endnote by one reviewer, and Rayyan by the other reviewer, and articles which either reviewer considered as potentially relevant were retrieved in full. Both reviewers determined eligibility on the basis of full text articles within Covidence. When discrepancies arose based on full text articles, these were discussed and the reviewers came to a consensus on inclusion/exclusion of studies. If agreement could not have been obtained, a third reviewer would have assessed the article, and the majority opinion would have prevailed (but this was not required).

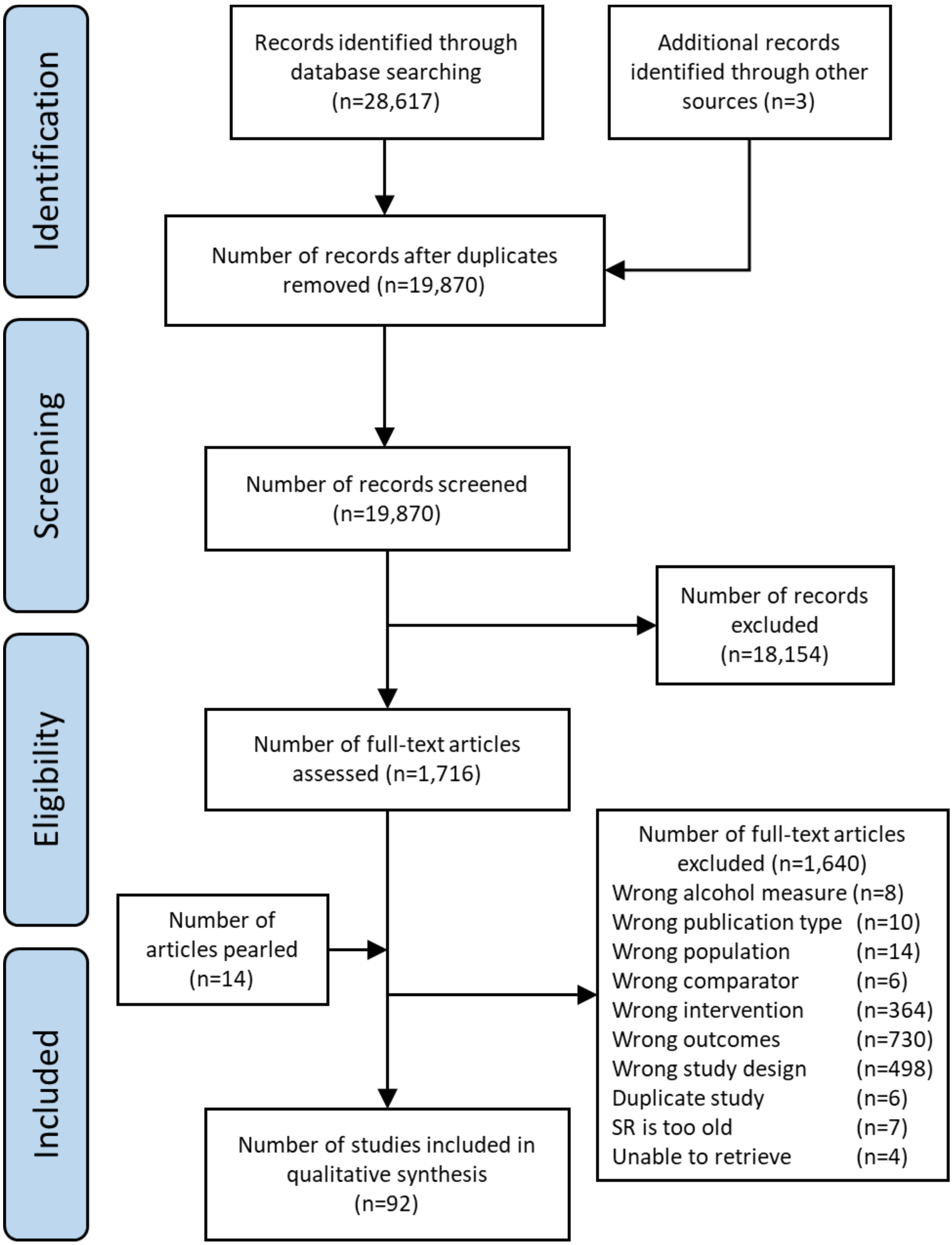

Figure 1 PRISMA flowchart showing the selection process for all the included studies (Liberati et al. 2009)

The study profiles for the 91 included studies are shown in Appendix B.
Studies that initially appeared to meet the inclusion criteria (potentially relevant) were subsequently excluded on the basis of the full text article, are shown in Appendix F. The Endnote libraries containing the initially retrieved citations can be supplied upon request.

4 Data extraction methods and tables

Data were extracted in duplicate by the reviewers into data extraction forms in Word which were designed specifically for this review. The data were put into two forms: study profile tables (see Appendix B), and study outcomes tables. (The reviewers had aimed to use Covidence for data extraction, however, Covidence was more time consuming than Word, so the reviewers switched to Word). Each reviewer then created a copy of their study outcomes tables, with the results removed, and the second reviewer then extracted the results in duplicate. A third reviewer then compared the outcomes extracted between reviewers, and where discrepancies arose, determined which outcomes were accurately extracted from the primary article.

Data were collected from each study on: authors, publication year, location, the funding source, study design, NHMRC aetiology level of evidence, risk of bias, study population characteristics (subgroups that were included), levels of alcohol consumption, mental health outcomes, inclusion/exclusion criteria, and follow-up period.

Descriptive statistics were extracted or calculated for all relevant outcomes in the individual studies – including numerator and denominator information, means and standard deviations, medians and inter-quartile ranges.

Relative effect measures (relative risks, odds ratios or hazard ratios), absolute risk differences, and associated 95% confidence intervals were extracted from individual comparative studies containing count data.

5 Methods used to critically appraise the quality of the included studies

Two reviewers initially appraised a small number of studies in duplicate, and discussed their classifications to promote consistency. They then each appraised half of the remaining studies, discussing the classification of risk of bias with the other reviewer if uncertain. Once all the studies had their risk of bias assessed, the distribution of risk of bias ratings were visually compared for the two reviewers. The average and spread of risk of bias classifications were very similar between reviewers.

6 Quality assessment of the included studies

Individual studies were critically appraised in terms of the risk of bias associated with their study design. Observational studies were assessed using the checklist adapted by the Centre for Public Health Excellence (CPHE), based on the GATE checklist. Systematic reviews would have been assessed using the AMSTAR 2 checklist, had any been included (Shea et al. 2017). The Cochrane Collaboration's tool for assessing risk of bias (Higgins et al. 2011) would have been used to appraise randomised controlled trials (RCTs) if any had been identified which met the inclusion criteria. The checklists are attached in Appendix D. The summary of the risk of bias of the included studies is shown in Table 50, page 171.

The research question was "What is the **association** between various levels and/or patterns of **alcohol consumption** and **mental health disorders?**"

The question was an aetiology question and aetiology study designs were expected to be identified (see Table 9). Aetiology studies are concerned with understanding the mechanisms that cause health outcomes (i.e. does alcohol consumption influence mental health status?). However, inferences are unlikely to be able to made about cause and effect, except where a time element can be captured ie mental health is normal at baseline and then alcohol consumption is measured and the impact on subsequent mental health status is recorded.

Table 9: NHMRC evidence hierarchy: designations of 'levels of evidence' for aetiology research questions

Level	Aetiology [a b]
I [c]	A systematic review of level II studies
II	A prospective cohort study
III-1	All or none [d]
III-2	A retrospective cohort study
III-3	A case-control study
IV	A cross-sectional study or case series

Source: (Merlin, Weston & Tooher 2009)

a. Definitions of these study designs are provided on pages 7-8 How to use the evidence: assessment and application of scientific evidence (NHMRC 2000b).

b. If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (i.e. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

c. A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

d. All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

7 The methods used to analyse, synthesise and summarise the results of the included studies

The intention was to meta-analyse the results of the identified studies where the populations, exposure definition and outcome measurement were similar enough for a meta-analysis to be informative. However, the included studies were too heterogeneous to meta-analyse, in regards to:

- the timing of baseline and follow-up questionnaires (i.e. age of participants included);
- the method of classifying alcohol consumption (i.e. as a continuous variable, as a dichotomous variable (drinker/abstainer or binge or heavy episodic drinker (HED)/non-HED drinker) or as a categorical variable (i.e. categories of daily, weekly or monthly consumption, or low, moderate, high)); and
- the statistics used to analyse the data.

The results are therefore synthesised with narrative summaries in appropriate subgroups and outcomes.

For each identified mental health outcome, the quality of the evidence contributing to that outcome will be assessed using GRADE. The GRADE approach involves considering the study design, the risk of bias, directness of evidence, inconsistency (heterogeneity), precision of effect estimates and risk of publication bias (and other biases) for each outcome, resulting in an overall quality of evidence depicted using the ⨁ symbol, with four ⨁⨁⨁⨁ indicating high quality, and one ⨁⊖⊖⊖ indicating very low quality. A Summary of Findings table containing the GRADE output will be constructed (Guyatt et al. 2013), and an evidence statement developed, reflective of the GRADE or confidence in the reported findings for each outcome, to be considered by the AWC and the ONHMRC.

The first step in the GRADE process is to identify whether the evidence was derived from a randomised controlled trial or other study types. Observational study designs are normally rated down by two points to 'low' quality, due the additional uncertainty of conclusions from observational studies, as compared to randomised trials. However, given the research question, randomisation may be not feasible or ethical (e.g. randomisation to large consumption of alcohol), and so prospective cohort studies were considered to be the most appropriate design (see Table 9). These were therefore only be rated down one point to 'moderate' quality rather than 'low' quality, and 'moderate' was used as the starting point for the quality of evidence. It was then decreased by 1 or 2 if there was inconsistency between studies, if the evidence was indirect (in regards to outcomes, population, setting, applicability to Australian context etc), if there was imprecision in the effect measure or publication bias (Table 10). Conversely, the quality rating was upgraded if there was a large magnitude of effect, if all plausible confounding would have reduced the demonstrated effect, or increased the effect if no effect was observed, or if there was a dose-response gradient identified (Table 11). The approach was consistent with that used in the 2017 Alcohol Guidelines report, as agreed to by NHMRC and the AWC (NHMRC Clinical Trials Centre 2017).

The GRADE system classifies risk of bias into categories of "not serious", "serious" or "very serious". The two reviewers assessing risk of bias of the individual studies also classified studies into three categories of bias, but these categories were "low risk of bias", "moderate risk of bias" and "high risk of bias", with separate categories for the internal validity of comparison between consumption groups, and the generalisability of the study population to the source population and Australia. The interval validity of the studies was used to determine the risk of bias, and cases of poor generalisability (rather than poor reporting) rated down the directness of the evidence.

Table 10 Factors that downgrade the quality of the evidence

Factor	Consequence
Limitations in study design or execution (risk of bias)[a]	↓ 1 or 2 levels
Inconsistency of results	↓ 1 or 2 levels
Indirectness of evidence	↓ 1 or 2 levels
Imprecision	↓ 1 or 2 levels
Publication bias	↓ 1 level

[a] based on quality assessment

Table 11 Factors that upgrade the quality of the evidence.

Factor	Consequence
Large magnitude of effect	↑ 1 or 2 levels
All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed	↑ 1 level
Dose-response gradient	↑ 1 level

Evidence statements derived from findings in the evidence base adopted consistent language to reflect the GRADE components. The Evidence Statements generally fit into one of the following categories:

I. *Consistent evidence of an association* – this wording was used when the body of evidence was deemed valid, applicable to the Australian context and consistently showed an association between alcohol consumption and mental health outcomes.
II. *The evidence shows no association* – this wording was used when the body of evidence was deemed valid, applicable to the Australian context, and demonstrated that there was no association between alcohol consumption and mental health outcomes.
III. *Limited evidence of an association* – this wording was used when it was deemed that there is limited confidence that the body of the evidence shows an association between alcohol consumption and mental health outcomes applicable to the Australian context.
IV. *No reliable evidence of an association* – this wording was used when the body of evidence could not confidently be deemed sufficiently valid or relevant to the Australia context, such

that the level of association between alcohol consumption and mental health outcomes cannot be determined. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include lack of consideration of: baseline physical and mental health status, age, sex, marital status, socioeconomic status, life events, occupation, type of area (urban/rural), presence of support group, smoking behaviour, illicit drug use, use of psychotropic drugs or therapy, and treatment for pre-existing mental health problems.

8 Applicability

The systematic review performed makes evidence statements, but does not make recommendations. The applicability of recommendations, and how they can be put into practice cannot therefore be discussed.

9 Editorial independence

The systematic review authors have no conflicts of interest to declare. Adelaide Health Technology Assessment is an independent research group from the School of Public Health, at the University of Adelaide.

The systematic review was funded by the NHMRC. The Office of the NHMRC provided comment on the systematic review protocol and will provide on the Evidence evaluation report and the Technical report.

The Alcohol Working Committee have declared their interests, which are published https://www.nhmrc.gov.au/health-topics/alcohol-guidelines/alcohol-working-committee.

No members of the Alcohol Working Committee have associations with the alcohol industry.

The systematic review protocol underwent independent methodological review to ensure that the processes used to derive, synthesise and appraise the evidence is appropriate, and that the subsequent review will be in accordance with the latest knowledge on alcohol and mental health.

10 Discussion of how comments from the independent methodological reviewer have been addressed.

The methodological reviewers considered there were several areas where the report could be improved.

- Be clearer about exposure measures, including clearly separating studies which measure binge drinking from those which measure overall consumption.
    - *The whole reporte was revised to redefine quantities of alcohol in terms of grams, and be explicit about what cut-offs each study used. The term 'binge drinking' has been removed from the document given the different definitions associated with this term.*
- Put more emphasis on studies at lower risk of bias and highlight these in the document, possibly excluding some studies based on failure to meet specific methodological requirements (e.g. adjusting for baseline depression)

- *More discussion of the risk of bias of studies was put into the report, and cases of heterogeneity were investigated to see whether risk of bias could contribute.*
- Incorporate the evidence statements into the GRADE chapter, and possibly also in the summary boxes.
  - *The evidence statements are all included in the 'Interpretation' column of the GRADE tables.*
- Improve the transparency of RoB assessments and GRADE assessments, both of which we would have expected to generally be lower.
  - *Each GRADE table now has the references for the individual studies, to make it easier to interpret how the GRADE was derived for each individual outcome. The text has more discussion of the risk of bias of studies.*
  - *The full risk of bias assessments for the included studies are available on request, but were not appended to the reports given the size of the document.*

The minor edits as suggested were all made.

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Appendix A Search strategy

Table 12 Full search strategy for Medline on the PubMed platform, searched on 14th May 2018

#1	(anxious[Title/Abstract] OR worry[Title/Abstract] OR worried[Title/abstract] OR anxiety[Title/Abstract] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed[Title/Abstract] OR mood[Title/Abstract])	501087
#2	("Mood Disorders"[Mesh] OR "Anxiety Disorders"[Mesh])	167689
#3	("alcohol use"[Title/Abstract] OR alcoholic[Title/Abstract] OR (alcohol AND drink*)[Title/Abstract] OR "alcohol consumption"[Title/Abstract])	36715
#4	("Alcohol-Related Disorders"[Mesh] OR "Alcohol Drinking "[Mesh] OR “Alcohol Abstinence”[Mesh] OR "Alcoholic Beverages”[Mesh])	164232
#5	(#1 OR #2)	557855
#6	(#3 OR #4)	178445
#7	(#5 AND #6)	12595
#8	(#5 AND #6) Filters: Publication date from 2007/01/01	5596

MeSH = Medical Subject Heading, based on a Medline/PubMed platform

Appendix B Study profiles

Table 13 Study profiles for longitudinal studies (level II aetiological evidence)

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
An & Xiang (2015) United States Health and Retirement Study (HRS)	To examine the relationship between heavy smoking, heavy drinking and depression in U.S. middle aged and older adults.	N=24,759 with no depression at baseline. Overall response rate 80% across waves.	**Inclusion criteria:** HRS participants born 1900-1953 (≥50 years old at baseline), and free from depression at first interview. **Exclusion criteria:** Age ineligibility, presence of specific condition at baseline, and/or missing covariates.	Mean age 60.5 51.0% male 79.9% non-Hispanic White 10.3% African American 6.9% Hispanic 70.3% married or living with partner 51.3% high school educated, 21.8% college, 10% high than college 18% heavy drinker 17.9% smoker 8.8% ever been diagnosed with psychiatric problems	Funding source not stated. Conflicts of interest NR
Armeli et al. (2015) United States	To examine the effect of drinking and motivations to drink on subsequent month's affect.	522/575 provided at least 1 year of data. Those excluded more likely to be men, and have AUD symptoms at Year 1.	**Inclusion criteria**: students studying Introductory Psychology at the University of Connecticut, who initially reported drinking alcohol ≥2 times in past month and provided at least 1 year of data. **Exclusion criteria**: NR	Mean age at baseline: 18.9±1.1 years Sex distribution not stated. 58% freshmen, 33% sophomores, 9% juniors or beyond	Supported by National Institute on Alcohol Abuse and Alcoholism Grant. Conflicts of interest NR
Augestad et al. (2008) Norway The Health	To assess potential gender differences in the association between physical activity and	77,310/85,100 (91%) returned the questionnaire 74,977/77,310 (97%) received the medical examination	**Inclusion criteria:** all residents in the county aged ≥20 years who were invited for health screening in 1984−1986 (HUNT 1) and in 1995−1997 (HUNT 2) and were aged 31−50 years in	HUNT reported physical activity in 1984−1986 (HUNT 1) and studied the association with occurrence of depression as reported at follow-up in 1995−1997 (HUNT 2). **N=3,353 women who were included**	Funding source NR Conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Survey in Nord-Trondelag (HUNT)	occurrence of depressive symptoms	21,235/74,977 subjects in HUNT 1 met the inclusion criteria 6,661/21,235 did not meet exclusion criteria and were included	HUNT 2 **Exclusion criteria:** those who did not participate in both surveys, HUNT 1 participants with diabetes, severe disability, using blood pressure medication, had had a myocardial infarct, angina or stroke, using painkillers, often nervous, depressive symptoms, those with missing information	20% aged 21−25 years, 26% aged 26−30 years, 28% aged 31−35 years, 26% aged 36−40 years, 71% <12 years education, 16% >12 years education, 3% underweight, 18% overweight, 1% obese, 41% living with a child, 4% living alone, 38% do physical activity <1 times/week, 33% do physical activity once/week, 22% do physical activity 2−3 times/week, 7% do physical activity almost daily, 30% do easy physical activity, 37% do moderate physical activity, 2% do vigorous physical activity, 40% current smokers, 5% are abstinent, 47% did not drink in last 2 weeks, 45% drank 1−4 times in last 2 weeks, 1% drank 5−10 times in last 2 weeks, 1% drank >10 times in last 2 weeks. **N=3,308 men who were included** 17% aged 21−25 years, 25% aged 26−30 years, 27% aged 31−35 years, 31% aged 36−40 years, 71% <12 years education, 18% >12 years education, <1% underweight, 35% overweight, 3% obese, 37% living with a child, 7% living alone, 44% do physical activity <1 times/week, 26% do physical activity once/week, 24% do physical activity 2−3 times/week, 6% do physical activity almost daily, 15% do easy physical activity, 42% do moderate physical activity, 7% do vigorous physical activity, 32% current smokers, 2% are abstinent, 25% did not drink in last 2 weeks, 66% drank 1−4 times in last 2 weeks, 4% drank 5−10 times in last 2 weeks, 3% drank >10 times in last 2 weeks.	
Baethge et al. (2008) United States McLean-Harvard First-Episode	To examine temporal patterns of associations of affective morbidity before, during and following the use of alcohol and cannabis.	N=166 patients. Response rate NR.	**Inclusion criteria:** patients aged ≥18 years old, with a first-lifetime, Structured Clinical Interview DSM-IV (SCID) diagnosed manic or mixed episode of type I Bipolar Disorder, consecutively admitted to McLean Hospital	Median age at intake: 28 (range 18 – 72) years 90 men, 76 women 45.2% met DSM-IV criteria for substance use disorder. Alcohol use exceeded occasional social drinking or met DSM-IV criteria for alcohol abuse at baseline or follow-up in 62% and cannabis used more than sporadically by 18.2% of subjects.	Supported by the Mental Health Research Association, the Max Kade Foundation, a Kenneth R. Rossano Predoctural

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Project			Institutional Review Board. **Exclusion criteria**: acute intoxication, withdrawal or delirium; previous hospitalisation; mental retardation (IQ<70) or organic mental disorder; ill>one year before intake; or >3 months of prior antipsychotic or mood stabiliser treatment.		Research Fellowship, the Atlas Foundation and NARSAD grants and NIH gratns, and the Bruce J Anderson Foundation the McLean Private Donors Research Fund. Maruicio Tohen is employed by Eli Lilly & Co; Ross J Baldessarini is consultant or research collaborator to Auritec, Biotrofix, IFI SpA, Janseen, JDS, Eli Lilly & Co., Merck, MK-Biopharmaceuticals, NeuroHealing, and Novartis Corporations.
Bahorik et al. (2016) United States	Investigated whether differences existed between patients with and without AUD in terms of marijuana use, depressive	N=307. Participation rate NR. Limited generalisability as all patients had been referred to a dependency recovery unit for either hazardous alcohol use or drug use.	**Inclusion criteria:** aged 18 or over, filled in PHQ-9, absence of mania/ psychosis, and drug use (illicit/non-prescribed) or hazardous drinking (3 drinks/day for women; 4 drinks/day for men) in past 30 days	Mean age 37 ± 13.0 years 70.3% women 38.1% White; 21.1% Hispanic, 14% Asian, 21.8% Black, 4.2% other race/ethnicity 42% married 48.5% had AUD 60% hazardous drinking at baseline	Supported by the National Institute on Alcohol Abuse and Alcoholism Conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	symptoms and functional outcomes		**Exclusion criteria**: safe alcohol use or no illicit drug use	40.7% use marijuana at baseline Patients without AUD more likely to use marijuana (48.1%) than those with AUD (32.8%)	
Bell & Britton (2015) UK	To examine the association between drinking habits in midlife and depression during long-term follow-up.	8,838/10,308 (86%) men and women from the original cohort had no depression at baseline 7,478/8,838 (85%) met the inclusion/exclusion criteria for this study British civil servants are not representative of the general population, particularly not blue-collar workers and the unemployed There was no difference between those retained and excluded by age. However, women and those from lower socioeconomic groups were more likely to be excluded	**Inclusion criteria:** British civil servants aged 35–55 years from the Whitehall II study **Exclusion criteria:** Participants with depression or missing the depression measurement at baseline, those with no depression information at subsequent follow-ups, those who were missing values for any of the drinking variables and covariates	British civil servants aged 35–55 years at base-line (1985–1988) from the Whitehall II prospective cohort study **N=7,478 included participants: baseline characteristics** Mean age 44.3±6.1 years, 71% male, 32% high socioeconomic position, 19% low socioeconomic position, 77% married/de facto, 15% single, 16% current smokers, 34% ex-smokers, 66% had a good diet, 73% were physically active, 77% had self-rated good health, 26% participated in HED, 4% were abstainers, 81% were moderate drinkers, 15% were hazardous drinkers, 30% were daily drinkers, 42% were weekly drinkers, 13% were monthly drinkers, 12% were occasional drinkers, 25% had depression during follow-up	The study was supported by a UK Economic and Social Research Council PhD studentship and grants from the European Research Council and the UK Medical Research Council/Alcohol Research UK Authors declared no conflicts of interest
Birkley et al. (2015) United States	To examine the temporal relationship between alcohol consumption and depressive symptomatology.	N=743/800 Retention rate of 93% at Wave 2 1,906/1,988 participated overall (including European American) Mean age not stated, although wave 1 in 5th graders, and they state the average age of 5th graders is 11 years old	**Inclusion criteria:** Elementary school children (5th graders) whose parents were participating in another study. This study focused on African American (AA) and Hispanic American (HA) children with a random sample of European American (EA) children. **Exclusion criteria:** NR	**African Americans (n=328; 41%)** 48.7% male; 20.1% >high school diploma; 4.4% unemployed, 11.8% adults poverty rate; 17.1% child poverty rate **Hispanic Americans (n=144; 18%)** 50.0% male; 18.8% >high school diploma; 3.6% unemployed, 9.3% adults poverty rate; 14.0% child poverty rate **European Americans (n=328; 41%)** 48.4% male; 14.5% >high school diploma; 2.7% unemployed, 6.9% adults poverty rate; 9.8% child	Supported by the National Institute on Alcohol Abuse and Alcoholism. Conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				poverty rate	
Boscarino et al. (2011) United States	To examine relationship between alcohol use before and following the World Trade Center (WTC) attacks in New York, and their relationship to PTSD and PTSD symptoms.	N=2,368 (63% cooperation) at baseline (13-15 months after WTC attack) At follow-up, 1,681/2,368 responded (71%) (25-29 months after WTC attack) Oversampling of groups who have lower follow-up (younger persons, men, Blacks and Lations)	**Inclusion criteria:** adults aged ≥18 years living in New York City on the day of the WTC attacks. **Exclusion criteria:** NR	22.7% 18-29 years; 32.9% 30 – 44 years; 32.5% 45 – 64 years, 11.9% 65+ 46.2% male 33.8% <$30,000; 46.5% $30,000 - $99,000; 16.1% $100,000+ 50.3% married 41.7% college graduate 43% White; 26% White, 24.1% Latino 36% low social support, 37.9% moderate social support, 26.2% high social support	Supported by the National Institute of Mental Health and the Pennsylvania Department of Health Conflicts of interest NR
Bots et al. (2008) Finland, Italy and the Netherlands Elderly (FINE) study	To identify modifiable risk factors for late-life depression.	526 who participated in both baseline examinations (1989-1991) and follow-up (1994-1995). 56 excluded due to depression at baseline.	**Inclusion criteria:** Men born between 1900 and 1920, who participated in the Seven Countries Study, and were survivors from one of 5 centers in Finland, Italy and the Netherlands. **Exclusion criteria**: cognitively impaired at baseline, or depressed at baseline.	Mean age 75.2 years at baseline (80.0 years at follow-up). 100% male **Not depressed at follow-up (n=467)** Mean education: 8.2±4.6 years; 21.0% single/divorced/widowed; 9.4% conjugal loss between study years; 53.8% moderate alcohol consumption at baseline; 21.6% high alcohol consumption at baseline; 15.3% smoked **Depressed at follow-up (n=59)** Mean education: 7.0±4.7 years; 25.4% single/divorced/widowed; 21.4% conjugal loss between study years; 36.0% moderate alcohol consumption at baseline; 26.0% high alcohol consumption at baseline; 15.3% smoked	Supported by a grant from the European Union. Conflicts of interest NR
Brennan et al. (2016) United States Health and Retirement	To examine prospective relationships between older adults' baseline health behaviours,	N=7,939 / 8,635 (excluding those who did not provide their own information). No data about larger study data (how representative, attrition etc).	**Inclusion criteria:** individuals aged 55 – 65 years **Exclusion criteria**: those whose information was provided by proxy informants	Mean age 59.80±3.16 years; 43.9% male; 80% White; 20% other; 73.1% married; 1.75±1.40mean number of medical conditions; 39.5%abstinent without history of drinking problems; 9.4% abstinent with history of drinking problems; 17% light drinkers; 20% moderate drinkers; 14.1% heavy drinkers; 5.5% participated in HED; 23.7%	Supported by the NIH, National Institute on Alcohol Abuse and Alcoholism and by Health Services

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Study	and subsequent depressive symptom trajectories.			history of drinking problems.	Research and Development, Department of Veterans Affairs The authors declare no conflicts of interest.
Brook et al. (2014) United States Harlem Longitudinal Development Study	To examine concurrent triple comorbid trajectories of tobacco, alcohol and marijuana (from time 2, T2 to time 5, T5)	N=816/1332 1332 at T1 (recruitment at T1 not described; mean age 14.1) 1190 at T2 (mean age 19.2 years) 662 at T3 (random sample due to budget restrictions; mean at 24.4 years) 838 at T4 (mean age 29.2 years) 816 at T5 (61% of original sample; mean age 32.3 years)	**Inclusion criteria:** participants attending schools in the East Harlem area of New York City. **Exclusion criteria:** no follow-up data at T5	Mean age at T2 19.2 years 52% African American, 48% Puerto Rican Further demographics not stated (*supplement to online version not available)*	Supported by the National Institute on Drug Abuse and by the National Cancer Institute. Conflicts of interest NR
Brook et al. (2016) United States Children and Adults in the Community study	To examine patterns of comorbid use of three substances of abuse (tobacco, alcohol, marijuana), and the associations between these patterns and psychopathology in adulthood.	N=973 recruited at Time 1, T1 at age 5 years Data from: 756 at T2 (1983, mean age 14.1±2.8) 739 at T3 (1985-6, mean age 16.3±2.8) 750 at T4 (1992, mean age 22.3±2.8) 749 at T5 (1997, mean age 27±2.8)	**Inclusion criteria**: randomly selected families from 2 New York counties in 1975, who participated in at least 2 waves of data collection between T2 and T7. **Exclusion criteria:** NR	Mean age at T7: 36.6±2.8 years 50% female 90% White, 8% African America, 2% Other	Supported by grants from the National Cancer Institute and the National Institute on Drug Abuse. The funders had no role in design, data collection, interpretation, drafting of manuscript, or

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
		673 at T6 (2002, mean age 31.9±2.8) 607 at T7 (2005-2006, ages 32-42) Participation rate not stated. A random community-based sample (selected in 1975). Close match between those sampled and the 1980 census with regard to demographics, racial distribution, family income, maternal education and family structure.			decision to submit. All authors declare no conflict of interest.
Bulloch et al. (2012) Canada	To evaluate the incidence of MDE in relation to different patterns of alcohol use	15,254 participants in Wave 1 (1994) By Wave 7 (2006) 12% were deceased 0.9% were institutionalised 22.8% were non-respondents 64.4% completed all 7 waves Differences between participants and non-participants NR	**Inclusion criteria:** Initial data collection took place in 1994 using face-to-face interviews of a nationally representative cohort of 17,276 household residents **Exclusion criteria:** those who had MDD at baseline	Participants in the longitudinal National Population Health Survey (NPHS) **N=15,254 participants in Wave 1 (1994)** 49% male, 12% aged 12−18 years, 11% aged 19−25 years, 40% aged 26−45 years,24% aged 46−65 years, 13% aged ≥66 years, 59% married, 29% never married, 60% currently employed, 50% had ≥1 chronic condition, 12% had severe or moderate pain, 18% had income in the lower quartile, 29% were smokers, 12% were non-drinkers, 10% were guideline drinkers, 61% participated in HED **N=13,175 participants in Wave 1 (1994) who did not have MDD** 48% male, 12% aged 12−18 years, 10% aged 19−25 years, 41% aged 26−45 years,25% aged 46−65 years, 13% aged ≥66 years, 60% married, 28% never married, 61% currently employed, 50% had ≥1 chronic condition, 11% had severe or moderate pain, 18% had income in the lower quartile, 28% were smokers, 11% were non-drinkers, 10% were guideline drinkers, 59% participated	Funding was provided by a grant from the Canadian Institutes for Health Research. Conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				in HED	
Byers et al. (2012) United States Study of Osteoporotic Fractures	To characterise the natural course of depressive symptoms among older women. Secondary objective was to examine if lifestyle factors known to be associated with late-life depression differentially predict depressive symptom trajectories.	7240/ 9704 women who had at least 2 measurements of depressive symptoms over 20 years	**Inclusion criteria:** older community-dwelling women from population-based listings in 4 areas of the United States **Exclusion criteria:** Unable to walk without help or undergone bilateral hip replacements.	Mean age 72.8±4.7 years at baseline (followed into their 80s and 90s) 100% female 99.7% White	Supported by the National Institute of Mental Health, National Institute on Aging and Public Health Service grants from the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Authors declared no conflicts of interest.
Cabello et al. (2017) Russia, Ghana, India and Mexico WHO's Study on Global AGEing and Adult Health (SAGE)	To determine whether people with unhealthy lifestyles are more likely to develop depression.	SAGE Wave 0 (2002-2004): 95% in Ghana, 94% in India, 100% in Mexico and 99% in Russia. Wave I (2007-2010): 81% in Ghana, 68% in India, 53% in Mexico and 84% in Russia.	**Inclusion criteria:** adults who responded to both wave 0 and wave I of SAGE. Nationally representative samples of adults aged 50 years and older and smaller sample 18-49. **Exclusion criteria:** NR	Sample characteristics for whole sample not provided. **Persistent depression (n=219):** Mean age: 51.4 ± 14.77 years 75% women, 50% unemployed, 38% Mexican, 1.2% Ghana, 2.8% Russia, 57.9% India 41.6% in lower 2 quintiles of household income 42.9% less than primary school education 30% healthy, 70% at least one health condition 92% never drink, 6% current drinkers, 2% heavy drinkers **Incident depression (n=594):** Mean age: 50.2 ± 15.4 years 67% women, 40.9% unemployed, 34% Mexican, 4.2% Ghana, 3% Russia, 58% India 36.7% in lower 2 quintiles of household income 41.2% less than primary school education 44% at least one health condition	SAGE is supported by the US national Institute on Aging through Interagency Agreements. Funding for this paper from People Programme of the European Union's Seventh Framework Programme and Centro de Investigacion Biomedica en Red en Salud Mental and the Instituto de Salud Carlos III.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				92% never drink, 6% current drinkers, 2% heavy drinkers	The authors have no conflicts of interest.
Cerda et al. (2016) United States Pittsburgh Youth Study (PYS)	Is there a within-person association between an increase in psychiatric problems and an increase in substance use among adolescent males?	503 boys (92.1% participation)	**Inclusion criteria:** boys aged 13-19 randomly selected from schools based on a comprehensive public school enrolment list from the Pittsburgh Board of Education. **Exclusion criteria:** NR	100% male 56% Black, 41% White, 3% Asian, Hispanic or mixed-race	Supported by National Institutes of Health Grants. Data collection supported by grants from the National Institute on Drug Abuse, National Institute on Mental Health, Pew Charitable Trusts, and Office of Juvenile Justice and Delinquency Prevention. The authors declare no conflicts of interest.
Chan et al. (2013) Australia	To evaluate the role of family conflict and subsequent depressed mood in predicting heavy alcohol use among adolescent girls.	1,239/2,416 (51%) of students agreed to participate and 16 were excluded 93.2% of Wave 1 sample participated in Wave 2 94.4% of Wave 2 sample participated in Wave 3 (87% retention overall). Participants who dropped out of the study were more likely to have: higher depressed	**Inclusion criteria:** First-year high school students (at Wave 1) from 12 metropolitan state and Catholic secondary schools in Victoria, a state-representative sample of schools **Exclusion criteria:** students who did not consent, lack of parental consent, absence from school on day of survey, providing invalid responses and incomplete data.	N=969 high school students from 12 metropolitan state and Catholic secondary schools in Victoria, who completed all three wave samples Characteristics at baseline **N=683 No HED** 59% female, 30% ethnic background, 19% had parents not living together, 17% had low commitment to school. **N=203 HED** 52% female, 24% ethnic background, 28% had parents not living together, 23% had low commitment to school.	Funding from the NHMRC, the Australian Research Council and the Alcohol Education and Rehabilitation Foundation, and the Grosvenor Settlement philanthropic trust. Conflict of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
		mood (p<0.001), higher family conflict (p<0.001), low school commitment (p<0.05), report lifetime alcohol use (p<0.001), and were less likely to live with both parents (p<0.001)	Participants who reported heavy alcohol use at Wave 1 were excluded from the key longitudinal regression analyses		
Chang et al (2016) United States Nurses' Health Study	Investigate a comprehensive array of potential risk/protective factors for late life depression.	N=21,728/121,700 women from Nurses Health study, after excluding those who died before 2000, did not return 2000 questionnaire, where depression could not be determined, who had depression, aged under 65 years, had no health examination at follow-up.	**Inclusion criteria:** female nurses aged 33 – 55 years in 1976 (analyses restricted to those over 65 years in 2000). **Exclusion criteria**: died before 2000, did not return 2000 questionnaire, where depression could not be determined, who had depression, aged under 65 years, had no health examination at follow-up.	Mean age 71.4± 4.1 years 92.5% White; 0.9% Black; 1.8% Other 6.2% current smokers 91.9% ≤1 comorbidity; 9.1% >2 comorbidities Largest no. of drinks in a single day: 41.1% none; 49.2% 1-2; 9.7 ≥	Supported by National Institutes of Health research grants. Funding support also received from Harvard Medical School Office for diversity Inclusion and Community Partnership Faculty Fellowship. The sponsors had no role in the design of the study, collection, management, analysis or interpretation of results. The authors have no conflicts of interest.
Cheng et al. (2016) China China Health	To provide the first estimates for the prospective association between	17,708 (80.5%) of individuals responded at W1 in 2011–2012. 15,628/17,708 (88%) were successfully re-interviewed	**Inclusion criteria:** 80 households were selected by simple random sampling from each of the 150 selected counties and all persons aged	**N=17,708 Wave 1 participants** 48% male, 24% current drinkers, 4% more than daily drinkers, 26% current tobacco use, 16% smoke ≥20 cigarettes/day, 13% nicotine dependence, 22% depressive symptoms, 5% excellent health. 17% good	Funded by the Chinese Medical Board of New York Conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
and Retirement Longitudinal Study (CHARLS)	depressive symptoms and a range of drinking- and smoking-related variables Logistic regression OR for predicting depression by alcohol consumption frequency	for W2 in 2013–2014 Individuals who were lost to follow-up were older (p<0.001) and more likely to report good health (p<0.001). There were no differences in gender, current drinking, alcohol withdrawal, heavy smoking, and the presence of depressive symptoms.	45 years or older from the selected household were asked to participate. **Exclusion criteria:** NR	health, 43% fair health, 26% poor health, 8% very poor health. **N=15,628 Wave 2 participants** 48% male, 24% current drinkers, 4% more than daily drinkers, 26% current tobacco use, 16% smoke ≥20 cigarettes/day, 14% nicotine dependence, 22% depressive symptoms, 6% excellent health. 17% good health, 44% fair health, 26% poor health, 7% very poor health.	NR
Chou et al. (2011) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	To provide estimates of the risks posed by the status of HED in the year prior to the 2001-2002 NESARC for subsequent occurrence of specific Axis I psychiatric disorders.	N=13,489 (middle aged and older subsample of NESARC, 43,093 in Wave 1) Attrition for older group not stated. Overall response for Wave 2 was 86.7% (excluding those who died, were deported, mentally or physically impaired, or on active duty in armed forces)	**Inclusion criteria:** aged 50 years and above who participated in both Waves 1 and 2 of the NESARC **Exclusion criteria:** NR	**Males (n=5,461)** Non-drinkers: 1,987 Current drinkers but no past year HED: 2,616 Past year HED <1 per month: 310 Past year HED ≥1 per month: 548 **Females (n=7,981)** Non-drinkers: 4,302 Current drinkers but no past year HED: 3,223 Past year HED <1 per month: 223 Past year HED ≥1 per month: 233 Demographics overall not provided (only what proportion of each category met the drinking categories).	No funding for this analysis. The NESARC was conducted and funded by the National Institute on Alcohol Abuse and Alcoholism, with supplemental support from the National Institute on Drug Abuse. The authors have no conflicts of interest.
Cisler et al. (2012) United states National	To examine the effect of interpersonal violence on risk of subsequent psychopathology	N=3,614/6,928 contacted (52%) Non-completers had more people living in household, more females, more single parents, more rural, parents	**Inclusion criteria:** adolescents aged 12 – 17 residing in the United States **Exclusion criteria:** NR	Mean age at wave 1: 14.63 ± 2.70 years 65% Caucasian; 15% African American; 11% Hispanic; 2% Native American, 3% Pacific Islander/Asian, 3% Other Mean annual household income = $46,093 ± $8, 775	Funding source and conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Survey of Adolescents – Replication (NSA-R)	(PTSD, depression, delinquency, problematic drinking), in the presence of the effects that these variables have on one another.	less concerned about violent crime, parents who had not talked with adolescent about how to avoid being molested, sexually abused, how to avoid drugs and alcohol. 2,511/3,614 measured at wave 2 1,653/3,614 measured at wave 3			
Cougle et al. (2015) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	To examine whether weekly use of alcohol, regardless of dependence status, was associated with onset of psychiatric diagnosis 3 years later.	43,093 participated in Wave 1 (81.01% response rate) 34,653 participated in Wave 2 (80.4%). Wave 2 responders did not differ from non-responders.	**Inclusion criteria:** non-institutionalised US citizens **Exclusion criteria**: NR	NR	No funding sources to declare. The authors declare no conflicts of interest.
Danzo et al. (2017) United States	To examine pathways connecting alcohol use and depression symptoms longitudinally from 6th to 9th grade.	N=593/782 families participated (73%). Unclear if only child per family recruited (i.e. whether there were 593 participants or higher).	**Inclusion criteria:** 6th graders from 3 urban middle schools **Exclusion criteria:** NR	Mean age: 11 years 10 months (wave 1); 13 years 1 month (wave 2); 14 years 1 month (wave 3) and 15 years (wave 4) 51% males 36% European Americans; 18% Hispanic or Latino; 15% African American; 7% Asian; 19% biracial or mixed identify; 2% Pacific Islander; 2% Native American 80% of participants' father and 79% mothers had ≥high school degree 87% children felt neighbourhood safe or very safe	Supported by the National Institute on Drug Abuse. Conflicts of interest NR
Dawson et al. (2008)	To illustrate the role of confounders in	22,122 included 34,653/ 39,959 eligible	**Inclusion criteria:** adults 18 years or older, representing the population residing in	**Characteristics by baseline risk drinking category.** **Never (n=13,507; 59.9%)**	NESARC sponsored by the National Institute on

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
United States National Epidemiologic al Survey on Alcohol and Related Conditions (NESARC)	attenuating the associations between frequency of risk drinking and harm.	responded (81% response rate) for Wave 1 86.9% reinterview rate for Wave 2 Those who drank at least once in year preceding included.	households and non-institutional group quarters in all 50 states and the District of Columbia, who had consumed at least one drink in the year immediately preceding the Wave 1 interview. **Exclusion criteria:** Missing frequencies of risk drinking at baseline.	Mean age 46.8 years 47.2% male 80.6% non-Hispanic white 69.1% married 76.8% employed 63.7% attended college **<1/month (n=3553; 16.7%)** Mean age 37.8 years 54.0% male 82.7% non-Hispanic white 62.8% married 90.4% employed 67.5% attended college **1-3/month (n=2001; 9.1%)** Mean age 36.0 years 57.9% male 80.3% non-Hispanic white 54.2% married 90.0% employed 61.4% attended college **1-2/week (n=1794; 8.5%)** Mean age 34.9 years 67.8% male 76.9% non-Hispanic white 47.3% married 91.3% employed 58.8% attended college **3-4/week (n=618; 2.8%)** Mean age 35.9 years 68.9% male 78.9% non-Hispanic white	Alcohol Abuse and Alcoholism, National Institutes of Health, and national Institute on Drug Abuse Authors declared no conflicts of interest.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				44.9% married 88.9% employed 55.9% attended college **Daily/near daily (n=649; 3.0%)** Mean age 41.7 years 75.7% male 77.5% non-Hispanic white 51.8% married 81.1% employed 45.9% attended college	
Edwards et al. (2014) UK Avon Longitudinal Study of Parents and Children (ALSPAC)	To examine the relationship between frequency of drinking during early adolescence (ages 13–15) with problems with depression and anxiety 2−4 years later	13,978 singleton/twins/ 14,062 pregnancies were still alive at 12 months 7,100 adolescents attended clinics at median ages of 12 years 10 months, 13 years 10 months, and 15 years 5 months. 4,292 adolescents self-administered the Clinical Interview Schedule–Revised (CIS-R) via computer at the median age of 17 years 10 months Missing outcome data were more common among boys, participants whose mothers had lower levels of education, individuals living in rented or subsidized housing, individuals in crowded homes, those with higher levels of conduct problems, and those whose mothers exhibited	**Inclusion criteria:** participant in the ALSPAC study with alcohol use data at age 13–15 years and depression/anxiety data at age 17 years 10 months **Exclusion criteria:** NR	**Adolescents from ALSPAC** Males: at age 13–15 years 61% had a low drinking frequency, 28% had a medium drinking frequency and 11% had a high drinking frequency; at age 17 years and 10 months 4% had depression and 7% had anxiety. Females: at age 13–15 years 58% had a low drinking frequency, 31% had a medium drinking frequency and 11% had a high drinking frequency; at age 17 years and 10 months 11% had depression and 15% had anxiety. No other baseline characteristics were provided However, housing tenure (owned/mortgaged, privately rented, subsidized housing rented from council/housing association), crowding status (the ratio of number of residents to number of rooms in house), maternal education (no high school qualifications, high school, beyond high school), maternal harmful alcohol use (Yes, no), conduct problems age 11 .(low, medium high), maternal depression factor score were investigated for multivariate analysis	Funded by funded by a National Institutes of Health Grant Conflicts of interest NR

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		harmful drinking at child age 12. Participants whose mothers had higher depression scores were more likely to be missing outcome data. Frequency of alcohol use was not associated with missing outcome data.			
Fleming et al. (2008) United States Raising Healthy Children project	To look at 4 types of associations between substance use and depression	N=951/ 1046 Those who dropped out were similar to those retained. Each time point had data on >97% of sample. All data available for 93% of participants.	**Inclusion criteria:** students from 10 public schools in a suburban Pacific Northwest school district. Participants had to complete at least one of the annual surveys from 8th to 11th grade. **Exclusion criteria:** NR	Mean age at baseline: 12.94 years (range 12 – 14) 81% White, 7% Asian or Pacific Islander, 5% Hispanic, 4% Black, 3% native American 38% receive free or reduced price school lunch in first year of project	Supported by the National Institute on Drug Abuse. Conflict of interest NR
Flensborg-Madsen et al. (2011) Denmark Copenhagen City Heart Study (CCHS)	To investigate in a large population sample the prospective association between self-reported amount of alcohol intake and the later risk of being registered at a hospital with anxiety disorders.	14,223 participants in 1976−78 (74% response rate) 12,698/14,223 (70%) participated in 1981−83 10,135/14,223 (61%) participated in 1991−93 No description of participant characteristics was provided	**Inclusion criteria:** The sample was randomly drawn from the Central Population Register, by use of the unique personal identification number, and invited by letter to answer self-administered questionnaires in the years 1976–1978 **Exclusion criteria:** NR	**N=18,146 individuals completing at least one of the three questionnaires in CCHS I–III** 5% registered with mood disorders, 2% with psychotic disorders, 2% with anxiety disorders, 3% with personality disorders, 2% with drug abuse, and 12% some kind of psychiatric disorder other than AUD.	Supported by research grants from the Lundbeck Foundation and the IMK Almene Fond Conflict of interest NR
Fröjd et al. (2011) Finland Adolescent	To explore whether associations between anxiety and alcohol are already evident in	3,278 (94%) of students participated in W1 1,609 girls and 1,669 boys 2,070/3,278 (63%) students participated in W2	**Inclusion criteria:** Ninth grade students (aged 15–16 years) from all Finnish-speaking secondary schools in two Finnish cities, Tampere and	Ninth grade students who participated in AMHCS. **N=2,070 students (baseline parameters)** 4% had anxiety, 9% had social phobia, 10% frequently drank alcohol, 3% were frequently drunk, and 3% used marijuana.	Supported by funding from the Pirkanmaa Hospital District, Yrjö Jahnsson Foundation and the

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Mental Health Cohort Study (AMHCS)	middle adolescence	28% of the girls and 46% of the boys were lost to follow-up Those with an intact family and those with better educated parents responded to the follow-up more frequently. General anxiety and higher levels of alcohol use were associated with a lower probability of responding	Vantaa **Exclusion criteria:** respondents who completed the survey facetiously	No other patient demographics were reported although baseline family structure and parental educational level were identified as confounders	Finnish Cultural Foundation. Conflict of interest NR
Gea et al. (2012) Spain "Seguimiento Universidad de Navarra" (SUN) project	To prospectively evaluate the influence of alcohol intake on incident depression in a Mediterranean cohort.	19,576 subjects were recruited up to February 2008 17,462/19,576 (89%) were successfully followed-up at least once N=2,769 abstainers (628 males) N=7,921 <10 g/day (3,017 males) N=2,240 10−25 g/day (1,462 males) N=689 >25 g/day (594 males) High alcohol intake (>25 g/day) was associated with being male (86% were male), older (mean age was 46 years), and with higher BMI (mean BMI 26 kg/m^2)	**Inclusion criteria:** university graduates who were recruited to the study and returned the biennial mailed questionnaires **Exclusion criteria:** energy intake out of predefined limits (800−4,000 Kcal/day in men and 500−3,500 Kcal/day in women), prevalent, personal history of previous depression, or use of antidepressants at baseline, incident depression in the first follow-up questionnaire	Participants in the SUN Project, recruited between 1999 and 2008. **N=13,619 participants without baseline or early incident depression** 58% female **N=628 male abstainers** Mean age 43±15 years, mean BMI 25±3, 13% current smokers, 29% ex-smokers, 59% married, 5% living alone, 3% unemployed **N=2,141 female abstainers** Mean age 36±11 years, mean BMI 22±3, 15% current smokers, 20% ex-smokers, 49% married, 5% living alone, 5% unemployed **N=3,017 males drinking <10 g/day** Mean age 42±13 years, mean BMI 25±3, 16% current smokers, 35% ex-smokers, 63% married, 5% living alone, 2% unemployed, mean alcohol intake 5±3 g/day, 2 g/day from wine, 2 g/day from beer and 1 g/day from spirits. **N=4,904 females drinking <10 g/day** Mean age 34±10 years, mean BMI 22±3, 25% current	The SUN Project has received funding from the Instituto de Salud Carlos III, the Navarra Regional Government and the University of Navarra. Two authors were supported by fellowships from the "Instituto de Salud Carlos III", and the Ministerio de Educación, Cultura y Deporte Authors declared no conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				smokers, 27% ex-smokers, 43% married, 7% living alone, 6% unemployed, mean alcohol intake 3±3 g/day, 1 g/day from wine, 1 g/day from beer and 1 g/day from spirits. **N=1,462 males drinking 10−25 g/day** Mean age 43±12 years, mean BMI 26±3, 26% current smokers, 37% ex-smokers, 64% married, 6% living alone, 2% unemployed, mean alcohol intake 16±4 g/day, 7 g/day from wine, 5 g/day from beer and 4 g/day from spirits. **N=778 females drinking 10−25 g/day** Mean age 37±11 years, mean BMI 22±3, 35% current smokers, 34% ex-smokers, 39% married, 10% living alone, 4% unemployed, mean alcohol intake 15±4 g/day, 6 g/day from wine, 5 g/day from beer and 3 g/day from spirits. **N=594 males drinking >25 g/day** Mean age 49±11 years, mean BMI 26±3, 27% current smokers, 53% ex-smokers, 80% married, 8% living alone, 2% unemployed, mean alcohol intake 41±19 g/day, 23 g/day from wine, 11 g/day from beer and 7 g/day from spirits. **N=95 females drinking >25 g/day** Mean age 42±9 years, mean BMI 22±3, 30% current smokers, 48% ex-smokers, 56% married, 14% living alone, 2% unemployed, mean alcohol intake 33±9 g/day, 17 g/day from wine, 12 g/day from beer and 4 g/day from spirits.	
Gea et al. (2013) Spain Prevention with	To prospectively assess the association between alcohol intake and incident depression using	7,447 met the inclusion criteria for trial 5,505/7,447 (74%) met inclusion criteria for this study Differences between those	**Inclusion criteria:** men aged 55−80 years, women and 60−80 years, free of cardiovascular disease at baseline and met at least one of the two following criteria: type 2 diabetes mellitus or the	N=5,505 participants from the PREDIMED Study without baseline or early incident depression **N=1,818 abstainers** 78% female, mean age 68.5±6.1 years, mean BMI 30.3±4.1 kg/m^2, 13% secondary school or higher education, 7% current smokers, 15% former smokers,	Funding has been received from research funding bodies and from companies involved in the food and

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Mediterranean Diet (PRED-IMED) Study	repeated measurements of alcohol intake.	included and those not included or lost to follow-up was NR	presence of three or more coronary heart disease risk factors. **Exclusion criteria:** Previous history of cardiovascular disease, any severe chronic illness, history of food allergy, intolerance to olive oil or nuts, drug addiction or chronic alcoholism, total energy intake out of predefined limits (800−4,000 Kcal/day for men and 500−3,500 Kcal/day for women), baseline prevalent depression, previous history of depression or use of antidepressant drugs, did not have alcohol use information	71% married, 12% living alone, mean total energy intake 2,054±511 Kcal/day, mean alcohol intake 0 g/day. **N=1,356 drinking <5 g/day** 59% female, mean age 67.0±6.1 years, mean BMI 30.0±3.9 kg/m^2, 23% secondary school or higher education, 12% current smokers, 24% former smokers, 78% married, 9% living alone, mean total energy intake 2,184±509 Kcal/day, mean alcohol intake 2.0±1.4 g/day, mean wine intake 1.3±1.4 g alcohol/day, mean beer intake 0.5±0.9 g alcohol/day, mean spirits intake 0.2±0.5 g alcohol/day. **N=1,279 drinking 5−15 g/day** 38% female, mean age 66.4±6.2 years, mean BMI 29.4±3.5 kg/m^2, 28% secondary school or higher education, 17% current smokers, 36% former smokers, 84% married, 7% living alone, mean total energy intake 2,330±511 Kcal/day, mean alcohol intake 9.8±2.7 g/day, mean wine intake 7.4±3.7 g alcohol/day, mean beer intake 1.7±2.7 g alcohol/day, mean spirits intake 0.6±1.5 g alcohol/day. **N=1,052 drinking >15 g/day** 12% female, mean age 65.6±6.1 years, mean BMI 29.3±3.3 kg/m^2, 36% secondary school or higher education, 29% current smokers, 44% former smokers, 89% married, 5% living alone, mean total energy intake 2,595±533 Kcal/day, mean alcohol intake 35±17 g/day, mean wine intake 25±16 g alcohol/day, mean beer intake 4.8±8.4 g alcohol/day, mean spirits intake 4.2±8.8 g alcohol/day.	alcohol industries Many or the authors have received lecture fees and/or served on the board of various companies involved in the food and alcohol industries
Goodwin et al. (2017) UK	To identify group trajectories of alcohol consumption in a young to mid-adulthood UK	4,500 participated in baseline study in 2002 1,392/2153 (65%) completed the baseline questionnaire 1,359/1,392 were contacted	**Inclusion criteria:** individuals who completed the full questionnaire at baseline and were contactable for follow-up assessments **Exclusion criteria:** individuals	A random sample of 4500 serving personnel from the Royal Navy, Army and Royal Air Force were allocated to receive either a full questionnaire or an abridged questionnaire in 2002 **N=667 included individuals: baseline characteristics** From baseline: 34% aged <30 years, 27% aged 30−34	Supported by the UK Ministry of Defence One of the authors is an Honorary

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	military population and to identify associations with mental disorder	for follow-up assessment 941/1,359 (69%) completed follow-up in 2004−2006 667/1,359 (49%) completed a follow-up in 2007−2009 There were significant differences in age and rank between those who took part in all 3 phases and those who dropped out.	who completed the full baseline questionnaire and both follow-up assessments	years, 39% aged ≥35 years, 8% female, 21% were officers, 25% naval service, 49% army, 27% RAF, 57% had a previous deployment, 29% current smokers, 88% had good/excellent health, 20% had a probable common mental disorder, 2% had probable PTSD, median (IQR) alcohol consumption 9 (4−20). From follow-up 1: 61% attained A levels, a degree or above, 84% married/de facto, 10% single, 44% had no family relationship adversity, 12% had childhood antisocial behaviour,	Civilian Consultant Advisor in Psychiatry to the British Army and a Trustee of Combat Stress
Grazioli et al. (2018) Switzerland Cohort Study on Substance Use Risk Factors (C-SURF)	To examine, cross-sectionally and longitudinally the direct and indirect influences of alcohol use, drinking coping motives, and depression on suicide attempts by young men	5,987/7,556 (79%) men who provided written informed consent filled in the baseline assessment in 2010−2012 5,479/5,987 (92%) completed the follow-up questionnaire in 2012−2014. 4,617/5,479 (84%) met inclusion criteria Non-respondents reported more alcohol use than respondents, when they were alcohol consumers, but non-respondents were less often alcohol users than respondents.	**Inclusion criteria:** participants were enrolled from 3 of the 6 army-recruitment centres, independent of their eligibility for military service, in the French and German parts of Switzerland (covering 21 of the 26 Swiss cantons). Due to mandatory army recruitment, virtually all men aged 19–20 in the 21 covered cantons were eligible **Exclusion criteria:** abstainers at the baseline or the follow-up assessment, those with missing values on key variables	**N=4,617 men in the C-SURF study, who met the inclusion/exclusion criteria for this study** Mean age 19.95±1.19 years, 49% obligatory school, 28% obligatory school plus basic apprenticeship or vocational school, 23% completed vocational school diploma, high school diploma or bachelor, 55% French speaking, 45% German speaking, total drinks per week at baseline 9.94±10.14, 51$ ≥1 HED in the past month.	Funded by the Swiss National Science Foundation Conflict of interest NR
Gustafson (2012) United States National Longitudinal	To determine the effect of adolescent HED (wave II) on depressive symptoms as	N=3194/15,197 (21%) who participated in wave II, III and IV 134 schools sampled, ranging in size from 100 to over 3000 students	**Inclusion criteria:** Adolescents in grade 8-12 in 1995 at wave II from 134 middle and high schools, who completed data as young adults **Exclusion criteria**: NR	At Wave II: 1,482 in 9th grade, 1,712 in 10th grade 45% male, 55% female 57% White, 21% African American, 3% Native American, 13% Hispanic 31.5% attended college at Wave III	Funding source not stated. Conflicts of interest NR

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Study of Adolescent to Adults Health (AddHealth)	measured at young adulthood (wave III) and adulthood (wave IV)				
Hiles et al. (2015) Australia Hunter Community Study	To explore the relationship between inflammatory markers, baseline lifestyle factors, and depressive symptoms.	1,410 3318 agreed to participate (44.5%) Gender and marital status match national profile. 2250 completed follow-up questionnaires. Those followed up had lower depressive symptoms than those lost to follow-up.	**Inclusion criteria:** Community-dwelling cohort of individuals aged 55 – 85 years, randomly selected from Australian electoral roll **Exclusion criteria:** NR	Mean age 65.6±7.1 years old 50.4% females 77.9% married or de facto/living with partner Mean CES-D 6.8±7.7 5.2% smoking 236 no use of alcohol 888 safe use of alcohol 139 hazardous use of alcohol 121 use at unknown quantity	Supported by the University of Newcastle's Strategic Initiative Fund, Gladys M Brawn Senior Research Fellowship scheme, Vincent Fairfax Family Foundation and the John Hunter Charitable Trust. The authors declare no conflicts of interest.
Hoffman et al. (2011) United States Spinal Cord Injury (SCI) Model System Longitudinal data set	To determine what demographic, injury-related, or other clinical variables predict clinically significant depression improvement or development of depression between 1 and 5	1035/1807 participants with spinal cord injuries who completed both 1 and 5-year follow-up	**Inclusion criteria:** participants attending one of 16 SCI Model System centers in the United States, aged 17 years or older, sustained a traumatic spinal cord injury, admitted within 1 year of injury, completed inpatient rehabilitation and discharge in geographic catchment area. **Exclusion criteria:** did not complete follow-up at 1 or 5 years	Mean age 37.1 ± 14.8 years 74.5% males 77.2% white; 18.1% African American; 4.7% Other Cause: motor vehicle 54.8%; fall 23.5%; violence 11%; sports 9.7%, pedestrian 1.1% Injury severity: paraplegia incomplete 17.8%; paraplegia complete 28.2%; tetraplegia incomplete 35.9%; tetraplegia complete 18%; minimal deficit 0.2% Education: high school or greater 81.2% 40.4% married	Supported by Department of Education, National Institute on Disability and Rehabilitation Research, SCI Model Systems: University of Washington, Baylor College of Medicine, University of Michigan, and

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	years post injury				Shepherd Model System. The authors declared no conflict of interest.
Hooshmand et al. (2012) Canada	To use a latent growth curve model approach to examine self-medication/acting out and failure hypotheses.	4,412 participants Participation rate 83% to 86% Participants who completed all surveys not significantly different from those with incomplete data.	**Inclusion criteria:** Students from 8 high schools in Ontario, Canada **Exclusion criteria:** NR	Grade 9: mean age 14 years ± 6 months Grade 10: mean age 15 years ± 5 months Grade 11: mean age 16 years ± 5 months Grade 12: mean age 17 years ± 5 months 49% female 92.4% born in Canada Ethnic backgrounds other than Canadian: 31% Italian, 18% French 25% of parents university graduates	Second author received funding from the Social Sciences and Humanities Research Council of Canada. No other conflicts of interest declared.
Hruska et al. (2017) United States	To examine whether the alcohol-related variables predicted PTSD symptoms severity.	80/84 eligible consented to participate (95.2%) 68/80 retained 6 weeks post-injury 36 patients provided sufficient information to analyse	**Inclusion criteria:** traumatic injury victims admitted to Level 1 trauma Center in Midwest, aged 18 – 65 years old; living within 30 miles of the hospital; having a Glasgow Coma Scale score >13 during trauma center admission; meeting Criterion A of the DSM-IV PTSD diagnostic criteria. **Exclusion criteria:** NR	Mean age 34.0±10.8 75% male 69.4% Caucasian, 30.6% African American Education: 36.1% with some college or 2-year degree Mean Injury Severity Score of 6.2 ± 5.4 Injury: 33.3% motor vehicle/cycle accidents; 33.3% assaults	Funding source NR. Conflicts of interest NR.
Jaffee et al. (2009) United States	To determine whether alcohol use during the current month will predict an increased likelihood of a	115/227 included. 51 did not meet full inclusion criteria, and 61 decided not to participate.	**Inclusion criteria:** current diagnosis of bipolar disorder and substance dependence other than nicotine, based on SCID; substance use within 60 days of intake; a mood stabilizer regimen for ≥2 weeks,	N=115 Mean age 39.9±10.9 years 46.1% female 92.2% White 55.8% completed college 52.6% employed	Grants from the National Institute on Drug Abuse. One author received grant support from Eli Lilly

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	depressive episode in subsequent month.		and ≥18 years of age, participating in one of 2 clinical trials of a manualised group therapy. **Exclusion criteria**: current psychosis, current danger to self or others; concurrent group treatment; residential treatment restricting substance use.	67% unmarried 79.8% bipolar I, 14.9% bipolar II, 5.3% bipolar not otherwise specified. 57.4% had both drug and alcohol dependence. 44.3% marijuana, 40.5% cocaine, 6.3% opioids, 5.1% sedatives/hypnotics, 1.3% amphetamines, 1.3% hallucinogens, 1.3% benzodiazepines	and Company.
Johnson et al. (2013) United States Chicago Health and Life Experiences of Women (CHLEW) study	To investigate whether higher levels of hazardous drinking are associated with higher levels of subsequent anxiety and depression in adult sexual-minority women.	Wave 1: 447 women Wave 2: 382 women (85.9%) Those lost to follow-up similar to baseline group, with exception that they were more likely to have less than high school education.	**Inclusion criteria:** women who self-identified as lesbian, ≥18 years of age, spoke English and resided in Chicago or surrounding suburbs. **Exclusion criteria:** NR	Mean age 37.5±11.7 (range 18 – 83) years 100% female 47% non-Hispanic White; 28% Black non-Hispanic; 20% Hispanic/Latina; 5% Asian/Pacific Islander, Native American or multiracial. 56% had bachelor's degree or higher 68% worked full time 25% earned <$20,000 per annum; 21% earned >$75,000 per annum 67% in committed relationship with female partner	Grants received from the National Institute for Alcohol Abuse and Alcoholism. Conflicts of interest NR
Kaysen et al. (2011) United States	To examine the impact of alcohol misuse on the course of PTSD in female crime victims.	N=47/64 completed all 3 time points 11 patients assessed but met exclusion criteria	**Inclusion criteria**: female assault victims in the Seattle metropolitan area (which met DSM-IV criterion A for PTSD); assault occurred within past 5 weeks; literate in English **Exclusion criteria**: current delusions or psychosis; lack of English literacy; more than 5 weeks post-trauma; did not meet assault criteria; and intoxication during in-person assessment.	Mean age 35.6 years±9.0 (range 19-53) 77% received at least high school diploma; 16% completed college or higher degree. 52% were single, 19% co-habiting or married; 18% separated/widowed/divorced 70% earned less than $10,000 annually. 29% African American; 44% Caucasian; 5% Asian/Pacific Islander; 15% Native American and 8% other. 12% Hispanic/Latino. Assaults: 24 sexual assaults (completed vaginal, oral or anal penetrative assault); 40 first-degree physical assault (experienced injury or felt perpetrator was trying to kill/injure her)	Grants received from the National Institute for Alcohol Abuse and Alcoholism and the Alcohol Beverage Medical Research Foundation. The authors declare no final relationships with commercial interests.

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Lang et al. (2007) UK	To assess the relationship between drinking and cognitive health in middle-aged and older people	19,924 individuals, aged ≥50 years in 2002, responded to HSE at baseline 11,392/19,924 (66%) participated all 3 waves 7,286/11.392 (64%) met inclusion criteria No comparison between participants and non-participants reported	**Inclusion criteria:** individuals aged 50 and over who participated in Waves 2 and 3 of ELSA and had CAGE scores of less than 2 **Exclusion criteria:** respondents who had scores of 2 or higher on the 4-item CAGE questionnaire in waves 2 or 3	Participants in all 3 waves of the English Longitudinal Study of Ageing (ELSA) who were eligible for this study **N=3,409 men: baseline characteristics** Mean age 61.7 years, mean number of comorbidities 0.21, mean BMI 27.2, mean number of close family members 1.06, mean number of close friends 2.13, 23% had ≤9 years of education, 14% had ≥14 years of education, 17% current smokers, 54% ex-smokers, 3% ex-drinkers, 1% never drinkers, 51% >0−1 drinks/day, 23% >1−2 drinks/day, 22% >2 drinks/day. **N=3,877 women: baseline characteristics** Mean age 63.0 years, mean number of comorbidities 0.18, mean BMI 27.5, mean number of close family members 1.44, mean number of close friends 2.08, 21% had ≤9 years of education, 10% had ≥14 years of education, 19% current smokers, 37% ex-smokers, 4% ex-drinkers, 4% never drinkers, 75% >0−1 drinks/day, 14% >1−2 drinks/day, 4% >2 drinks/day.	Funding source NR Authors declared no conflicts of interest
Luppa et al. (2012) Germany	To determine the incidence, risk factors and the course of depressive symptoms in latest life within a German population-based prospective study of individuals aged 75 years and older over an 8-year follow-up period	1,265/1,692 (75%) participated at baseline (1997/98) 860/1,265 (68%) participants at 8-year follow-up were eligible for this study The 1,265 subjects did not differ from the remainder of the sample in terms of age (U=263.49, p=0.45), gender (χ^2=0.39, p=0.53) or marital status (χ^2=5.03, p=0.17).	**Inclusion criteria:** subjects were identified by systematic random sampling from an age-ordered list provided by the local registry office, and subjects living in nursing homes were included by proportion **Exclusion criteria:** patients who refused to participate in follow-up, had proxy interviews, were deceased, could not be located, had invalid or incomplete assessment of depression	The Leipzig Longitudinal Study of the Aged (LEILA75+) is a population-based prospective study of a large cohort of older adults in Leipzig, Germany **N=860 participants without depressive symptoms at baseline** 72% women, 12% had a high educational level, 53% were widowed, 9% were living in a nursing home, 36% were living with someone, 14% had poor/very poor health, 51% had satisfactory health, 7% had had a myocardial infarction, 7% had had a stroke, 23% had been hospitalised in the last 12 months, 34% had had at least one stressful life event in the last 6 months, 6% had at-risk drinking levels.	Funded by the Interdisciplinary Centre for Clinical Research Leipzig Authors declared no conflicts of interest
Mackie et al. (2011)	To clarify whether early alcohol use	806 students recruited were randomised to intervention or	Students who scored one SD above the school mean on one	**Students who participated in the no-intervention arm of the London school-based study**	Supported by Action on Addiction, the

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
UK	effects the rate of change of psychological symptoms	no-intervention 411 no-intervention group 393/411 (96%) met inclusion criteria 80.1% of students completed the survey at the first follow-up (W2) 76.9% of students completed the survey at W3 63.8% of students completed the survey at W4 Comparisons between participants and non-participants were NR	of the four subscales of the Substance Use Risk Personality Scale (SURPS: hopelessness, anxiety sensitivity, impulsivity, and sensation seeking) and a low risk group who did not score more than 1 SD above the school mean were included in original RCT. **Inclusion criteria:** Only those randomised to the no-intervention comparison group **Exclusion criteria:** students who reported unreliable data (responding inconsistently across the survey or positively to a sham drug item)	37.2% Caucasian, 32.6% Black, African ⁄ Caribbean, 10.8% Asian, 11.3% mixed race, and 8.2% other Only 15% (n = 59) of participants were consistent non-drinkers at all time points in this study. 49.3% (n = 194) of participants were non-drinkers at Wave 1, 36.6% (n = 144) at W2, 34.9% (n = 137) at W3, and 27.9% (n = 110) at W4 The percentage of students who reported HED naturally increased from 26.5% at W1 to 36.7% at W4. Mean Q×F scores: W1=4.36±4.82, W2=4.97±5.54, W3=4.77±5.80, W4=5.29±6.05. Mean depression scores: W1=14.67±6.97, W2=14.43±6.90, W3=14.12±6.86, W4=14.09±6.39. Mean anxiety scores: W1=11.79±4.71, W2=11.30±4.14, W3=11.31±4.07, W4=11.14±4.07. **N=126 alcohol users: baseline characteristics** 48% female, mean age 13±0.8 years, mean hopelessness score 14.02±4.02, mean anxiety sensitivity score 11.76±2.93, mean impulsivity score 13.22±2.90, mean sensation seeking score 16.72±3.38. **N=139 non-alcohol users: baseline characteristics** 53% female, mean age 13±0.7 years, mean hopelessness score 12.77±3.64, mean anxiety sensitivity score 12.24±3.21, mean impulsivity score 12.17±2.99, mean sensation seeking score 16.32±3.48.	National Institute for Health Research Biomedical Research for Mental Health, the Maudsley NHS Foundation Trust. One author was funded by an MRC⁄ESRC Interdisciplinary Post-doctoral Research Fellowship Conflict of interest NR
Magnusson Hanson et al. (2016) Sweden Swedish Work Environment Survey (SWES) and	To examine whether unhealthy behaviours are intermediaries in the longitudinal relationship between job demands, decision authority,	9,214 participants in the 2003 SWES 5,985/9,214 (65%) participated in Wave 1 of SLOSH in 2006 11,441/18,756 (61%) 2003 and 2005 SWES participants participated in SLOSH Wave 2 in 2008	**Inclusion criteria:** individuals included in SWES 2003 and 2005: from the entire country stratified by county, citizenship, gainfully employed and 16−64 years of age at the time of enrolment Participants who responded and were working at least 30%	Participants who responded and were working at least 30% in SLOSH Waves 2−5, from 2008 to 2014 **N=3,706 participants: baseline characteristics** Mean age 47.6±8.9 years (range 20−67), 43% male, 1% unskilled manual workers, 6% skilled manual workers, 44% assistant non-manual employees, 7% intermediate non-manual employees, 40% professionals or upper-level executives, 2% self-employed, 79% married/cohabiting, 21% single, 8% current smokers, 5%	Financed by Swedish Research Council for Health, Working life and Welfare Authors declared no conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Swedish Longitudinal Occupational Survey of Health (SLOSH)	and social support and depressive symptoms.	10,078 (57%) participated in Wave 3 in 2010 9,880 (57%) participated in Wave 4 in 2012 8,757 (52%) participated in Wave 5 in 2014 3,706 participants who responded and were working at least 30% in all four waves from 2008 to 2014 In comparison with those who were excluded, those who were included had a higher proportion of women, older persons, and people with university education.	in all four waves from 2008 to 2014 **Exclusion criteria:** those who did not respond to all four waves and those who worked less than 30% in any of the waves	excessive alcohol consumption, 7% unhealthy diet, 16% physically inactive.	
Mason et al. (2008) United States Project Family (some families in Preparing for the Drug Free Years)	To investigate the effects of different dimensions of alcohol involvement in late adolescence on past-year MDD in early adulthood.	429 (49%) of 883 families agreed to participate Compared to sample with 90% response rate, few differences (so is representative)	**Inclusion criteria:** families of 6th grade students in rural communities of a Midwestern state. **Exclusion criteria:** NR	Mean age of children: 11 years at baseline 52% female >95% White 83% families were dual-parent structure 61% of mothers and 58% of fathers had post-high-school education Median household income in 1993 was $32,000	Supported by the National Institute on Alcohol Abuse and Alcoholism. Conflicts of interest NR.
Mason & Spoth (2011) United States Project Family	To examine whether predictive relationships among alcohol use, adverse consequences, and subjective	208 families at wave 1 (51% of invited families) Data based on wave 5 (age 16, n=151), and wave 6 (age 18; n=157) Compared to sample with 90% response rate, few	**Inclusion criteria:** control families of Project Family (6th grade students in 11 rural schools located in Midwestern United States). **Exclusion criteria:** NR.	Mean age of children” 11.34 years at baseline 52% female >95% White	Supported by the National Institute on Alcohol Abuse and Alcoholism. Conflicts of interest NR.

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	well-being that have been observed during young adult years operate in a similar or different manner during the teen years.	differences (so is representative)			
McCarty et al. (2012) United States Developmental Pathways Project	To explicate the associations between depressive symptoms and alcohol use in early adolescence	N=2,187/2,920 eligible students (74.9%)	**Inclusion criteria:** 6th graders who had a 3rd grade reading comprehension or higher, from 4 Seattle-area public schools. **Exclusion criteria:** NR	Mean age: 12.0 (range 11.0 – 13.6) years 51.6% male 39.5% Non-Hispanic White; 24.9% Black; 24.1% Asian/Pacific Islander; 10.1% Hispanic; 1.4% Native American 33.4% low income (<$34,000); 35.5% mid income (%35,000-$74,999); 31.1% high income (>$75,000) 27.3% single parent household 42% lifetime history of any substance use disorder among biological parents	Source of funding not stated. Conflicts of interest NR.
Meng (2017) Canada	To investigate characteristics associated with the earlier onset of first depressive episode in a large, population-based, prospective cohort study	17,726 participants initially included in the NPHS cohort. 12,355/17,726 (69.7%) completed all nine cycles 12,227/12,355 (99%) participants met inclusion criteria Compared to non-selected survey subjects, the study sample had a higher proportion of older population, women, Caucasians, people living married or in a common-law relationships, people with higher income	**Inclusion criteria:** aged ≥12 years at baseline who had been followed-up to 2010/2011; depressed-free at the baseline and had depression values (Yes/No) during the follow-ups; no reported history of Alzheimer's disease or other dementias. **Exclusion criteria:** NR	Baseline characteristics of the 12,227 participants were NR Characteristics examined in this study included socio-demographic factors (age, sex, race, marital status, income, education, and immigration status), history of chronic disease, and lifestyle factors (type of drinkers, level of physical activity, and type of smokers). The variable of "history of chronic disease" was dichotomous. Participants reporting any of the following long-term conditions that had been diagnosed by a health professional, were seen as having a history of chronic disease: arthritis or rheumatism, high blood pressure, asthma, chronic bronchitis, or other lung or breathing condition, diabetes, epilepsy, heart disease, angina, effects of a heart attack, effects of stroke, paralysis,	Start-up funding from the Douglas Hospital Research Centre and the scholar award from the Fonds de recherché Sante du Québec Author declared no conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
		and better education, immigrants, regular drinkers and smokers, less active people, and people suffering with chronic diseases		incontinence, Alzheimer's disease or other dementias, osteoporosis or brittle bones, glaucoma, digestive conditions, kidney failure or disease, cerebral palsy, spina bifida, cystic fibrosis, multiple sclerosis, deformity, orthopaedic impairment or absence of arms, legs, hands or feet, cancer, or any other long-term condition.	
Meng et al. (2017) Canada Zone d'Épidémiolog ie Psychiatrique du Sud-Ouest de Montréal (ZEPSOM)	To explore psychosocial risk factors for depression and quantify the effect of risk factor modifications on depression incidence	1,814/2,433 (75%) included in this study form Wave 1 (2006−7) 1,357/1,814 (75%) completed Wave II (2008−9) 956/1,814 (53%) completed Wave III (2010−11) In comparison with the unselected participants, the analysis sample contained more younger adults, males, married/de facto people, people with higher income and higher education, immigrants, abstainers and fewer people with a family history of mental health problems (p<0.05). Compared with those not eligible for this study, the analysis sample tend to live in areas having lower rates of: low income, unemployment for those aged 25 years and older, visible minorities and fewer numbers of cultural community centres,	**Inclusion criteria:** 2,433 randomly selected individuals aged 15–65 years from a total combined population of 269,720 were included in ZEPSOM **Exclusion criteria:** lifetime diagnosis of MDE at baseline, incomplete surveys at Wave II and/or III	A population-based cohort study: ZEPSOM, consists of a representative community sample of five neighbourhoods in the South-West sector of Montreal. **N=1,357 individuals in the 2-year follow-up group** **50.3% were female:** mean age 41.9 years, 51% were married, 31% were single, 21% had low income, 67% had post-secondary degree, 16% had not completed secondary education, 74% born in Canada, 30% had FH of mental health problems, 10% were abstainers, 10% were former drinkers, 23% were occasional drinkers, 57% were regular drinkers. Mean GIS measures in 500 m buffer zone from place of residence: 65% crime rate, 17% prevalence of low income, 8% unemployment rate for those aged ≥25 years, 20% visible minority population, 2.1 cultural community centres, 0.3 community organisations, 0.3 medical clinics, 0.3 mental health related services, 0.6 physical activity places. **49.7% were male:** mean age 40.9 years, 51% were married, 37% were single, 16% had low income, 64% had post-secondary degree, 15% had not completed secondary education, 72% born in Canada, 28% had FH of mental health problems, 6% were abstainers, 10% were former drinkers, 16% were occasional drinkers, 69% were regular drinkers. Mean GIS measures in 500 m buffer zone from place of residence: 66% crime rate, 18% prevalence of low income, 8% unemployment rate for those aged ≥25 years, 20% visible minority population, 2.2 cultural	The Zone d'Épidémiologie Psychiatrique du Sud-Ouest de Montréal study was funded by the Canadian Institute of Health Research. This study was partially funded by a start-up fund from Douglas Mental Health University Institute. Authors declared no conflicts of interest

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		community organisations, medical clinics, mental health-related services and physical activity places (p<0.05)		community centres, 0.3 community organisations, 0.3 medical clinics, 0.3 mental health related services, 0.6 physical activity places. **N=956 individuals in the 4-year follow-up group** 47.8% were male and 52.2% were female. The characteristic between males and females remained the same (except for crime rate) as what were found in the 2-year follow-up group.	
Meririnne et al. (2010) Finland Adolescent Depression Study	To clarify the impact of the core alcohol use phenomenon of drunkenness-oriented drinking, in terms of weekly drunkenness on course of adolescent unipolar depression.	197/218 adolescents with unipolar depressive episode at baseline (who were not found to have bipolar disorder during follow-up)	**Inclusion criteria:** depressed adolescents, referred from schools, health care centers, and social and family counselling services to adolescent psychiatric outpatient clinics. **Exclusion criteria:** change in diagnosis to bipolar disorder during the study.	**No/occasional users (n=81)** 19.8% male; mean age 16.2±1.5 years; 27.2% of parents upper middle class; 37% lower middle class; 27.2% working class; 34.6% MDD part remiss/mild/moderate; 38.2% MDD severe/psychotic; 16.0% dysthymia/double depression' 11.1% other depressions; 64.4% single MDD; 35.6% recurrent MDD; mean age of 1st mood disorder: 13.2±2.6 years; 69.1% any comorbid diagnosis; mean BDI score at baseline: 20.8±7.9 **Regular users (n=81)** 17.3% male; mean age 16.3±1.8 years; 27.2% of parents upper middle class; 34.6% lower middle class; 32.1% working class; 40.7% MDD part remiss/mild/moderate; 38.3% MDD severe/psychotic; 9.9% dysthymia/double depression' 11.1% other depressions; 70.3% single MDD; 29.7% recurrent MDD; mean age of 1st mood disorder: 13.3±2.8 years; 69.1% any comorbid diagnosis; mean BDI score at baseline: 23.6±10.3 **Excessive users (n=35)** 20.0% male; mean age 17.1±1.5 years; 20.0% of parents upper middle class; 37.1% lower middle class; 25.7% working class; 45.7% MDD part remiss/mild/moderate; 42.9% MDD severe/psychotic; 8.6% dysthymia/double depression' 2.9% other depressions; 64.5% single MDD; 35.5% recurrent MDD; mean age of 1st mood disorder: 13.7±2.7 years; 85.7% any comorbid diagnosis; mean BDI score at baseline: 22.4±8.7	Supported by the Hospital District of the University of Helsinki, the Peijas Hospital, the Yrjö Jahnsson Foundation, and the Sigrid Juselius Foundation. Conflicts of interest NR.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Mushquash et al. (2013) Canada	To accurately conceptualise HED, depressive symptoms, and their interrelations	Recruitment procedure NR Participant profile resembles other samples from Dalhousie University	**Inclusion criteria:** NR **Exclusion criteria:** NR	**N=200 undergraduate women from Dalhousie University** Mean age 19.86±3.02 years, mean 2.10±1.16 years of university education, lived in Canada for mean 18.29±5.76 years; 88.0% Caucasian, 47% single, 41% dating, 40% HED at week 1, 40% HED at week 2, 34% HED at week 3, 36% HED at week 4. **Wave 1:** mean depressive symptoms POMS-D 3.81±3.05, DACL 2.28±3.06, CES-D 16.94±4.89; mean HED frequency 0.74±1.10, mean HED severity 5.75±1.66. **Wave 2:** mean depressive symptoms POMS-D 3.43±3.01, DACL 2.00±3.78, CES-D 16.45±4.74; mean HED frequency 0.65±0.92, mean HED severity 5.61±1.60. **Wave 3:** mean depressive symptoms POMS-D 3.01±3.00, DACL 1.69±2.69, CES-D 15.86±4.50; mean HED frequency 0.54±0.87, mean HED severity 5.66±2.09. **Wave 4:** mean depressive symptoms POMS-D 2.95±3.14, DACL 1.75±2.91, CES-D 15.98±4.85; mean HED frequency 0.54±0.81, mean HED severity 5.47±1.57.	Funded by a Dalhousie University Department of Psychiatry Research grant Authors declared no conflicts of interest
Needham (2007) United States National Longitudinal Study of Adolescent Health	To examine depression and substance use as dynamic interrelated trajectories, conditioned by gender.	N=10,828/ 20,745 school students who responded to wave I (1995), wave II (1996) and wave III (2001-2002) and had valid sampling weights.	**Inclusion criteria:** Adolescents (grade 7-11) at wave I, who completed data at wave II and III as young adults **Exclusion criteria**: NR	At Wave I: (grades 7-11) 53% female 53% White, 21% Black, 16% Latina/o Mean age=15.3 years Parental education: 12% less than high school; 29% high school; 58% more than high school 40% non-intact family structure Mean CES-D depressive symptoms: 15.2	Funding received from Robert Wood Johnson Foundation health & Society Scholars program. Conflicts of interest NR
Onwuameze et al. (2013)	To prospectively evaluate risk	N=257/300 farmers available for analyses	**Inclusion criteria:** principal farm operators who met the US	Mean age = 56 years 98% male	Dr Paradiso received grant or

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United States Iowa Certified Safe Farm (CSF) study	factors for depressed mood among a cohort of farmers.	Reasonably generalizable to Iowa farmers in general (higher proportion of males, larger mean hog herd size, larger total acres farmed).	Department of Agriculture farm criteria (>$1000 in agricultural product sales per year). **Exclusion criteria**: NR	100% White	research support from the Dana Foundation, the Mallinckrodt Foundation, NARSAD, and the National Institute on Aging.
Otten et al. (2018) Netherlands	To longitudinally examine the effect of the 5-HTTLPR genotype on the association between depressive symptoms and alcohol use in a Dutch community sample.	428 families participated at baseline 416/428 (97%) families participated at Wave 2 404/428 (94%) families participated at Wave 3 356/428 (83%) families participated at Wave 4 326/428 (76%) families participated at Wave 5. 288/428 (67%) fathers met the inclusion criteria 306/428 (71%) mothers met the inclusion criteria	Families consisting of two parents and two adolescents aged 12−16 years old were recruited via 22 municipality registers in the Netherlands. **Inclusion criteria:** Parents from the included families with data for their 5-HTTLPR genotype who were born in the Netherlands. **Exclusion criteria:** NR	Parents from the 428 families included in the Family and Health study. **N=288 males** Mean age 46.2±3.95 years (range 37−61) at Wave 1, mean number of alcoholic beverages consumed in the previous week: 12.89±10.27 at Wave 1, 12.48±10.36 at Wave 2, 12.69±10.42 at Wave 3, 14.46±11.49 at Wave 4, 13.76±10.89 at Wave 5, mean depressive symptoms score: 2.22±0.58 at Wave 1, 2.22±0.61 at Wave 2, 2.25±0.63 at Wave 3, 2.13±0.68 at Wave 4, 2.08±0.70 at Wave 5. **N=306 females** Mean age 43.8±3.55 years (range 35−56) at Wave 1, mean number of alcoholic beverages consumed in the previous week: 6.01±6.35 at Wave 1, 5.71±6.16 at Wave 2, 6.14±6.75 at Wave 3, 6.68±6.75 at Wave 4, 6.26±6.48 at Wave 5, mean depressive symptoms score: 2.42±0.56 at Wave 1, 2.42±0.57 at Wave 2, 2.44±0.60 at Wave 3, 2.36±0.68 at Wave 4, 2.31±0.63 at Wave 5.	Funded by grants from the Dutch Organization of Scientific Research Conflict of interest NR
Paljärvi et al. (2009) Finland Health and Social Support	To determine what aspect of drinking pattern would be the best predictor for depressive symptoms.	25,902 responded to the HSS postal survey in 1998 at Wave 1 (40% response rate) 19,629/25,902 (80%) responded in 2003 at Wave 2 The original sample included	**Inclusion criteria:** men and women of working age who completed a postal survey in 1998 and in 2003 **Exclusion criteria:** respondents with missing information on measures of alcohol consumption or	**N=15,926 responded who completed Wave 1 and Wave 2 of the HSS survey** **Baseline characteristics:** 59% women, 25% aged 20−24 years, 23% aged 30−34 years, 25% aged 40−44 years, 27% aged 50−54 years, 88% Finnish speakers, 12% Swedish speakers, 20% FH of alcohol problems, 48% had at least a college education, 19% were living alone, 12% were divorced,	Supported by a grant from the Finnish Foundation for Alcohol Studies and grants from the Academy of Finland Authors declared no

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(HSS) study		overrepresentations from one geographic area and from one minority language group. Excluding the over-representations, the population does not differ significantly from the Finnish general population	symptoms of depression. Abstainers were excluded because reasons for abstaining are a probable source of unmeasured confounding	7% were unemployed, 7% had a low level of social support, 22% had a high level of subjective stress	conflicts of interest
Pardee et al. (2014) United States	To examine associations between alcohol use and facets of anxiety in a longitudinal community sample of middle adolescents.	N=387 adolescent-caregiver pairs Recruited through random digit dialling within Erie County, NY. Attrition of 4.4% across waves 2 and 3.	**Inclusion criteria:** NR **Exclusion criteria:** NR	Mean age: 12.09 (range 11-13) years 55% female 83% White/non-Hispanic Median family income \$70,000 (range \$1,500 - \$500,000).	Supported by the National Institute on Drug Abuse. Conflicts of interest NR.
Parrish et al. (2016) United States California Families Project	To examine cross-lagged relations between frequency of alcohol use and internalizing symptoms.	N=620/674 Mexican-origin youth 73% of eligible families agreed to participate. Those who dropped out did not differ significantly from participating youth on gender, generational status or family income.	**Inclusion criteria:** Mexican-origin youth aged 14, in 5th grade, living with his or her biological mother **Exclusion criteria:** NR	Age 14 at baseline 50% female Other demographics not stated	Funding source not stated. Conflicts of interest NR.
Patwardhan et al. (2017) Finland Northern Finland Birth Cohort 1986	To examine associations between cumulative contextual risk in childhood and depression in	8,755/9,479 babies initially recruited, 8,755 parents provided consent 6,963/8,755 were eligible for this study (73% of the original birth cohort)	**Inclusion criteria:** required data to measuring the cumulative contextual risk **Exclusion criteria:** NR	Participants came from the NFBC-1986 study on health and well-being. For the current study, alcohol use data were drawn from a self-reported adolescent survey at age 16 years, and depression outcomes from the Finnish Hospital Discharge Register data **N=6.963 total participant characteristics** 49% male, cumulative contextual risk factors: 4% had	Supported by National Institute on Drug Abuse (NIDA), National Institutes of Health grant Conflict of interest

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(NFBC-1986)	early adulthood, testing two mediating mechanisms, alcohol use and perceived social support from friends and family	Compared to the birth cohort, the analysis sample had participants with slightly higher cumulative risk and lower ratings of anxious-fearful behaviour at age 8. The analysis sample did not differ from a birth cohort in the rates of depression diagnosis, gender ratio, ratings of internalizing problems at age 16, adolescent alcohol use and perceived social support.		teenage mothers, 13% mothers smoked while pregnant, 11% mothers drank while pregnant, 7% participants lived with a single parent at age 7, 12% had an unemployed mother at age 7, 11% had an unemployed father at age 7, 13% had fathers with <9 years of education, 6% had mothers with <9 years of education, mean age 16.0 (range 14.58−16.96) at time of adolescent data collection, mean number of times drank alcohol in the past 12 months 2.18±1.85, mean number of times been drunk in the past 12 months 1.67±1.71, mean number of HED in the past 30 days 0.74±1.08, 6% diagnosed with depression. For males: Mean number of times drank alcohol in the past 12 months 2.12±1.86, mean number of times been drunk in the past 12 months 1.61±1.72, mean number of HED sessions in the past 30 days 0.73±1.09, 5% diagnosed with depression. For females Mean number of times drank alcohol in the past 12 months 2.24±1.84, mean number of times been drunk in the past 12 months 1.73±1.71, mean number of HED sessions in the past 30 days 0.74±1.07, 9% diagnosed with depression.	NR
Paulson et al. (2018) United States Health and Retirement Study (HRS)	To examine the relationship between moderate alcohol use and depressive symptoms over 8 years.	N=3177 Complete HRS set includes 37,319 adults >50 years old	**Inclusion criteria:** adults 50 and older **Exclusion criteria:** below age 65 at 2006 wave, reported drinking >4 drinks/sitting; missing CRP values at 2006 wave, or CRP values above 10µg/mL; and identified as heavy drinkers (>14 drinks/week)	Mean age: 74.3±7.0 years 57.3% female Mean education: 12.3±2.1 years 86.9% White/Caucasian; 10.5% Black/African American, 2.6% other Mean drinks per occasion: 1.14±2.2 Mean occasions per week: 0.49±0.9 27.3% had comorbidities	Funding source not stated. Conflicts of interest NR.
Pesola et al.	To explore the	The core sample consisted of	**Inclusion criteria:** adolescents	N=4,863 adolescents from the Avon Longitudinal Study	Funded by The

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(2015) UK	developmental relationship between harmful drinking and depressed mood in adolescence	14,541 pregnancies. 14,062/14,541 live births 13,988/14,062 children alive at 1 year of age. 5,126/9,996 (51%) questionnaires were returned at age 16 years The ALSPAC cohort is similar to the overall UK population as indicated by comparisons with the 1991 census	who responded to the questionnaires when aged 16 years and who had complete information for both alcohol and depression measures. **Exclusion criteria:** NR	of Parents and Children (ALSPAC) who were assessed between the ages of 14 and 16 years. Although regression analysis was adjusted for background covariates: financial difficulties, family education level, parents' alcohol consumption, and parents' depression, conduct problems scale (SDQ) and deviant peers, no baseline characteristics were provided	European Foundation for Alcohol Research and Mental Health Research Network Cymru Authors declared no conflicts of interest
Piasecki et al. (2017) United States Social and Emotional Contexts of Adolescent Smoking Patterns project	To extend the literature between hangover and depression.	N=986/1,263 who provided both baseline and follow-up. 1,344 had agreed to participate from 3,654 invited. i.e. those followed up are only 26% of invited sample.	**Inclusion criteria:** all 9th and 10th graders attending 16 Chicago-area schools at baseline. This article looks at wave 6 (time 1) and wave 7 (time 2). **Exclusion criteria:** NR	Mean age 22.4±0.8 years (range 20.2 – 25.5 years) 69.3% White; 18.3% Black; 4.4% Asian, 1.6% Native Hawaiian/Pacific Islander, 0.6% Native American, 5.9% more than one category; 15.3% Hispanic	Supported by the National Cancer Institute of the National Institutes of Health. Conflicts of interest NR
Powers et al. (2014) United States	To identify predictors of PTSD symptomatology in those exposed to trauma.	N=227/327 who provided follow-up information 3 months later	**Inclusion criteria:** adults ≥18 years old, admitted to a Level I trauma center between March 2012 and June 2013, able to provide contact phone number for follow-up. **Exclusion criteria:** traumatic brain injury and/or premorbid cognitive deficits (e.g. dementia, Alzheimer's), inability	Mean age: 46±18 years 64% male 68% White, 81% non-Hispanic 35% married 35% high school diploma, 44% Associate's degree or higher 55% premorbid diagnosis Cause of injury: 11% gunshot; 24% motor vehicle; 6% aggravated assault; 12% motorcycle; 10%	Funded by the Stanley Seeger Foundation and the National Institute on Drug Addiction Conflicts of interest NR

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			to understand spoken English or Spanish.	pedestrian/bike; 29% fall; 10% other 39% positive AUDIT-C	
Powers et al. (2016) Australia	To identify longitudinal patterns of HED and whether HED preceded depressive symptoms in the short-term (1–6 years) and long-term (10–15 years).	8,197/14,247 (58%) of women aged 18−23 years in 1996. 6,579/8,197 were eligible for wave 1 of this study 5,348/6,579 (81%) were eligible for wave 2 6,466/6,579 (98%) were eligible for wave 3 Participants at the2009 survey were older (47% versus 43%) and more likely to have post-school education (32% versus 26%), and were equally likely to be employed and never married in 1996 than non-respondents. Thus, participants over-represented more educated women.	**Inclusion criteria:** women randomly selected from the Medicare database, which covers all permanent residents of Australia. Women living in rural and remote areas of Australia were intentionally oversampled **Exclusion criteria:** women who did not complete all three surveys, depressive symptoms at the first (1996) survey, missing depressive symptoms at the other 2 surveys.	N=8,197 Women randomly selected from the Medicare database who completed a mailed survey of the Australian Longitudinal Study on Women's Health (ALSWH) in 1996 (aged 16−21 years), according to HED pattern N=6,466 women who completed all 3 surveys (1996, 2000 and 2009) **N=1,998 Never drank alcohol** 49% aged 18−20 years, 51% aged 21−23 years, 44% rural, 18% had monetary stress, 6% experienced violence, and 20% had depressive symptoms. **N=1,376 Rarely drank alcohol** 51% aged 18−20 years, 49% aged 21−23 years, 47% rural, 22% had monetary stress, 9% experienced violence, and 19% had depressive symptoms. **N=1,417 Drank alcohol monthly** 53% aged 18−20 years, 47% aged 21−23 years, 50% rural, 22% had monetary stress, 9% experienced violence, and 17% had depressive symptoms. **N=2,134 Drank alcohol weekly** 56% aged 18−20 years, 44% aged 21−23 years, 50% rural, 27% had monetary stress, 10% experienced violence, and 18% had depressive symptoms. **N= 1,272 Drank alcohol more often than weekly** 55% aged 18−20 years, 45% aged 21−23 years, 51% rural, 27% had monetary stress, 16% experienced violence, and 26% had depressive symptoms.	Supported by grants from the Australian Government Department of Health and the New South Wales Department of Health Drug and Alcohol Council Research Grants Program. Authors declared no conflicts of interest
Read et al. (2016) United States	To examine the relative stability of trauma symptoms,	N=944/1,234 college students 1002 invited to participate completed the baseline survey (September freshman	**Inclusion criteria:** Participants who endorsed at ≥1 Criterion A trauma; and ≥1 symptom each from PTSD symptom Clusters	Mean age 18.11±0.44 64.1% female 72% non-Hispanic Caucasian, 12% Asian, 9% Black, 2.4% Hispanic/Latino; >1% America Indian/Native	Supported by the National Institute on Drug Abuse, National Institute of

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	focusing on trauma exposure and alcohol involvement.	year, T1)	B, C and D (n=649). In addition, 585 who did not meet trauma criteria were invited for follow-up. **Exclusion criteria:** NR	Alaskan,>1% Hawaiian, 3.3% multiracial	Mental health and National Institute on Alcohol Abuse and Alcoholism. Conflicts of interest NR.
Read et al. (2014) United States	To delineate the role of coping in prospective associations between PTSD symptoms and alcohol use and consequences in a sample of trauma-exposed young adults.	N=734 drawn from larger longitudinal study on PTSD and substance use. 58% response rate	**Inclusion criteria:** incoming freshmen at 2 mid-size universities in the north-eastern and south-western United States, with prior trauma exposure at time of college entry. Participants who endorsed at ≥1 Criterion A trauma (with and without PTSD symptomatology) **Exclusion criteria:** NR	Mean age 18.11±±0.46 Sex distribution not stated. 71% non-Hispanic Caucasian; 11% Asian, 11% Black, 3% Hispanic/Latino, 3% multiracial; <1% other	Supported by the National Institute on Drug Abuse. Conflicts of interest NR.
Ruggles et al. (2017) United States Veterans Aging Cohort Study	To identify whether temporal patterns underlie associations between depression, smoking, unhealthy alcohol use and other substance use.	5479/7327 met criteria of having ever drank alcohol and smoked cigarettes	**Inclusion criteria:** United States veterans receiving care in the Veterans Health Administration (both HIV infected and HIV uninfected). **Exclusion criteria:** Patients who reported never smoking or drinking alcohol.	**HIV+** Mean age 49.8 ± 8.3; 97.3% male; 19% White, 67.5% Black, 13.5% other; 55.7% Hepatitis C infection; 30.7% died; 45.5% AUDIT-C ≥4; 32% PHQ-9 ≥8; 33.9% illicit substances **HIV-** Mean age 51.4%; 94.5% male; 22.8% White, 63.8% Black, 13.5% other; 34.4% Hepatitis C infection; 18.3% died; 50.5% AUDIT-C ≥4; 30.2% PHQ-9 ≥8; 26.8% illicit substances	Funding source NR The authors have no conflicts of interest to declare.
Scholes-Balog et al. (2015) Australia Internation-al	To examine the longitudinal relationships between depressive symptoms and	N=927 Victorian students who were involved in the IYDS N=916 Grade 6 N=804 Grade 9 N=791 grade 11	**Inclusion criteria:** The youngest Victorian sample was chosen for the current study. **Exclusion criteria:** absence of parental or student consent	N=927 Victorian students who were involved in the IYDS **N=440 grade 6 males** Mean age was 11.98±0.4, mean SMFQ (depression) scored 5.76±5.44, mean cigarette use scored 1.13±0.49, mean alcohol use scored 3.22±11.86, mean illicit substance use scored 1.05±0.44, mean family conflict	Financial support was provided by the National Institute on Drug Abuse for the IYDS data collection, the

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Youth Development Study (IYDS)	frequency of substance use among adolescents	Grade 6 Females used significantly less cigarettes and alcohol than Grade 6 boys. Females also experienced less poor family management, antisocial behaviour and positive parental attitudes towards drugs than Grade 6 boys		scored 1.93±0.76, mean antisocial behaviour scored 1.12±0.45, mean academic failure scored 1.85±0.57, and mean positive parental attitude towards drug use scored 1.29±0.50. **N=476 grade 6 females** Mean age was 11.91±0.39, mean SMFQ (depression) scored 5.85±5.58, mean cigarette use scored 1.07±0.31, mean alcohol use scored 1.68±4.73, mean illicit substance use scored 1.01±0.1, mean family conflict scored 1.91±0.8, mean antisocial behaviour scored 1.02±0.45, mean academic failure scored 1.78±0.52, and mean positive parental attitude towards drug use scored 1.14±0.32.	National Institute on Alcoholism and Alcohol Abuse and an Australian NHMRC Project Grant. Continued data collection in Victoria has been supported by two Australian Research Council Discovery Projects Authors declared no conflicts of interest
Schuler et al. (2015) United States National Longitudinal Study of Adolescent to Adult Health	To elucidate critical age windows in which these associations are strongest and concurrent treatment may be most beneficial.	N=6070/ 6504 Unclear why the number was so small, given individuals only needed to provide data at one time point.	**Inclusion criteria:** Individuals who provided substance use and depressive symptoms data during at least one wave, aged 12-31. **Exclusion criteria**: NR	51% female 70% White, 19% Black, 12% Hispanic, 11% other	Funding received from National Institute on Drug Abuse and National Cancer Institute. Funding source had no role in study. Authors had no conflicts of interest.
Schultz et al. (2014) United States	To identify predictors of worsening mental health, including PTSD and alcohol use in a national sample of veterans	N=1040/1833 met criteria contacted 596 completed usable survey (time 1) and 512 (86%) completed time 2 survey.	**Inclusion criteria:** veterans returned from deployment in Iraq or Afghanistan, surveyed between 3 and 12 months after returning from deployment. **Exclusion criteria:** NR	40.2% male 50% active duty, 25% national guard, 25% other reserve Age: 22.1% <26; 29.7% 26 – 34; 31.5% 35 – 44; 12.3% ≥45 years 12.3% Hispanic; 75.3% White; 16.9% African American; 7.8% other/multiple 28.9% single (never married); 54.5% married/with partner; 16.6% separated/ divorced/ widowed 11.5% high school grad; 49.6% some college / vocational	Supported by VA HSR&D Grant The authors had no financial disclosures.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				education; 38.1% bachelor degree or more 83.6% employed Time in military: 19% <5 years; 29.9% 5 – 10 years; 50.2% ≥10 years 56.8% Army; 17.8% Navy; 21.5% Air force; 3.9% Marines	
Skogen et al. (2016) Norway Norwegian Longitudinal Health Behaviour Study (NLHB)	To identify trajectories of alcohol consumption and intoxication from age 13–18 years, and to examine to what extent they were associated with symptoms of depression	1,102/1,242 adolescents were available for analysis of drinking frequency 1,095/1,242 were available for analysis of drinking to intoxication The study sample is considered representative of the birth-cohort attending ordinary school with regard to gender and residence distribution There were no differences between responders and non-responders across waves for symptoms of depression, smoking, alcohol use, BMI or parental socioeconomic status but more girls completed all waves compared with boys	**Inclusion criteria:** aged 13 years in 1990 **Exclusion criteria:** NR	N=1,102 adolescents from the NLHB study Characteristics at age 13 years: 45% female, mean depression score 2.3±0.9, 1.1% consumed alcohol weekly, 0.4% drank to intoxication ≥11 times in the last 6 months. Characteristics at age 14 years: 45% female, mean depression score 2.2±1.0, 5.1% consumed alcohol weekly, 3.0% drank to intoxication ≥11 times in the last 6 months. Characteristics at age 15 years: 45% female, mean depression score 2.4±1.1, 9.1% consumed alcohol weekly, 7.9% drank to intoxication ≥11 times in the last 6 months. Characteristics at age 16 years: 48% female, mean depression score 2.1±1.0, 10.8% consumed alcohol weekly, 13.2% drank to intoxication ≥11 times in the last 6 months. Characteristics at age 18 years: 51% female, mean depression score 2.4±1.1, 25.5% consumed alcohol weekly, 31.8% drank to intoxication ≥11 times in the last 6 months.	Funding source NR Conflict of interest NR
Sloan et al. (2011) United States National Longitudinal	To determine whether frequent participants in HED, at 17-25 years, experience poorer mental	7,757/ 12,686 youths interviewed in 2008 and 1979.	**Inclusion criteria:** National sample, with Black, Hispanic, and White youths with low incomes oversampled. Aged 14-22 years in 1979. Alcohol consumption first asked in	Mean age 20.6 years 52% female 31% Black, 19% Hispanic 21% married, 4.3% divorced/other 19% smoked marijuana, 6.9% other drugs	Supported by the National Institute on Alcohol Abuse and Alcoholism. Conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Study of Youth 1979 (NLSY79)	health.		1982. **Exclusion criteria**: NR	94% no health limitation. Baseline data from 1979-1984. Outcomes data from 2008. Matched an individual engaged in frequent HED with his or her nearest match who engaged in occasional HED and other drinkers and abstainers (2 control groups).	NR
Sui et al. (2009) United States Aerobics Center Longitudinal Study (ACLS)	To examine the longitudinal association between cardiorespiratory fitness and depressive symptoms.	N=14,343 participants. 73.4% male No description of the numbers excluded or who did not respond at follow-up.	**Inclusion criteria:** Normal resting electrocardiograms and able to complete exercise stress test to at least 85% of their age-predicted maximal heart rate during 1970 and 1995. **Exclusion criteria**: mental disorder (depression, anxiety, thoughts of suicide, nervous breakdown, difficulty sleeping, nervous disorder, psychiatric counselling), cardiovascular disease (myocardial infarction, stroke),or cancer.	Most were Caucasian, relatively well educated and from middle and upper socio-economic area. **Men (n=11,258)** Mean age 45±9.5 36.8% stressful occupation 13.4% smoker 41.7% ≥5 drinks/week **Women (n=3,085)** Mean age: 44.6±10.3 17.9% stressful occupation 8.8% smoker 25.1% ≥5 drinks/week	Funding source NR Conflicts of interest NR
Sullivan et al. (2011) United States Veterans Aging Cohort Study (VACS)	To determine the impact of varying levels of alcohol consumption and alcohol-related categories on depressive symptoms over time in patients with and without HIV infection.	2,446/ 3,192 (those excluded had fewer than 2 follow-up assessments, missing detail on outcomes, or never had a drink their life.	**Inclusion criteria:** HIV-infected patients and age- race- and site-matched HIV uninfected patients in general medicine clinics. **Exclusion criteria:** never had a drink in their life	**All patients (n=2446)** Mean age 50.2±9.2 years (range 22 – 87 years); 95.2% male; 57.3% Black; 32.3% White, 10.4% Other; 23.4% married, 26.4% divorced, 8.8% separated, 27.9% never married, 8.9% living with partner; 28.2% employed; 92.1% high school or greater; 10.7% homeless; 52.7% HIV infected; 24.5% Hepatitis C infected **Low-risk drinkers** Mean age 49.8 years (range 22 – 87 years); 94.2% male; 56.2% Black; 33.6% White, 10.2% Other; 24.4% married, 25.6% divorced, 8.0% separated, 28.7% never married, 9.2% living with partner; 30.9% employed; 93.5% high school or greater; 7.7% homeless; 55.9% HIV infected;	Supported by National Institute on Alcohol Abuse and Alcoholism, th National Institute of Aging, the Robert Wood Johnson Foundation Physician Faculty Scholars Program. All authors declare no conflicts of interest.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
				18.0% Hepatitis C infected **High risk drinkers** Mean age 50.9 ±8 years (range 28 - 82 years); 97.5% male; 59.7% Black; 29.3% White, 10.9% Other; 21.2% married, 27.9% divorced, 10.7% separated, 26.1% never married, 8.2% living with partner; 22.5% employed; 88.9% high school or greater; 17.3% homeless; 52.1% HIV infected; 38.7% Hepatitis C infected	
Sullivan et al. (2008) United States HIV – Longitudinal Interrelationships of Viruses and Ethanol (HIV-LIVE)	To determine if current alcohol dependence and alcohol consumption affect depressive symptoms in people with HIV infection.	N=400 Participation rate not stated. Recruitment from other studies, a HIV intake clinic, HIV Primary Care and Specialty Clinic and additional healthcare centres, homeless shelters, drug treatment programs, subject referrals and flyers.	**Inclusion criteria:** HIV infection documented by HIV antibody test; current or past alcohol problems supported by ≥2 positive responses to the CAGE questionnaire or study physician's determination of alcohol abuse or dependence; the ability to speak English or Spanish; a score >20 on the MMSE; capable of giving informed consent and answering questions. **Exclusion criteria:** NR	Mean age 43±7.4 years (range 21 – 71) 75% males 41% Black; 33% White, 19% Hispanic, 7% other races/ethnicities 25% homeless 59% Hepatitis C positive 64% illicit drug use 10% alcohol dependent 31% heavy drinking; 11% moderate drinking; 58% no alcohol consumption Mean CES-D score 22±12.9 (range 0-56)	Supported by the National Institute on Alcohol Abuse and Alcoholism of the NIH, National Institute on Drug Abuse and the Robert Wood Johnson Physician Faculty Scholars Program. Conflicts of interest NR.
Tait et al. (2012) Australia Dynamic Analyses to Optimise Ageing - DYNOPTA	To examines the relationship between alcohol consumption and depressive symptoms in older adults, particularly the oldest old	39,104/45,234 (86%) people had depression, alcohol consumption, and disability data at baseline and were living in the community at each follow-up. The contributing datasets and their baseline samples were: ALSA (n=2,087); ALSWH (n=26,137); AusDiab (n=7,296); HILDA (n=6,164); MELSHA (n=1,000); and PATH (n=2,550).	**Inclusion criteria:** Six of the nine Australian longitudinal studies contributing to the DYNOPTA project collected the key variables used in this study. **Exclusion criteria:** people missing baseline data	N=39,104 participants in DYNOPTA contributed data **N=17,668 aged 45−54 years** 88% female, 10% left school at <15 years, 83% had partners, 95% were not physically limited, 18% were current smokers, 29% ex-smokers, 79% had a low risk alcohol status, 13% were abstinent, 5% had a long-term health risk from excessive alcohol use, 2% had short-term injury risk from excessive alcohol use; 11% had probable depression. **N=5,255 aged 55−64 years** 50% female, 18% left school at <15 years, 79% had partners, 92% were not physically limited, 13% were	DYNOPTA was funded by an NHMRC Grant Work on this paper was supported by an NHMRC Grant and an NHMRC Research Fellowship Authors declared no conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
		On each measure, there were significant differences in the proportions by age group. In particular, the decline in current smoking and the increase in the proportion that was abstinent from alcohol at age 85 or older (38%) compared with younger age groups were notable.		current smokers, 37% ex-smokers, 72% had a low risk alcohol status, 8% were abstinent, 10% had a long-term health risk from excessive alcohol use, 10% had short-term injury risk from excessive alcohol use; 9% had probable depression. **N=13,060 aged 65−74 years** 87% female, 41% left school at <15 years, 63% had partners, 89% were not physically limited, 8% were current smokers, 33% ex-smokers, 64% had a low risk alcohol status, 30% were abstinent, 5% had a long-term health risk from excessive alcohol use, 2% had short-term injury risk from excessive alcohol use; 9% had probable depression. **N=2,620 aged 75−84 years** 60% female, 50% left school at <15 years, 59% had partners, 86% were not physically limited, 7% were current smokers, 39% ex-smokers, 65% had a low risk alcohol status, 28% were abstinent, 5% had a long-term health risk from excessive alcohol use, 2% had short-term injury risk from excessive alcohol use; 8% had probable depression. **N=501 aged ≥85 years** 50% female, 57% left school at <15 years, 40% had partners, 80% were not physically limited, 5% were current smokers, 40% ex-smokers, 56% had a low risk alcohol status, 38% were abstinent, 5% had a long-term health risk from excessive alcohol use, 1% had short-term injury risk from excessive alcohol use; 9% had probable depression.	
Tanaka et al. (2011) Japan	To investigate the association between risk factors and future development of depression in a	11,565/12,630 (92%) people completed the 1993 survey 9,650/12,630 (76%) completed the 2000 follow-up survey 9,201/9,650 (95%) were	**Inclusion criteria:** middle-aged and elderly persons living in the village of Komochi and the downtown area of the city of Isesaki who were identified based on the municipal resident	N=9,201 participants in the Komo-Ise study of middle-aged and elderly persons who were included in the analysis. **N=4,326 men (baseline characteristics)** 18% aged 40-44 years, 16% aged 45-49 years, 17% aged 50-54 years, 16% aged 55-59 years, 19% aged 60-	Supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science,

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	large-scale longitudinal setting	included in this study	registration file in 1993 **Exclusion criteria:** people who did not complete both surveys, those who were depressed at baseline (1993) or had a chronic mental illness.	64 years, 13% aged65-69 years, 43% rural, 15% had junior college, college or higher education, 3% had no occupation, 89% married 3% living alone, 38% enjoyed neighbours, 75% participated in activities, 60% had good friends, 94% perceived their health status as excellent, good or fair. 33% had a chronic disease, 3% had a BMI <18.8, 22% had BMI ≥25, 3% slept <6 hours, 3% slept >9 hours, 29% never smoked, 19% ex-smokers, 52% current smokers, 21% never consumed alcohol, 54% drank lightly, 26% were heavy drinkers, 53% physically inactive, 2% were depressed at follow-up **N=4875 women (baseline characteristics)** 15% aged 40-44 years, 16% aged 45-49 years, 16% aged 50-54 years, 19% aged 55-59 years, 19% aged 60-64 years, 14% aged65-69 years, 39% rural, 7% had junior college, college or higher education, 28% had no occupation, 82% married 5% living alone, 49% enjoyed neighbours, 74% participated in activities, 71% had good friends, 94% perceived their health status as excellent, good or fair. 34% had a chronic disease, 5% had a BMI <18.8, 23% had BMI ≥25, 6% slept <6 hours, 1% slept >9 hours, 89% never smoked, 2% ex-smokers, 9% current smokers, 56% never consumed alcohol, 40% drank lightly, 2% were heavy drinkers, 59% physically inactive, 2% were depressed at follow-up	and Technology, Japan, and a Gerontology and Health Grant from Gunma Prefecture Authors declared no conflicts of interest
Tsai et al. (2013) Taiwan Taiwan Longitudinal Study on Aging (TLSA)	To determine the ability of lifestyle factors in predicting the development of depressive symptoms in ≥53 year old Taiwanese.	4,049/4,412 (92%) people aged ≥60 years completed survey in 1989 2,462/3,041 (81%) people aged 50−66 years completed survey in 1996. 4,440/6,511 (53%) completed the 1999 survey (baseline for this study) 3,132/4,440 (71%) completed	**Inclusion criteria:** people from either cohort who completed the 1999 survey **Exclusion criteria:** people who had either surveys completed by proxy or had incomplete CES-D data, those with depressive symptoms at baseline	N=4,122 participants in TLSA included a population-based random sample of subjects aged ≥60 years in 1989, with a second sample drawn from the 50−66-year old population in 1996 who completed the 1999 survey. **N=849 with depressive symptoms at baseline** 60% female, 25% aged 53−64 years, 41% aged 65−74 years, 35% aged ≥75 years, 87% had ≤6 years education, 2% had ≥13 years education, 55% were not physically active, 8% were physically active 1−2 times/week, 37% were physically active ≥3 times/week,	The study received no funding support from any source. Authors declared no conflicts of interest

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
		the 2007 survey There was no comparison between responders and non-responders		21% were current smokers, 14% ex-smokers, 6% currently chewed betel nuts, 5% chewed betel nuts previously, 87% drank alcohol <1 times/week, 11% drank alcohol moderately (≥1 times/week, <2 drinks/time), 2% drank heavily (≥1 times/week, ≥2 drinks/time), 81% drank tea ≤2 times/week, 19% drank tea ≥3 times/week. **N=3,273 without depressive symptoms at baseline** 57% female, 40% aged 53−64 years, 37% aged 65−74 years, 24% aged ≥75 years, 75% had ≤6 years education, 7% had ≥13 years education, 36% were not physically active, 7% were physically active 1−2 times/week, 58% were physically active ≥3 times/week, 26% were current smokers, 16% ex-smokers, 6% currently chewed betel nuts, 5% chewed betel nuts previously, 80% drank alcohol <1 times/week, 17% drank alcohol moderately (≥1 times/week, <2 drinks/time), 2% drank heavily (≥1 times/week, ≥2 drinks/time), 64% drank tea ≤2 times/week, 35% drank tea ≥3 times/week.	
Van Gool et al. (2007) Netherlands Maastricht Aging Study (MAS)	To examine whether healthy lifestyles are associated with absence of depressed mood	1,823/3,449 (53%) respondents returned the questionnaire between 1993 and 1995 (baseline) 1,376/1,823 (75%) participants underwent reassessments 6 years later 1,169/3,449 (34%) of the respondents were included in this study Women and older individuals were oversampled to ensure adequate representation of these groups in follow-up measurements.	**Inclusion criteria:** Individuals, aged 24 to 81 years, were randomly recruited from the Registration Network Family Practices, a primary care research sampling frame consisting of 9,919 individuals whose native language is Dutch. **Exclusion criteria:** medical conditions that interfered with their normal cognitive functioning at their entry into the MAS study	The longitudinal MAS, an ongoing investigation examining determinants of normal cognitive aging. **N=1,169 respondents who were included in this study** 48% female, 42% aged 24−44 years, 41% aged 45−64 years, 17% aged 65−81 years, 81% married/de facto, 37% had a low level of education, 29% had a high level of education, 93% were not impaired, 33% had no chronic diseases, 34% had one chronic disease, 33% had ≥2 chronic diseases, 35% never smoked, 38% were ex-smokers, 27% current smokers, 22% spent >30 minutes/day on physical exercise, 49% did no physical exercise, 33% were overweight, 14% drank no alcohol, 80% drank ≤2 drinks/day, 7% drank ≥3 drinks/day, Mean Symptom Checklist 90 score 20.5±6.1.	Supported in part by a grant from the Dutch Ministries of Education and Health and Welfare, via the Steering Committee for Gerontological Research Conflict of interest NR
van Zaane et	To investigate the	158/180 (88%) BP patients	**Inclusion criteria:** aged 18−75	**N=137 participant sociodemographic and clinical**	Funded by the

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
al. (2014) Netherlands	temporal relationship between alcohol use and short-term mood-switching probabilities in BP patients	entered baseline assessment 137/158 (87%) participated for at least two months 125/158 (79%) participated for at least six months 104/158 (66%) completed the full 12 months. Analyses were based on the 137 patients with follow-up data for at least two months. No significant differences were found in the sociodemographic and clinical data at baseline, including illness severity symptoms and alcohol and other drug use, between those who completed the full study and those with at least 2 months of follow-up data.	years; meet DSM-IV criteria for BD-I or BD-II with or without comorbid AUD; have no serious physical illness that might influence the diagnosis or course of BD; be able and willing to participate in the study for one year; and have adequate command of the Dutch language. **Exclusion criteria:** participation for less than 2 months	**characteristics at baseline** Mean age 45.9±10.2 years, 54% males, 66% had BP-I, 34% had BP-II, mean age of onset of BD 24.1±9.9 years, mean duration of BD 21.7±11.5 years, mean number of depression episodes, 15.1±23.4, mean number of manic episodes 13.8±21.5, 31% had rapid cycling, 67% with a partner, 60% had an annual income <€20.00047% has educational level ≤ high school, 90% had jobs that did not match qualifications, 48% were unable to work, 44% had lifetime AUD, 20% had current AUD, 38% had lifetime AD, 18% had current AD, 21% had lifetime DUD, 6% had current DUD; 34% had lifetime anxiety disorder, 14% had current anxiety disorder, mean age of onset of AUD 24.7±9.6 years, mean number of daily drinks 1.96±2.36 (range 0−14), mean number of daily drinks for males 2.45±2.84 (range 0−14), mean number of daily drinks for females 1.43±1.51 (range 0−6), 8% had history of alcohol-induced depression, 7% had history of alcohol-induced (hypo)mania, 22% had ≥1 suicide attempts	Geestelijke Gezondheidszorg InGeest Institute of Psychiatry and Mental Health and Stichting tot Steun, the Netherlands, and by unrestricted grants from Eli Lilly International, USA, and Bristol-Myers Squibb, the Netherlands. Two authors have received unrestricted grants and/or speakers' fees from some of the following: Eli Lilly & Co, Bristol-Myers Squibb, AstraZeneca, GlaxoSmithKline, Janssen-Cilag, Lundbeck, Wyeth, Organon, Pfizer, and Servier
Weyerer et al. (2013) Germany Study on Ageing, Cognition,	To determine incidence and predictors of late-life depression	10,850/22,701 (48%) patients were eligible 6,619/10,850 (61%) were randomly selected 3,214/6,619 (49%) participated at baseline 2,910/6,619 (44%) had no	Patients were recruited by 138 GPs in six study centres **Inclusion criteria:** age ≥75 years, the absence of dementia, and at least one contact with the GP within the last 12 months.	**N=2,512 participants demographic characteristics at baseline** 64% women, mean age 79.6±3.5 years (range: 75−99), 51% were living alone, 45% were widowed, 44% were married, 6% were never married, 5% were divorced, 60% had a low level of education (elementary school), 28% had a middle level of education, 12% a high level of	Funded by the German Federal Ministry of Education and Research and supported by the INTERREG IVB project 'Health and

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Dementia in Primary Care Patients (AgeCoDe Study)		depression at baseline and were included 2,512/2,910 (86%) completed both follow-ups	**Exclusion criteria:** cannot consent, irregular patient, deaf or blind, severely ill, language barrier.	education. **N=2,512 participants at follow-up** 43% had a new incidence of depression, 37% in women and 46% in men, 35% in those aged 75−79 years, 48% in those aged 80−84 years, 75% in those aged ≥85 years	Demographic Changes' Authors declared no conflicts of interest
Wilkinson et al. (2016) United States National Longitudinal Study of Adolescent to Adults Health	Aim 1: To test the direction of association between adolescent substance use and depression (self-medication or stress model). Aim 2: Examine potential mediators and moderators of relationship between substance use and depressive symptoms.	N=12,107 who participated in Wave 1, III (18-25 years) and IV (24-32 years) with complete data on variables of interest	**Inclusion criteria:** Adolescents in grades 7-12 in 1994-95 at wave 1 from 2 large schools and 14 small schools **Exclusion criteria:** NR	**Males (N=5,474)** Race=65.8% white, 14.9% black, 12.2% Hispanic; Parental education=11.9% less than high school; 26.1% high school graduate, 30% some college, 32.1% college graduate or higher **Females (N=6,521))** Race=66.5% white, 16% black, 11.4% Hispanic; Parental education=11.5% less than high school; 28.2% high school graduate, 28.7% some college, 31.6% college graduate or higher	Grant funding by the National Institute on Drug Abuse, using data from Add Health, funded by grant from Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. The authors had declared no conflicts of interest
Wymbs et al. (2014) United States Development al Pathways Project (DPP), same population as	To test whether gender moderated prospective associations between early substance use and later depressive symptoms.	N=2,187/2,920 eligible students (74.9%)	**Inclusion criteria:** 6th graders who had a 3rd grade reading comprehension or higher, from 4 Seattle-area public schools. Data from when they were in 8th, 9th and 12th grade. **Exclusion criteria:** NR	Mean age at intake: 12.0 (range 11.0 – 13.6) years (Mean age 14 in Year 8) 51.6% male 39.5% Non-Hispanic White; 24.9% Black; 24.1% Asian/Pacific Islander; 10.1% Hispanic; 1.4% Native American 33.4% low income (<$34,000); 35.5% mid income (%35,000-$74,999); 31.1% high income (>$75,000) 27.3% single parent household	Supported by the National Institute on Alcohol Abuse and Alcoholism, National Institute of Mental Health and the National Institute on Drug Abuse.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
McCarty et al. (2012)				42% lifetime history of any substance use disorder among biological parents	Conflicts of interest NR
Zhang et al. (2017) Germany Dresden Predictor Study	To test the predictive validity of four health-related factors for new onsets of MDD	3,065/5,203 eligible at baseline 1,881/3,065 completed interview and questionnaire at baseline 2118/2788 at follow-up completed interview and questionnaire	**Inclusion criteria:** German, female, age 18 – 25 at baseline **Exclusion criteria:** Affected disorder at baseline.	N=1,196 women who completed both surveys and interviews Mean age = 21.03±1.73 years; 37.2% low SES; 64% middle SES; 8.5% high SES **N=1,118 no MDD at follow-up** Smoker=22% **N=78 with incident MDD at follow-up** Smoker=33%	Funding source and conflicts of interest NR.

AUD = alcohol use disorder; AUDIT = Alcohol Use Disorder Identification Test; AUDIT-C = Alcohol Use Disorders. Identification Test – Consumption; BAI = Beck's Anxiety Inventory; BDI = Beck's Depression Inventory; BMI = body mass index; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD = general anxiety disorder; HIV = human immunodeficiency virus; HR = hazard ratio; ICU = intensive care unit; IQR = inter-quartile range; MDD = major depressive disorder; NR = not reported; OR = odds ratio; PHQ-9 = nine question Patient Health Questionnaire; PTSD = post-traumatic stress disorder; SCID = Structured Clinical Interview for DSM-IV; WHO = World Health Organisation.

Table 14 Study profile for case-control study (level III-3 aetiological level of evidence)

Study / Country	Study Aim	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Conner et al. (2017) USA	To compare post-mortem toxicology results for alcohol and non-alcohol drugs, alone and in combination, in suicide decedents and motor vehicle accident victims	**Inclusion criteria:** Individuals in New Mexico ages 18−54 years that died in 2012 by suicide or motor vehicle collisions **Exclusion criteria:** those with missing or out-of-range data, poisoning suicides, Asians, Pacific Islanders and African Americans were excluded from analysis due to their low numbers	**N=185 suicide victims** 18% women, 51% white, 38% Hispanic, 11% Indigenous, 44% aged 18−34 years, 56% aged 35−54 years, 24% had alcohol and drug in blood, 40% had alcohol alone, 5% had a drug alone, and 42% had neither. **N=161 motor vehicle accident victims (Comparator)** 29% women, 30% white, 49% Hispanic, 21% Indigenous, 44% aged 18−34 years, 56% aged 35−54 years, 4% had alcohol and drug in blood, 44% had alcohol alone, 5% had a drug alone, 47% had neither.	Funding source NR Authors declared no conflicts of interest

NR = not reported

Table 15 Study profiles for cross-sectional studies (level IV aetiological evidence)

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Gart & Kelly (2015) United States Youth Risk Behavior Survey	To explore the relationship among depressive symptoms, use of illegal substances, alcohol and tobacco use, and how they contribute to suicidal ideation and behaviour in adolescents.	N=15,363 (No. who did not participate was not stated) 7,708 females	Inclusion: not stated Exclusion: not stated	Mean age: 16±1.2 years 7,708 female (50.1%) 3,774 9th grade; 3,693 10th grade; 4,133 11th grade, 3,699 12th grade 40.1% Caucasian; 18% African-American; 14.5% Hispanic	Funding source not stated. Authors declare no conflict of interest.
Glasheen et al. (2015) United states National Survey on Drug Use and Health data	To examine past year suicidal thoughts, plans and attempts among HED and non-HED adults with and without past year MDEs	N=136,500 adults (≥18 years). No. eligible to participate not stated.	**Inclusion:** adults (≥18 years) who had had at least one drink in past month **Exclusion:** people of no fixed address, active-duty military personnel, or residents of institutional group quarters.	46% females, 54% males 5% females reported suicidal thoughs, 1% had suicidal plans, <1% attempted suicide 4% males reported suicidal thoughts, 1% had suicidal plans, <1% attempted suicide	Funded by the Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. No conflicts of interest to declare.
Heberman et al. (2016) United states Department of Defense Survey of Health-Related Behaviors among Active Dute Military	To examine associations among drinking motives, alcohol use, PTSD, depression and suicidality in a representative sample of US Army soldiers	N=3,813/10,400 (36.6%) active duty members, who were lifetime alcohol users, and completed all survey items	**Inclusion:** active duty soldiers who completed all relevant survey items and were lifetime alcohol users. **Exclusion:** not completing all items, or being abstaining from alcohol.	3,813 soldiers who completed all relevant survey items and were lifetime alcohol users. 43% were aged 17 to 25 (n=1,600) 87% male (n=2,840) 67% non-Hispanic White 31% had high school education or less 43% unmarried 80% enlisted 32% heavy drinkers 5% light/moderate drinkers were suicidal 8% of heavy drinkers were suicidal	Funding source and conflicts of interest not stated.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
Personnel (DoD HRB)					
Kim & Kim (2010) Korea 2006 Korean Youth Risk Behavior Survey	To examine the association between early initiation of alcohol drinking, cigarette smoking and sexual intercourse with suicidal ideation and suicide attempts.	N=71,404/78,593 potential participants interviewed (90.0%) 7,520 (10.5%) excluded due to missing data	**Inclusion:** sample of public and private middle and high school students in grades 7 to 12 in all regions of Korea (234 cities and districts) **Exclusion:** missing data	63,884 adolescnets 32,417 males 31, 467 females age range 13 – 19 years Mean age: 16.2±1.7 years	Funding source not stated. The authors declare no financial conflict of interest.
Lawrence et al. (2010) United States HIV/AIDS Clinic Cohort Observational Database project	To identify factors associated with self-reported suicidal ideation in HIV-infected individuals	N=1,216/1,268 patient reported outcome sessions (and patients).	**Inclusion:** convenience sample of patients at 2 HIV/AIDS clinics in Washington and Seattle, who attended at least 1 routine primary care appointment and completed their first Patient Reported Outcomes survey before February 2009. **Exclusion:** those who did not answer the suicidal ideation question. .	Mean age: 44±10 years 53% white 79% male Mean CD4 count: 454±277 cells/mm^3 80% on antiretroviral 170/1216 (14%) reported suicidal ideation	Supported by the UAB Center for AIDS Research, CNICS and the Mary Fisher CARE Fund, UW Center for AIDS Research, and the National Institutes of Mental Health. Four authors received research or consulting funding from pharmaceutical companies (Bristol-Myers Squibb, Gilead, Merck, Tibotec, GlaxoSmithKlein, Monogram Biosciences, Panacos, Pfizer, Progenics, Roche, Serono, Tanox, Trimeris,Vertex, and Boehringer Ingelheim Pharmaceuticals. Other authors had no conflicts of

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
					interest.
Peltzer & Pengpid (2015) Kiribati, Samoa, Solomon Islands and Vanuatu Global School-Based Health Survey (GSHS)	To investigate the correlations between early initiation of smoking, alcohol and drug use with suicidal ideation and suicide attempts.	N=6,540 school-going adolescents Response rate for Kiribati 85%; Samoa 79%, Solomon Islands 85%, Vanuatu 72%.	**Inclusion:** existing data from the Global School-Based Health Survey from four Pacific Island countries in Oceania. Schools were selected with probability proportional to their reported enrolment size. In the second stage, classes in selected school randomly selected, and all students were eligible to participate irrespective of their age. **Exclusion:** not stated.	6540 adolescents predominantly aged 13-16 years 51.3% males 25.8% suicidal ideation, 34.9% suicide attempts 15.7% early smoking initiation 13.8% early alcohol initiation 12.9% early drug use initiation 31.7% had one or more psychological distresses (no close friend, mostly or always feeling lonely, or mostly or always being worried/anxiety)	
Schilling et al. (2009) United States Signs of Suicide (SOS) program in 2001-2002	To examine the association between self-reported alcohol use and impulsive suicide attempts among adolescents.	N=31,953 Only 38% of schools implementing the SOS program returned the screening forms for analysis. However, sample returned closely matched US distribution of race and sex.	**Inclusion:** Data from the SOs program, consisting of screening forms from students attending 225 of 594 schools in the U.S. **Exclusion:** participants with missing values of item measures used in the analyses	48.3% male, 51.7% female 71.1% white, 11.9% black, 10% Hispanic, 2% Asian, 1.3% Indian, 3.7% Multiracial 2.8% aged ≤13 years; 21.5% aged 14, 30.4% aged 15, 22% aged 16, 15.8% aged 17, 7.6% ≥18 years old Grades 7 to 12 29.2% reported heavy episodic drinking in past year 12.2% reported drinking while down in past year 4.9% had attempted suicide	Not stated.
Souza et al. (2010) Brazil	To examine the prevalence of suicidal ideation as well as risk	N=1,039/1,145 adolescents 106 (9.26%) refused	**Inclusion:** All adolescents aged 11 to 15 years from 79 randomly selected census tracts in the urban area of	48.2% male, 51.8% female 20.1% aged 11, 20.9% aged 12, 19.5% aged 13, 20.02% aged 14, 19.2% aged 15 years 32.4% lowest SES; 37.1% median SES, 30.5%	All authors employed by universities. No conflicts of interest.

Study / Country	Study Aim	Participation rate / Generalisability	Inclusion/exclusion criteria	Population characteristics	Funding source / Conflict of interest
	factors in a representative sample of adolescents aged 11 to 15 from Pelotas, a southern Brazilian city.		Pelotas, Brazil **Exclusion:** Adolescents who refused to participate, or parents did not consent.	highest SES 21.7% had consumed alcohol in last month 7.2% had used tobacco in last month 14.6% with conduct disorder 2.3% with high depressive symptoms 14.1% had suicidal ideation	

MDEs = major depressive episodes; SES = socio-economic status

Appendix C Study outcomes tables

The effect of alcohol consumption on developing depression and depressive symptoms (general population)

All ages

Table 16 Depression outcomes from studies that reported on population-based cohorts of mixed gender and with a broad age range

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Adolescents, adults and elderly adults				
Bulloch et al. (2012) Canada Population-based longitudinal National Population Health Survey (NPHS) of household residents	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 2 years Wave 3: 4 years Wave 4: 6 years Wave 5: 8 years	N=17,276 nationally representative cohort of household residents aged ≥12 years 13,175/17,276 participants in Wave 1 (1994) who did not have MDE 9.6% (95% CI 8.9–10.4) reported excessive alcohol consumption No differences in baseline characteristics between those with and without MDE	**Alcohol consumption** was evaluated by answers given to specific survey questions and quantity of alcohol consumed in a 7-day diary. <u>Excessive drinking</u> was defined as drinking exceeding moderate drinking guidelines (14 drinks in a week for men and 7 for women) and were identified by entries in a 7-day diary of alcohol consumption <u>HED</u> was defined as ≥5 drinks on one occasion **MDE** was measured using CIDI-SFMD questionnaire. The cut-off for MDE requires endorsement of five of nine specified depressive symptoms during the same 2-week period in the preceding year.	**HR (95% CI) for MDE risk over 6 years for respondents with excessive alcohol consumption compared to those with low drinking levels in 1996** Exceeding guidelines: HR=1.0 (0.7, 1.4), NS HR_{adj}=0.9 (0.7, 1.3), NS HED: HR_{adj}=1.1 (0.9, 1.3), p=0.52 (adjusted for gender, age, marital status, employment status, having a chronic condition, being in pain and having a low income)
Magnusson Hanson et al. (2016) Sweden Population-based	**Level:** II **Quality:** CPHE 21/34 **Internal validity:** High risk of bias	N=3,706 participants in the Swedish Longitudinal Occupational Survey of Health (SLOSH) study Waves 2−5 N=179 with excessive alcohol	**Excessive alcohol consumption** was determined using AUDIT in 2008. <u>Excessive alcohol consumption</u> was defined as men reporting drinking ≥21 units and women ≥14 units weekly or drinking ≥6 units per occasion at least	**Standardized bivariate SEM cross-lagged coefficients** The relationship between excessive alcohol consumption in 2008 and depressive symptoms two years later was not significant β=0.092, NS

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Swedish Longitudinal Occupational Survey of Health (SLOSH) included individuals aged 16−64 years who were employed	**External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 3 or 5 years Wave 3: 5 or 7 years	consumption	weekly based on AUDIT. The CAGE questionnaire was used to determine alcohol use in 2010, 2012 and 2014 and does not provide data to determine alcohol consumption frequency or quantity **Depressive symptoms** were measured with a brief subscale from the SCL-90, the SCL-CD_6.	
Meng (2017) Canada Population-based National Population Health Survey (NPHS) included individuals aged ≥12 years	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: every 2 years for 16 years	N=12,227 NPHS participants who completed all 9 waves and did not have depression at baseline	**Type of drinker** was based on the participant's drinking frequency, including regular drinker, occasional drinker, former drinker, and abstainer. **First depressive episode** was assessed using the Composite International Diagnostic Interview Short Form, to assess the presence of MDD diagnostic symptoms in the 12-months prior to the interview. A 90% predicative probability cut-off point had been validated and was used to indicate the incidence of first depressive episode.	**Univariate HR (95% CI) for type of drinker associated with earlier onset of the first depressive episode** Occasional/former/abstainer HR=1.00 (reference) Regular drinker HR=0.88, (0.778, 0.995) p=0.041
Meng et al. (2017) Canada Population-based Zone d'Épidémiologie Psychiatrique du Sud-Ouest de Montréal (ZEPSOM) included individuals aged	**Level:** II **Quality:** CPHE 30/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: Wave II: 2 years	N=1,357 randomly selected individuals aged 15–65 years who completed Wave II (2008−9) N=1212 included in analysis N=646 females included in analysis N=956 randomly selected individuals aged 15–65 years who also completed Wave III (2010−11) N=877 included in analysis N=327 males included in analysis	**Type of drinker** was determined by number of drinks consumed weekly or monthly. Abstainer: no alcohol consumed Former drinker: no alcohol in the past year Occasional drinker: <1 drink/month Regular drinker: ≥1 drink/month **MDD** was measured using the CIDI questionnaire	**RR (95% CI) of incident major depressive disorder during the 2-year follow-up (Wave II) by alcohol consumption level** Abstainer RR=1.0 (Reference) Former drinker RR=0.15 (0.12, 0.19), p<0.001 Occasional drinker RR=1.28 (1.12, 1.45), p<0.001 Regular drinker RR=0.51 (0.44, 0.58), p<0.001 **RR (95% CI) of incident major depressive disorder during the 4-year follow-up (Wave III) by alcohol consumption level** Abstainer RR=1.0 (Reference) Former drinker RR=0.28 (0.23, 0.33), p<0.001 Occasional drinker RR=1.56 (1.40, 1.75), p<0.001

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
15–65 years	Wave III: 4 years	N=550 females included in analysis		Regular drinker RR=0.68 (0.61, 0.76), p<0.001
Adults and elderly adults				
Cabello et al. (2017) Russia, Ghana, India and Mexico WHO's Study on Global AGEing and Adult Health (SAGE)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: 5-8 years	N=7,908 adults who responded to both wave 0 and wave I of SAGE. Nationally representative samples of adults aged 50 years and older and smaller sample 18-49.	**Alcohol consumption:** defined by question about whether they ever consumed a drink containing alcohol. If the answer was yes, then a separate question was posed about how many drinks they had each day the previous week. Heavy drinkers defined as having at least 5 (for men) or 4 (for women) on at least one day in previous week. **MDD** as defined by diagnostic criteria for ICD-10, regarding symptoms over past 12 months	N=6349 (excluding lifetime depression at wave 0) **OR (95%CI) of incident MDD using logistic regression:** Never drinkers: OR_{adj}=1.0 (Reference) Non-heavy drinkers: OR_{adj}=0.93 (0.57, 3.67), p=0.78 Heavy drinkers: OR_{adj}=1.59 (0.67, 3.75), p=0.29 N=7,908 (including lifetime depression at wave 0) **OR (95%C) of persistent depression using logical regression**: Reference: never drinkers Non-heavy drinkers: OR_{adj}=0.98 (0.36, 2.61), p=0.96 Heavy drinkers: OR_{adj}=4.72 (1.03, 21.72), p=0.04 $OR_{adj:}$ adjusted for demographics, presence of physical chronic condition, BMI, general health status and country
Cougle et al. (2015) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** H9igh risk of bias (poor reporting on population) **Follow-up**: 3 years Wave 1: 2001-2002 Wave 2: 2004-2005	N=34,653 adults, aged 18 years and older, (nationally representative survey of non-institutionalised US citizens)	**Weekly alcohol consumption** by AUDADIS-IV (dose not stated) **Depressive disorder** defined as combination of MDD and dysthymia by AUDADIS-IV	**OR (95%CI) for incident depressive disorder at wave 2** Reference: not stated (assume consumption of alcohol less than weekly) Weekly alcohol: OR_{adj}=0.88 (0.83, 0.94), p<0.001 Adjusted for age, income, marital status, gender, ethnicity, education, and psychiatric comorbidity.
Sullivan et al. (2011)	**Level:** II **Quality:**	N=2,446 Veterans with or without HIV, aged 22 to 87 years, either	**HED** defined as consuming 6 or more drinks on one occasion 3 or more times	**Generalized estimating equation model to assess association of baseline alcohol use and MDD over time**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
United States Veterans Aging Cohort Study (VACS)	CPHE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 6 years	low risk drinkers or unhealthy drinkers (complete abstainers were excluded) 95% male Mean age 50.2±9.7 years N=1,339 with HIV N=1,677 low-risk drinkers N=769 unhealthy drinkers	during past year. **Hazardous drinking** defined as AUDIT score 5 (females) or 7 (males) **Non-hazardous drinking** defined as consuming alcohol in previous year but not HED or hazardous drinking. **Unhealthy drinking** defined as either hazardous drinking, HED or alcohol abuse or dependence **MDD** defined as score of PHQ-9 >9	Reference: non-hazardous drinkers Estimate (standard error), OR (95% CI), p-value: Hazardous drinking β=0.93 (0.33) OR_{adj}=2.53 (1.34, 4.81), p<0.001 HED β=0.76 (0.19) OR_{adj}=2.14 (1.49, 3.07), p<0.001 Past alcohol use β=0.26 (0.21) OR=1.15 (0.93, 1.42) OR_{adj}=1.30 (0.86, 1.96), p=0.21 Participants of HED have more severe depressive symptoms than non-hazardous drinkers OR_{adj}: adjusted for correlated outcome data, gender, race, and age
Van Gool et al. (2007) Netherlands Primary care-based Maastricht Aging Study (MAS), included adults aged 24 to 81 years.	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: 6 years	N=1,169 respondents, aged 24 to 81 years, from the MAS study were included in this study N=164 depressed at follow-up N=1,005 not depressed at follow-up N=161 0 drinks/day N=928 ≥2 drinks/day N=80 ≥3 drinks/day Individuals who did not take part in the study were significantly older, more likely to be female, widowed, have low levels of education, report impairments, be overweight, have more chronic diseases, undertake fewer minutes of physical activity per day, and have more symptoms of	Alcohol consumption was calculated according to participants' reports of the number of glasses of alcohol (representing approximately 10 g of alcohol) they drank per day on average (>10 glasses, 7−10 glasses, 3−6 glasses, 1−2 glasses, or none) and the average number of days per week they consumed alcohol (every day, 5−6 days, 3−4 days, 1−2 days, <1 day). Participants were grouped into the following categories: Non-drinkers: 0 drinks/day Regular drinkers: ≤2 drinks/day, Excessive alcohol use: ≥3 drinks/day. Transitions in alcohol use over time were categorized as: (1) still drinks alcohol (2) initiated alcohol use (3) quit drinking alcohol	**RR (95% CI) for baseline drinking level as determinants of depressed mood at follow-up** None: RR=1.0 (Reference) ≤2 drinks/day RR_{adj1}=0.92 (0.55, 1.54) RR_{adj2}=1.15 (0.68, 1.96) ≥3 drinks/day RR_{adj1}=1.49 (0.68, 3.24) RR_{adj2}=2.48 (1.08, 5.69), p<0.05 Mean no. of drinks per day (continuous variable) RR_{adj1}=1.07 (0.95, 1.21) RR_{adj2}=1.17 (1.03, 1.32), p<0.05 **RR (95% CI) for transitions in drinking behaviour between baseline and follow-up as determinants of depressed mood at follow-up** Still does not drink alcohol RR=1.0 (Reference) Still drinks alcohol RR_{adj1}=0.63 (0.37, 1.09) RR_{adj2}=0.80 (0.45, 1.41) Initiated alcohol use RR_{adj1}=0.17 (0.04, 0.73), p<0.05 RR_{adj2}=0.18 (0.04, 0.76), p<0.05

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		depression.	(4) still does not drink alcohol **Depressive mood** was assessed using the CES-D questionnaire A CES-D threshold score of ≥16 was used to define depressed mood	Quit drinking alcohol RR_{adj1}=1.35 (0.60, 3.01) RR_{adj2}=1.29 (0.57, 2.91) RR_{adj1}: adjusted for baseline depressive symptomatology. RR_{adj2}: adjusted for baseline depressive symptomatology, age, gender, marital status, educational level, instrumental activities of daily living status, and number of chronic diseases.

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; AUDIT = Alcohol Use Disorder Identification Test; BMI = body mass index; CI = confidence interval; CAGE = Cut-Annoyed-Guilty-Eye; CIDI = Composite International Diagnostic Interview; CIDI-SFMD = Composite International Diagnostic Interview for major depressive episodes; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; HIV = human immunodeficiency virus; HR = hazard ratio; ICD-10 = International Classification of Diseases, 10th revision; MDD = major depressive disorder; MDE = major depressive episode; NS = not significant; OR = odds ratio; PHQ-9 = nine question Patient Health Questionnaire; RR = relative risk; SCL-90 = Hopkins Symptom Checklist; SEM = structural equation models.

Table 17 Depression outcomes from studies that reported on males and/or females with a broad age range separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Adolescents, adults and elderly adults				
Meng (2017) Canada Population-based National Population Health Survey (NPHS) included individuals aged ≥12 years	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: every 2 years for 16 years	N=12,227 NPHS participants who completed all 9 waves and did not have depression at baseline N~5, 893 men (48.2%) N=6,334 women (51.8%)	**Type of drinker** was based on the participant's drinking frequency, including regular drinker, occasional drinker, former drinker, and abstainer. **First depressive episode** was assessed using the Composite International Diagnostic Interview Short Form, to assess the presence of MDD diagnostic symptoms in the 12-months prior to the interview. A 90% predicative probability cut-off point had been validated and was used to indicate the incidence of first depressive episode.	**Univariate HR (95% CI) for type of drinker associated with earlier onset of the first depressive episode for females** Occasional/former/abstainer HR=1.00 (reference) Regular drinker HR=0.916 (0.796, 1.054), p=0.221 **Univariate HR (95% CI) for type of drinker associated with earlier onset of the first depressive episode for males** Occasional/former/abstainer HR=1.00 (reference) Regular drinker HR=0.794 (0.635, 0.992), p=0.042 **Multivariate HR (95% CI) for type of drinker associated with earlier onset of the first depressive episode for males** Occasional/former/abstainer HR_{adj}=1.00 (reference) Regular drinker HR_{adj}=0.794 (0.641, 0.983), p=0.035 Adjusted for age, length of follow-up, ethnicity, chronic disease and physical activity
Meng et al. (2017) Canada	**Level:** II **Quality:** CPHE 30/34	N=1,357 randomly selected individuals aged 15–65 years who completed Wave II (2008−9)	**Type of drinker** was determined by number of drinks consumed weekly or monthly.	**RR (95% CI) of incident major depressive disorder during the 2-year follow-up (Wave II) by alcohol consumption level for femlaes**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Population-based Zone d'Épidémiologie Psychiatrique du Sud-Ouest de Montréal (ZEPSOM) included individuals aged 15–65 years	**Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: Wave II: 2 years Wave III: 4 years	N=1212 included in analysis N=646 females included in analysis N=956 randomly selected individuals aged 15–65 years who also completed Wave III (2010−11) N=877 included in analysis N=327 males included in analysis N=550 females included in analysis	Abstainer: no alcohol consumed Former drinker: no alcohol in the past year Occasional drinker: <1 drink/month Regular drinker: ≥1 drink/month **MDD** was measured using the CIDI questionnaire	Abstainer RR=1.0 (Reference) Former drinker RR=0.11 (0.07, 0.15), p<0.001 Occasional drinker RR=1.49 (1.25, 1.77), p<0.001 Regular drinker RR=0.75 (0.63, 0.89), p=0.001 **RR (95% CI) of incident major depressive disorder during the 4-year follow-up (Wave III) by alcohol consumption level for females** Abstainer RR=1.0 (Reference) Former drinker RR=0.21 (0.17, 0.27), p<0.001 Occasional drinker RR=1.19 (1.05, 1.35), p=0.008 Regular drinker RR=0.75 (0.66, 0.85), p<0.001 **RR (95% CI) of incident major depressive disorder during the 4-year follow-up (Wave III) by alcohol consumption level for males** Abstainer RR=1.0 (Reference) Former drinker RR=0.26 (0.18, 0.37), p<0.001 Occasional drinker RR=2.62 (1.93, 3,56), p<0.001 Regular drinker RR=0.45 (0.33, 0.62), p<0.001
Adults and elderly adults				
Johnson et al. (2013) United States Chicago Health and Life Experiences of Women (CHLEW) study	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** High risk of bias **External validity:** Low risk of bias **Follow-up**: 4 years	N=382 adult women who identify as lesbian (aged 18-83 years) Mean age 37.9±11.8 years N=98 any HED at baseline N=210 any intoxication at baseline	**Hazardous drinking** by combining indicators of heavier drinking and adverse consequences. HED: ≥1 occasions of drinking ≥6 drinks/day Subjective intoxication: ≥1 or more occasions of having consumed "enough to feel drunk – that is, when drinking noticeably affected your thinking, talking and behaviour" based on past 12-month reports. Adverse drinking consequences (e.g. driving while drunk, complaints about drinking by partner) and symptoms of	**Longitudinal effects of hazardous drinking and depression on one another.** Hazardous drinking (wave 1)-depressive symptoms (wave 2): standardized coefficient: β=0.18, p<0.05 Adjusted for baseline depression.

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			potential alcohol dependence (e.g. memory lapses, inability to stop or reduce consumption). **Depressive symptoms** measured using the National Institute of Mental Health Diagnostic Interview Schedule	
Onwuameze et al. (2013) United States Iowa Certified Safe Farm (CSF) study	**Level:** II **Quality:** CPHE 16/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up**: 3 years	N=257 farmers from Iowa (98% male), mean age 56 years from certified safe farms N=251 male	**Alcohol consumption** based on >9 alcohol drinks per week **Depression** based on non-validated question of "how would you rate your level of depression in the last quarter?" (very low, low, average, high or very high). Depression classified as high or very high.	**Univariate analysis of depression risk factors** Alcohol (>9 drinks/week): RR=0.94 (95%CI 0.79, 1.13), p=0.51 Alcohol use did not predict depressed mood in these farmers
Ruggles et al. (2017) United States Veterans Aging Cohort Study	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: 6 years (but OR based on survey 1 year prior)	N=5,479 Veterans with or without HIV, who reported having drank and smoked cigarettes at some point in their life. N=2,878 HIV positive Mean age 49.8±8.3 years 97% male N=2,601 HIV negative Mean age 51.4±9.0 years 95% male	**Unhealthy alcohol use** defined by score ≥4 on AUDIT-C **MDD** defined as score of ≥8 on PHQ-9	**Logistic regression analysis of unhealthy alcohol use on preceding survey and current depression** Healthy alcohol use: OR_{adj}=1.0 (Reference) Unhealthy alcohol use: OR_{adj1}=1.09, p=0.10 OR_{adj2}=1.09, p=0.08 OR_{adj3}=1.10, p=0.06 OR_{adj4}=1.10, p=0.13 Adjusting for: HIV status, number of years from enrolment, depression status at baseline, current alcohol use, smoking, and for stimulant use (1 only), marijuana use (2 only), opioid use (3 only) and heroin use (4 only).
Sui et al. (2009) United States Aerobics Center Longitudinal Study (ACLS)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:**	N=3,085 healthy women N=11,258 healthy men Aged 20–81 years (no mental/mood disorders at baseline, no cardiovascular disease, no cancer)	**Alcohol consumption** ≥5 drinks/week vs <5 drinks/week **Depressive symptoms** on the CES-D (≥16 considered to have depressive symptoms)	**OR (95% CI) for depressive symptoms in females** Alcohol consumption: <5 drinks/week: OR_{adj}=1.0 (Reference) ≥5 drinks/week: OR_{adj}=1.00 (0.75, 1.33) **OR (95% CI) for depressive symptoms in males** Alcohol consumption:

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	Moderate risk of bias **Follow-up**: 12 years			<5 drinks/week: OR_{adj}=1.0 (Reference) ≥5 drinks/week: OR_{adj}=1.01 (0.87, 1.18) Adjusted for age, baseline examination year and survey response year.

CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CIDI = Composite International Diagnostic Interview; CPHE = Centre for Public Health Excellence; HIV = human immunodeficiency virus; HR = hazard ratio; MDD = major depressive disorder; OR = odds ratio; RR = relative risk;

Adolescents

Table 18 Depression outcomes from studies that reported on adolescents of both genders together

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Birkley et al. (2015) United States Youths sampled from urban, suburban, and rural school districts in the Southeast	**Level:** II **Quality:** CPHE 16/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up**: 1 year	N=800 fifth grader school students (average age 11 years) 328 African Americans (AA) 144 Hispanic Americans (HA) 328 European Americans (EA)	**Alcohol consumption** on the Drinking Styles Questionnaire. Children classified as either "drinker" or "non-drinker", depending on whether they had ever consumed ≥1 drink **Depressive symptoms** on the CES-D, scored from 0−60. Scores were used on a continuum to model the degree of depressive symptomatology	**Standardised and unstandardised coefficient for SEM path between drinker status (time 1) and depressive symptoms (time 1):** EA: Standardised β=0.08 Unstandardised *b*=0.20 AA: Standardised β=0.10 Unstandardised *b*=0.25 HA: Standardised β=0.07 Unstandardised *b*=0.14 **Standardised and unstandardised coefficient for SEM path between drinker status (time 1) and depressive symptoms (time 2):** EA: Standardised β=0.04 Unstandardised *b*=0.73 AA: Standardised β=0.11 Unstandardised *b*=2.16, p<0.05 HA: Standardised β=−0.08 Unstandardised *b*=−1.65 **Standardised and unstandardised coefficient for SEM path between drinker status (time 2) and depressive symptoms (time 2):** EA: Standardised β=0.20 Unstandardised *b*=1.14, p<0.01 AA: Standardised β=0.32 Unstandardised *b*=2.12, p<0.05 HA: Standardised β=0.07 Unstandardised *b*=0.44 **Bivariate correlation between drinking status and depressive symptoms**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				T1→T1 T1→T2 T2→T2 AA: phi=0.07 phi=0.12* phi=0.25*** HA: phi=0.02 phi=0.01 phi=0.16 EA: phi=0.13* phi=0.14* phi=0.21*** *p<0.05, ***p<0.001
Chan et al. (2013) Australia High school-based study of year 8 students at entry	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: Wave 2: 1 year Wave 3: 2 years	N=969 high school students from 12 metropolitan state and Catholic secondary schools in Victoria, who completed all three wave samples N=683 No HED N=203 HED Participants who dropped out of the study were more likely to have higher depressed mood (p<0.001) and report lifetime alcohol use (p<0.001)	**HED** was measured using the item "How many times have you had five or more alcoholic drinks one after the other?" from the CTCY survey and was scored as 0=none, 1=once in the last 2 weeks, 2=two times in the last 2 weeks, 3=three to five times in last 2 weeks, and 4=six or more times in the last 2 weeks. The results were dichotomised to a binary scale. <ins>HED</ins> was defined as ≥5 drinks/session at least once in the last 2 weeks **Depressed mood** was measured using the CES–D20 scale. The response was a 4-point Likert scale where 0=not at all, 1=some or a little, 2=occasionally, and 3=most or all the time. The total of the 20 items were subjected to square-root transformations to correct for skewness. Thresholds NR.	**Bivariate correlation between HED and depressed mood at each of the three waves.** Spearman's rank coefficient for HED at Wave 1 (year 8) and depression at: Wave 1 (age 13) rho=0.20, p<0.001 Wave 2 (age 14) rho=0.15, p<0.001 Wave 3 (age 15) rho=0.09, p<0.01 Spearman's rank coefficient for HED at Wave 2 (year 9) and depression at: Wave 2 (age 14) rho=0.21, p<0.001 Wave 3 (age 15) rho=0.08, p<0.05 Spearman's rank coefficient for HED at Wave 2 (year 9) and depression at: Wave 3 (age 15) rho=0.13, p<0.05
Cisler et al (2012) United States National Survey of Adolescents – Replication (NSA-R)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of	N=3,614 adolescents aged 12−17 years residing in the United States who participated in Wave 1 of the National Survey of Adolescents-Replication (NSA-R). Mean age at wave 1 14.6±2.7 years N=2,511 participated in Wave 2 N=1,653 participated in Wave 3	**HED frequency:** participants were asked "Considering all types of alcoholic beverages, how many times during the past 30 days did you have five or more drinks on an occasion? HED frequency was used as a continuous variable and log transformed to correct for skewness **Major depressive symptoms**	**Multiple linear regression analyses:** **predicting depression at wave 2 (mean age 15.9 years) from wave 1 HED** Original data (n=2,511) β=0.01, t=-0.01 Multiple imputation (n=3,614) β=0.01, t=0.13 **predicting depression at wave 3 (mean age 17.1 years) from wave 1 HED** Original data (n=1,653) β=−0.06, t=-2.47, p<0.05

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	bias **Follow-up**: 15.3±4.6 months between wave 1 and 2 14.4±2.7 months between wave 2 and 3 29.0±4.5 between wave 1 and 3		adolescents were asked 13 questions about the presence of DSM-IV symptoms of depression over the last 12 months.	Multiple imputation (n=3,614) β=−0.04, t=-2.41, p<0.05 Adjusted for ethnicity, sex, age, interpersonal violence, PTSD, delinquency, baseline depression.
Gustafson (2012) United States National Longitudinal Study of Adolescent to Adults Health (Add Health)	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 6 years between wave II and III and 6 years between wave III and IV	N=3,194/15,197 school students who participated in wave II (in 1996), III (in 2002) and IV (in 2008) of the Add Health study Mean age at T1 15.41±0.83 years 55% female 32% college attendance at T2 73% no HED at T1 48% no HED at T2 47% no HED at T3 Did not control for other substances	**HED**: defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) **Depressive symptoms:** 5 items of the CES-D scale recorded as a continuous average score ranging from 0-3.	**Effect of HED at Wave II on depressive symptoms at wave III and IV** **Pearson correlations for HED at T1 and:** depressive symptoms at T1: r=0.141, p<0.01 depressive symptoms at T2: *r*=0.069, p<0.01 depressive symptoms at T3: *r*=0.029
Hooshmand et al. (2012) Canada Students from eight high schools encompassing a school district in Ontario	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up:** 3 years	N=4,412 adolescents in starting in Grade 9, followed until Grade 12 (ages 14 – 17 years)	**Alcohol frequency** from 1 (never) to 8 (every day) used as a continuous variable **Alcohol amount per session** from 1 <1 drink) to 6 (over 10 drinks) used as a continuous variable **Depressive symptoms** on the CES-D (20 items on scale of 1 to 5) as a continuous variable	**Correlations between alcohol variables (G9) and depressive symptoms (G9, to G12)** Alcohol frequency (G9) – depression (G9): *r*=0.22, p<0.05 Alcohol amount (G9) – depression (G9): *r*=0.09, p<0.05 Alcohol frequency (G9) – depression (G10): *r*=0.11, p<0.05 Alcohol amount (G9) – depression (G10): *r*=0.10, p<0.05 Alcohol frequency (G9) – depression (G11): *r*=0.10, p<0.05 Alcohol amount (G9) – depression (G11): *r*=0.07, p<0.001

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			Alcohol frequency, amount and depressive symptoms all exhibited acceptable skewness and kurtosis and were analysed using maximum likelihood estimation.	Alcohol frequency (G9) – depression (G12): *r*=0.11, p<0.05 Alcohol amount (G9) – depression (G12): *r*=0.14, p<0.05 **Correlations between alcohol variables (G10) and depressive symptoms (G10 to G12)** Alcohol frequency (G10) – depression (G10): *r*=0.17, p<0.05 Alcohol amount (G10) – depression (G10): *r*=0.16, p<0.05 Alcohol frequency (G10) – depression (G11): *r*=0.11, p<0.05 Alcohol amount (G10) – depression (G11): *r*=0.12, p<0.05 Alcohol frequency (G10) – depression (G12): *r*= 0.10, p<0.05 Alcohol amount (G10) – depression (G12): *r*=0.11, p<0.05 **Correlations between alcohol variables (G11) and depressive symptoms (G11 to G12)** Alcohol frequency (G11) – depression (G11): *r*=0.11, p<0.05 Alcohol amount (G11) – depression (G11): *r*=0.11, p<0.05 Alcohol frequency (G11) – depression (G12): *r*=0.09, p<0.05 Alcohol amount (G11) – depression (G12): *r*=0.08, p<0.001 **Correlations between alcohol variables (G12) and depressive symptoms (G12)** Alcohol frequency (G12) – depression (G12): *r*=0.12, p<0.05 Alcohol amount (G12) – depression (G12): *r*=0.04 Depressive symptoms and alcohol use increased across adolescence. **Dual trajectory latent growth curve analysis** Alcohol frequency intercept–depression slope: β=−0.02, NS Alcohol frequency intercept–depression intercept: β=0.21, p<0.001 Alcohol amount intercept – depression slope: β=0.04, NS Alcohol amount intercept – depression intercept: β=0.15, p<0.01 Alcohol use and depressive symptoms intercepts highly correlated (i.e. cross sectional correlations), but alcohol use did not predict change in depressive symptoms. The failure hypothesis (health-risk behaviours influencing depression) was

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				not supported.
Mackie et al. (2011) United Kingdom London secondary school-based study	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 6 months Wave 3: 12 months Wave 4: 18 months	N=393 students met inclusion criteria N=61 low risk for substance abuse N=73 scored high for hopelessness N=89 scored high for anxiety sensitivity N=81 scored high for impulsivity N=89 scored high for sensation seeking Mean age 13 years, 9 months at W1 Slightly more boys (53.5%) than girls (47.5%) reported consuming alcohol at W1. Students who scored higher in H and IMP were more likely to be consuming alcohol and HED at T1.	**Alcohol Use** was assessed using a quantity by frequency (Q×F) composite score as a continuous variable. Quantity was assessed by asking participants how many alcoholic drinks they would consume on a typical day in which they drank (none to ≥10). Frequency was assessed by asking participants how often they have an alcoholic drink (never to almost daily). HED was assessed by asking participants whether they had consumed ≥5 (for males) or ≥4 (for girls) drinks on one occasion in the past 6 months. The Q×F measure demonstrated a positive skew as some participants reported little or no alcohol use, so a natural log transformation was used for analyses. **Depression** was assessed using the Brief Symptom Inventory (BSI). Depressive symptoms were assessed by six items (i.e. feeling lonely, sad, worthless, hopeless about the future, having no interest in things, and thoughts of ending your life). Participants were asked to rate the frequency of each item occurrence on a five-point scale (not at all, a little bit, moderately, quite a bit, often) in the previous 6 months. A 6-month time frame was used instead of the standard 7 days to fit in with the	**Bivariate Correlations of Q×F Alcohol Use with Depression** Wave 1 Q×F: depression at: W1 r=0.20, p<0.001 W2 r=0.13, p<0.05 W3 r=0.08 W4 r=0.11 Wave 2 Q×F: depression at W2 r=0.12, p<0.05 W3 r=0.07 W4 r=0.12 Wave 3 Q×F: depression at W3 r=0.14, p<0.05 W4 r=0.18, p<0.05 Wave 4 Q×F: depression at W4 r=0.28, p<0.001 Q×F and depression were moderately correlated **Parameter Estimates for Unconditional Linear Growth Models** Q×F: Intercept β=0.42, p<0.01 Slope β=0.02, p<0.05 Intercept-Slope covariance β=−0.001 Depression: Intercept β=14.60, p<0.01 Slope β=−0.23 Intercept-Slope covariance β=-6.91, p<0.01 Q×F significantly increased over time Depression revealed a nonsignificant decrease over time **SEM regression analysis of causal relationship between alcohol use and depression** High initial levels in Q×F alcohol use did not predict change in depression: Q×F intercept-depression slope β=0.03, p=0.45

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			6-month follow-up periods.	
Mason et al. (2008) United States Project Family (some families in Preparing for the Drug Free Years)	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years and 6 years	N=429 adolescents followed up for 2 years (from 10th grade to 12th grade), including intervention arm participants in Project Family. Alcohol assessment at Wave 5 (age 16 years) and Wave 6 (age 18 years) Mean alcohol consumption at: Age 16 was 1.46 drinks/month Age 18 was 2.33 drinks/month N=71 participated in HED at age 16 N=126 participated in HED at age 18 MDD assessed at Wave 7 (age 22 years) N=24 met criteria for MDD	**Alcohol consumption:** based on question about how many times they had consumed beer, wine, wine coolers or distilled spirits in past month. Responses on a 5-point scale (1): "I don't drink alcohol" to (5): "more than 6 drinks". **HED:** by question about "In the past month, how many times have you had three or more drinks (beer, wine or other liquor) in a row?" Drinking quantity frequency and HED frequency were categorical variables **Depressed mood** on the 8-item Child Behaviour Checklist-Youth Self-Report. Depressed-mood scales were computed as the average response to all items. **MDD** on the Diagnostic Interview Schedule with reference to DSM-IV criteria. MDD was a dichotomous variable that was coded 1 for those who met criteria in the past year and 0 for those who did not.	**SEM correlations between alcohol variables (age 16) and depressive symptoms (age 16)** Alcohol quantity: β=0.11, p<0.05 Alcohol frequency: β=0.19, p<0.01 HED: β=0.11 **SEM correlations between alcohol variables (age 16) and depressive symptoms (age 18)** Alcohol quantity: β=0.10 Alcohol frequency: β=0.22, p<0.001 HED: β=0.14, p<0.05 **SEM correlations between alcohol variables (age 16) and MDD (age 22)** Alcohol quantity: β=0.21, p<0.01 Alcohol frequency: β=0.08 HED: β=0.13, p<0.05
Mason & Spoth. (2011) United States Project Family	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years	N=151/208 control participants from Project Family N=208 Wave 1: age 11 years N=151 Wave 5: age 16 years N=157 Wave 6: age 18 years Alcohol assessment at Wave 5 (age 16 years) and Wave 6 (age 18 years)	**Alcohol consumption:** based on (1) the number of times they had consumed beer, wine, wine coolers, or other liquor within the past month; (2) the quantity of alcohol usually consumed each time on a scale ranging from 0:"I don't drink alcohol" to 5: "More than 6 drinks." Responses to these two items were standardized and summed to compute a quantity-	**SEM correlations between alcohol variables (age 16) and depressive symptoms (age 16)** Alcohol quantity-frequency: β=0.24, p<0.05 HED: β=0.20, p<0.05 Drunkenness: β=0.11 **SEM correlations between alcohol variables (age 16) and depressive symptoms (age 18)** Alcohol quantity-frequency: β=0.27, p<0.05 HED: β=0.27, p<0.05

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	and 6 years		frequency index. **HED:** by question about "In the past month, how many times have you had three or more drinks (beer, wine or other liquor) in a row?" To normalize the distribution, responses were categorized into (0) = "0", (1) = "1," and (2) = "2 or more." **Drunkenness** by how many times in the past month they had been drunk from drinking beer, wine, wine coolers or other liquor. Responses were categorized into (0) = "0", (1) = "1," and (2) = "2 or more." **Depressive symptoms** was measured with 8 self-reported items on the Child Behaviour Checklist-Youth Self-Report that were averaged to compute an overall scale	Drunkenness: β=0.28, p<0.05 **SEM correlations between alcohol variables (age 16) and depressive symptoms (age 18)** Alcohol quantity-frequency: β=0.06 HED: β=0.05 Drunkenness: β=0.20, p<0.05
McCarty et al. (2012) United States Developmental Pathways Project	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 3 years (yearly follow-up)	N=512 6th graders from 4 Seattle-area public schools. 48% female Mean age 12.0 years (range 11.0−13.6)	**Alcohol consumption:** based on the Customary Drinking and Drug Use Record Given the limited amount and variability of alcohol use defines as "more than just a sip or taste," a binary variable was created to indicate whether adolescents reported any use of alcohol within the past 6-months. **Depressive symptoms** based on the depression module of the Diagnostic Interview Schedule for Children (DISC). Depressive symptoms endorsed as occurring within the past year were summed to form depressive symptom counts, which ranged from 0 to 22,	**SEM cross-lagged path inter-correlations** Alcohol (6th grade) and Depressive symptoms (6th grade): β=0.23, p<0.01 Alcohol (6th grade) and Depressive symptoms (7th grade): β=0.13, p<0.01 Alcohol (6th grade) and Depressive symptoms (8th grade): β=0.16, p<0.01 Alcohol (6th grade) and Depressive symptoms (9th grade): β=0.17, p<0.01 Alcohol (7th grade) and Depressive symptoms (7th grade): β=0.19, p<0.01 Alcohol (7th grade) and Depressive symptoms (8th grade): β=0.08 Alcohol (7th grade) and Depressive symptoms (9th grade):

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				β=0.02 Alcohol (8th grade) and Depressive symptoms (8th grade): β=0.18, p<0.01 Alcohol (8th grade) and Depressive symptoms (9th grade): β=0.17, p<0.01 Alcohol (9th grade) and Depressive symptoms (9th grade): β=0.15, p<0.01
Needham (2007) United States National Longitudinal Study of Adolescent Health (Add Health)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up:** 1 year between wave I and wave II, and 6 years between wave II and wave III	N=10,828 school students who responded to wave I (1995), wave II (1996) and wave III (2001-2002) and had valid sampling weights. Mean age at wave 1 15.28±1.61 years N=5,728 females N=5,100 males Did not control for other factors	**HED:** defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) **Depressive symptoms:** were assessed by summing 9 items on the CES-D scale	In general, there was a decline in depressive symptoms in transition from adolescence to young adulthood (mean of slope: B=−0.20, p<0.001) The intercept of HED predicts rate of change in depressive symptoms. Those who drank more heavily at wave I, had a faster rate of decline in symptoms of depression across the transition to adulthood.
Parrish et al. (2016) United States California Families Project	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years	N=620 Mexican-origin youth living in California, age 14 at baseline 50% female 16% of participants at age 14 had tried alcohol at least once in the last 3 months. Mean=1.12±0.34, range 1.00–3.67 23% of participants at age 16 had tried alcohol at least once in the last 3 months. Mean=1.19±0.45, range 1.00–	**Frequency of alcohol use:** how many times in past 3 months they had used or tried (more than just a few sips) beer, wine or wine coolers, or liquor using a 5-point scale (1="Never"; 5="Almost every day or every day"). Frequency of alcohol use was computed as a continuous variable by taking the mean of the three drink types **Depressive symptoms** using the 8-item Anhedonic Depression subscale of the Mini-Mood and Anxiety Symptom Questionnaire.	**SEM cross-lagged latent variable regression models.** **Standardised estimates of structural coefficients in bivariate models:** Frequency of alcohol use (age 14) and Depressive symptoms (age 16): Unadjusted β=0.05, p<0.05 Adjusted β=0.04 Adjusted for gender and generational status and delinquency

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		4.00	Participants rated how much they "felt or experienced" each symptom "during the past week" using a 5-point scale at age 14 and a 4-point scale at age 16 (continuous variable).	
Patwardhan et al. (2017) Finland Population-based Northern Finland Birth Cohort 1986 (NFBC1986) study on health and well-being participants	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: prenatal, aged 8 years, aged 16 years, up to 28 years	N=6.963 adolescent participants Depression diagnosis rates in females are approximately twice as high as in males	**Alcohol use** at age 16 years was a continuous variable based on three items from adolescent self-report survey referring to the frequency (How many times during the past 12 months have you had at least one drink of alcohol?), intensity (How many times in the past 12 months have you been drunk?), and HED in the past 30 days measured on the 7-point scale (α=0.91). **Depression diagnosis** was obtained from the Finnish Hospital Discharge Register data that contains official medical records of diseases and related health problems through to approximately age 28 years. Depression diagnoses for every participant were dichotomized to indicate the presence or absence of depression diagnosis.	**Correlation between alcohol use at age 16 years and a diagnosis of depression up to age 28 years** rho=0.072, $p<0.001$ **SEM β coefficient (standardised) in the final fully saturated model of the full path analysis sample (N=6,963) for alcohol use leading to depression** β=0.10 (95% CI 0.05, 0.15), $p<0.001$
Pesola et al. (2015) United Kingdom Population-based birth cohort from Avon Longitudinal Study of Parents and Children	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of	N=5,126 adolescents aged 16 years who returned the questionnaires N=4,863 adolescents with complete information on the outcome measures were included in the analysis 60% female	**Harmful drinking** was measured at age 14 years using the adolescent version of the Semi-Structured Assessment for the Genetics of Alcoholism. Four items were used to estimate a harmful drinking measure: (1) frequency of drinking without parents' permission; (2) frequency of having a whole drink; (3) largest	**Spearman correlations for scales' scores for cases with complete information (n=1,883)** Drinking age 14 years – depressed mood age 14 years: rho=0.13, $p<0.05$ Drinking age 14 years – depressed mood age 16 years: rho=0.33, $p<0.001$ **SEM coefficient β (95% CI) for harmful drinking at the age of 14 years predicting depressed mood 2 years later**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
(ALSPAC) using waves from ages 13 to 16 years	bias **Follow-up from baseline**: annually, main analysis from ages 14 to 16 years	Young people who returned their questionnaires were more likely to be female, from a family with higher social class and have a higher education level. Adolescents who were less likely to return the questionnaires were more likely to be smokers and to report an onset of alcohol use before the age of 13 years.	number of whole drinks within a 24-hour period; and (4) whether the adolescent had ever been drunk (α=0.78). <u>Harmful drinking</u> thresholds NR. Descriptive statistics were calculated by summing the questionnaire items for complete cases. **Depressed mood** was measured using the Short Mood and Feelings Questionnaire. The questionnaire comprises 13 items (α=0.91 at age 16). Thresholds NR. Descriptive statistics were calculated by summing the questionnaire items.	Total effect: Step 0 β=0.092 (0.05, 0.13), p<0.001 Step 1 β=0.079 (0.04, 0.12), p<0.05 Step 4 β=−0.026 (−0.07, 0.01) Indirect effect: Step 0 β=0.087 (0.07, 0.12), p<0.05 Step 1 β=0.087 (0.06, 0.11), p<0.05 Step 4 β=0.039 (0.02, 0.06), p<0.05 Direct effect: Step 0 β=−0.005 (−0.05, 0.04) Step 1 β=−0.008 (−0.06, 0.11) Step 4 β=−0.065 (−0.11, −0.02), p<0.05 Indirect/direct ratio: step 0=95%, step 1=91%, step 4=38% Step 0: unadjusted for covariates. Step 1: adjusted for background covariates (financial difficulties, family education level, parents' alcohol consumption, and parents' depression). Step 4: adjusted for background covariates, conduct problems scale, deviant peers at age 13 years and depressed mood at age 14 years.
Scholes-Balog et al. (2015) Australia School-based study of early, mid-, and late adolescents (IYDS)	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 3 years Wave 3: 5 years	N=927 Victorian students who were involved in the IYDS N=916 Grade 6 Males mean alcohol frequency: 3.22±11.86 Females mean alcohol frequency: 1.68±4.73 N=804 Grade 9 Males mean alcohol frequency: 3.25±2.18 Females mean alcohol frequency: 3.32±2.22 N=791 grade 11 Males mean alcohol frequency: 4.65±2.44	**Alcohol use** was measured by asking on how many occasions in the past year participants had more than a few sips of alcohol. Response options were scored on an 8-point scale ranging from never (1) to 40+ times (8). <u>Mean frequency of alcohol use</u>: (having more than a few sips of alcohol in the past year) **Depressive symptoms** were measured using the SMFQ, which consists of 13 items rated on a 3-point scale based on occurrence within the past 30 days. Summed scores range from 0 to 26, with higher scores indicating higher levels of depressive	**SEM cross-lagged path coefficients (β) for alcohol use leading to depressive symptoms** Alcohol use Grade 6, Depression at Grade 6: β=0.015 Alcohol use Grade 6, Depression at Grade 9: β=−0.051 Alcohol use Grade 9, Depression at Grade 9: β=0.143, p<0.001 Alcohol use Grade 9, Depression at Grade 11: β=−0.035 Alcohol use Grade 11, Depression at Grade 11: β=0.049

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		Females mean alcohol frequency: 4.36±2.26.	symptoms	
Skogen et al. (2016) Norway A birth-cohort from the Norwegian Longitudinal Health Behaviour Study (NLHB) for adolescents aged 13 years in 1990	**Level:** II **Quality:** CPHE 20/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 1 year Wave 3: 2 years Wave 4: 3 years Wave 5: 5 years	N=1,102 adolescents, aged 13 years, were available for analysis of drinking frequency N=1,095 were available for analysis of drinking to intoxication	**Alcohol consumption measures** were available at ages 13–16 and 18 years and were based on the questions, 'How often do you drink?' and 'How often have you been drunk the last 6 months?' **Frequency of alcohol consumption** categories were based on the highest frequency of 'Every week': Stable low: stable less than weekly alcohol consumption between ages 13 and 18 years Early onset high: weekly alcohol consumption at age 13−14 years Early onset low: less than weekly alcohol consumption at age 13−14 years **Drinking to intoxication** categories were based on a binary variable indicating 'No time' versus '≥1 times': Late onset: no drinking to intoxication prior to age 18 years Early onset: drank to intoxication at age 13−14 years Early onset stable: started drinking to intoxication at age 13−14 years and continues to do so at age 18 years **Symptoms of depression** were assessed using a 7-item depression inventory and all responses were rated on a 6-point scale. The mean depression score was	**Linear regression coefficients (95% CI) for the association between symptoms of depression at ages 15−18 years and different alcohol consumption trajectories from age 13 years:** Age 15: Stable low — Reference Early onset high — β=0.40 (0.16, 0.65), p<0.05 Early onset low — β=0.15 (−0.09, 0.39) Late onset — β=0.14 (−0.12, 0.41) Age 16: Stable low — Reference Early onset high — β=0.35 (0.10, 0.61), p<0.05 Early onset low — β=0.09 (−0.16, 0.33) Late onset — β=0.16 (−0.12, 0.44) Age 18: Stable low — Reference Early onset high — β=0.37 (0.13, 0.61), p<0.05 Early onset low — β=0.24 (0.02, 0.47), p<0.05 Late onset — β=0.11 (−0.16, 0.38) **Linear regression coefficients (95% CI) for the association between symptoms of depression at ages 15−18 years and drinking to intoxication trajectories from age 13 years:** Age 15: Late onset — Reference Intermediate onset — β=0.04 (−0.11, 0.19) Early onset — β=0.30 (0.11, 0.49), p<0.05 Early onset stable — β=0.29 (−0.12, 0.69) Age 16: Late onset — Reference Intermediate onset — β=0.10 (−0.07, 0.26) Early onset — β=0.16 (−0.06, 0.37) Early onset stable — β=0.56 (0.11, 1.01), p<0.05 Age 18: Late onset — Reference Intermediate onset — β=0.08 (−0.08, 0.24) Early onset — β=0.27 (0.06, 0.48), p<0.05

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			standardised [mean: 0, SD: 1] at each wave and the alcohol class membership variables were employed as categorical indicators in multiple linear regression analyses	Early onset stable β=0.23 (−0.22, 0.68) Regression coefficients were adjusted for gender and were estimated as difference in standard deviations from reference group. For the alcohol consumption measure, increased symptom levels of depression was reported at all time-points in the 'early onset high' trajectory compared with the 'stable low' (β=0.35–0.40), while the 'early onset low' trajectory reported increased levels of depression at age 18 years (β=0.24). For the drinking to intoxication measure, the 'early onset' trajectory reported increased symptom levels of depression at ages 15 and 18 years compared with the 'late onset' trajectory (β=0.27–0.30), while the 'early onset stable' trajectory reported increased levels of depression at age 16 years (β=0.56).

CES-D = Center for Epidemiological Studies Depression Scale; CPHE = Centre for Public Health Excellence; CTCY = The Communities That Care Youth; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; MDD = major depressive disorder; NR = not reported; NS = not significant; PTSD = post-traumatic stress disorder; SD = standard deviation; SEM = structural equation models; SMFQ = Short Mood and Feelings Questionnaire

Table 19 Depression outcomes from studies that reported on male and/or female adolescents separately

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Danzo et al. (2017) United States 6th grade student from three urban public middle schools	**Level:** II **Quality:** CPHE 28/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 3 years	N=593 families (unclear if 593 participants), where a child was 6th grade at baseline, from 3 urban middle schools. N=593 6th grade youths were included in this study 49% male (~291 females) 51% male (~302 males) Mean age of child 11 years 10 months in Wave 1	**Alcohol use:** was based on survey about their substance use and included the question "How many alcoholic drinks did you have last month?" (continuous variable) **Depressive symptoms:** 14-item self-report measures assessing depressive symptoms including sad, moody, or hopeless, and trouble sleeping. Participants rated the frequency of each symptom in the past month on a 5-point	**Bivariate Pearson correlations for females** Alcohol use 6th grade Depression 6th grade: r=0.34, p<0.05 Alcohol use 6th grade Depression 7th grade: r=0.13, p<0.05 Alcohol use 6th grade-Depression 8th grade: r=0.20, p<0.05 Alcohol use 6th grade-Depression 9th grade: r=0.07 Alcohol use 7th grade-Depression 7th grade: r=0.29. p<0.05 Alcohol use 7th grade-Depression 8th grade: r=0.30. p<0.05 Alcohol use 7th grade-Depression 9th grade: r=0.19, p<0.05 Alcohol use 8th grade-Depression 8th grade: r=0.38. p<0.05 Alcohol use 8th grade-Depression 9th grade: r=0.30. p<0.05

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
			scale ranging from "never or almost never" to "always or almost always". For analyses, the average across items was used.	Alcohol use 9th grade-Depression 9th grade: r=0.33. p<0.05 **Bivariate Pearson correlations for males** Alcohol 6th grade Depression 6th grade: r=0.10 Alcohol 6th grade Depression 7th grade: r=0.02 Alcohol 6th grade-Depression 8th grade: r=0.02 Alcohol 6th grade-Depression 9th grade: r=−0.04 Alcohol 7th grade-Depression 7th grade: r=0.12 Alcohol 7th grade-Depression 8th grade: r=0.17. p<0.05 Alcohol 7th grade-Depression 9th grade: r=0.00 Alcohol 8th grade-Depression 8th grade: r=0.28. p<0.05 Alcohol 8th grade-Depression 9th grade: r=0.12 Alcohol 9th grade-Depression 9th grade: r=0.09 **SEM cross-lagged path models examining direct effects of alcohol use on depressive symptoms for females:** Past-year alcohol use predicted elevated depressive symptoms: Alcohol use 6th grade Depression 7th grade: β=0.16, p<0.05 Alcohol use 7th grade-Depression 8th grade: β=0.14. p<0.05 **SEM cross-lagged path models examining indirect effects of alcohol use on depressive symptoms for females:** Alcohol use 6th grade Depression 9th grade (mediated by 7th grade alcohol use and 8th grade depression): β=0.08, SE-0.03, p<0.05. **SEM cross-lagged path models examining direct and indirect effects of alcohol use on depressive symptoms for males:** No cross-domain influence of alcohol use on depressive symptoms (or vice versa)
Edwards et al. (2014) United Kingdom Population-based	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of	N=7,100 adolescents, aged 13−15 years, has data on frequency of alcohol use available N=3,630 females N=3,470 males	**Alcohol use:** participants attended clinics and answered questions related to their alcohol use via computerized questionnaires. Participants' reports of drinking	**Logistic regression OR (95% CI) for the impact of medium and high alcohol drinking on depression compared with low alcohol drinking for females** Low alcohol use: OR=1.00 (Reference) Medium alcohol use OR=1.70 (1.14, 2.53), p<0.05

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Avon Longitudinal Study of Parents and Children (ALSPAC), during adolescence	bias **External validity:** Moderate risk of bias **Follow-up from baseline**: Median 2 years and 5 months	N=2,105 low drinking frequency N=1,114 medium drinking frequency N=411 high drinking frequency N=4,292 adolescents has data on depression and anxiety at age 18 years N=2,414 females	frequency was classified into three categories (none, occasional, or weekly use). This measure (assessed at three ages) was subjected to longitudinal latent class analysis to capture drinking frequency over time (ages 13–15), yielding three categories (low, medium, and high). **Depression-dependent variables:** the Clinical Interview Schedule–Revised (CIS-R) was self-administered via computer. Last-month mild, moderate, and severe depressive episodes were assessed and Individuals who met ICD criteria for a depressive episode were coded 1, otherwise they were coded 0.	OR_{adj}=1.63 (1.04, 2.55), p<0.05 High alcohol use OR=2.37 (1.42, 3.93), p<0.05 OR_{adj}=1.93 (1.08, 3.44), p<0.05 Males OR_{adj}: adjusted for crowding (persons/room), maternal education, maternal depression factor score Females OR_{adj}: adjusted for housing tenure (mortgaged/owned/ rented/subsidised rental), conduct problems at age 11, maternal depression factor score **Logistic regression OR (95% CI) for the impact of medium and high alcohol drinking on depression compared with low alcohol drinking for males** Low alcohol use: OR=1.00 (Reference) Medium alcohol use OR=1.74 (0.91, 3.36) OR_{adj}=2.25 (1.09, 4.66), p<0.05 High alcohol use OR=2.16 (0.92, 5.08) OR_{adj}=2.54 (1.06, 6.10), p<0.05 Males OR_{adj}: adjusted for crowding (persons/room), maternal education, maternal depression factor score Females OR_{adj}: adjusted for housing tenure (mortgaged/owned/ rented/subsidised rental), conduct problems at age 11, maternal depression factor score
Fleming (2008) United States Raising Healthy Children project	**Level:** II **Quality:** CPHE 20/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: yearly for 3 years	N=885 students from public schools in Pacific Northwest of U.S. (grade 8 at baseline) Mean age 12.94 years (range 12−14) at baseline N=412 girls N=473 boys 59% girls and 68% boys did not drink alcohol in the past year 16% girls and 11% boys drank alcohol in past year but not in the past month	**Alcohol frequency**: based on previous year consumption; 0=no use; 1=some use in past year but none in past month; 2=once or twice in past month; 3=3-5 times in past month; 4=6-19 times in past month, and 5=20 or more times in past month. **Depressive symptoms** on the shortened version of the Seattle Personality Questionnaire (SPQ) included 6 questions that were answered YES!, yes, no, and NO! The mean of the six items was obtained to	**Latent growth curve analysis correlations between alcohol and depressive symptoms for females** Alcohol grade 8-Depressive symptoms grade 8: β=0.26 Alcohol grade 8-Depressive symptoms grade 9: β=0.21 Alcohol grade 8-Depressive symptoms grade 10: β=0.16 Alcohol grade 8-Depressive symptoms grade 11: β=0.23 Alcohol grade 9-Depressive symptoms grade 9: β=0.27 Alcohol grade 9-Depressive symptoms grade 10: β=0.22 Alcohol grade 9-Depressive symptoms grade 11: β=0.18 Alcohol grade 10-Depressive symptoms grade 10: β=0.23 Alcohol grade 10-Depressive symptoms grade 11: β=0.22

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
		17% girls and 12% boys drank alcohol 1−2 times in the past month 4% girls and 4% boys drank alcohol 3−5 times in the past month 3% girls and 4% boys drank alcohol 6−19 times in the past month 1% girls and 1% boys drank alcohol ≥20 times in the past month	create a scale with a range from 0 to 3.	Alcohol grade 11-Depressive symptoms grade 11: β=0.14 **Latent growth curve analysis correlations between alcohol and depressive symptoms for males** Alcohol grade 8-Depressive symptoms grade 8: β=0.10 Alcohol grade 8-Depressive symptoms grade 9: β=0.13 Alcohol grade 8-Depressive symptoms grade 10: β=0.06 Alcohol grade 8-Depressive symptoms grade 11: β=0.05 Alcohol grade 9-Depressive symptoms grade 9: β=0.16 Alcohol grade 9-Depressive symptoms grade 10: β=0.06 Alcohol grade 9-Depressive symptoms grade 11: β=0.02 Alcohol grade 10-Depressive symptoms grade 10: β=0.08 Alcohol grade 10-Depressive symptoms grade 11: β=0.05 Alcohol grade 11-Depressive symptoms grade 11: β=0.05 Although caution should be exercised in comparing correlation coefficients across groups, most of the correlations are larger in magnitude for girls than for boys. **Dual-Process Growth Model Parameter Estimates** Level of depressive symptoms with level of substance use Girls: *B*=0.268 (SE=0.055), p<0.01, β=0.340 Boys: *B*=0.084 (SE 0.050), β=0.12
Needham (2007) United States National Longitudinal Study of Adolescent Health (Add Health)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 1 year between wave I and	N=10,828 school students who responded to wave I (1995), wave II (1996) and wave III (2001-2002) and had valid sampling weights. Mean age at wave 1 15.28±1.61 years N=5,728 females N=5,100 males	**HED**: defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) **Depressive symptoms:** were assessed by summing 9 items on the CES-D scale	**Unstandardised coefficients (SD) from dual latent growth models for females** Intercept(HED) → Slope (Depressive symptoms): *B*=−0.11 (0.01), p<0.001 **Unstandardised coefficients (SD) from dual latent growth models for males** Intercept(HED) → Slope (Depressive symptoms): *B*=−0.06 (0.03), p<0.05 The intercept of HED predicts rate of change in depressive

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
	wave II, and 6 years between wave II and wave III	Did not control for other factors		symptoms. Those who drank more heavily at wave I, had a faster rate of decline in symptoms of depression across the transition to adulthood.
Pesola et al. (2015 United Kingdom Population-based birth cohort from Avon Longitudinal Study of Parents and Children (ALSPAC) using waves from ages 13 to 16 years	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: annually, main analysis from ages 14 to 16 years	N=5,126 adolescents aged 16 years who returned the questionnaires N=4,963 adolescents with complete information on the outcome measures were included in the analysis N=2,918 females N=1,945 males Young people who returned their questionnaires were more likely to be female, from a family with higher social class and have a higher education level. Adolescents who were less likely to return the questionnaires were more likely to be smokers and to report an onset of alcohol use before the age of 13 years.	**Harmful drinking** was measured at age 14 years using the adolescent version of the Semi-Structured Assessment for the Genetics of Alcoholism. Four items were used to estimate a harmful drinking measure: (1) frequency of drinking without parents' permission; (2) frequency of having a whole drink; (3) largest number of whole drinks within a 24-hour period; and (4) whether the adolescent had ever been drunk (α=0.78). Harmful drinking thresholds NR. Descriptive statistics were calculated by summing the questionnaire items for complete cases. **Depressed mood** was measured using the Short Mood and Feelings Questionnaire. The questionnaire comprises 13 items (α=0.91 at age 16). Thresholds NR. Descriptive statistics were calculated by summing the questionnaire items.	**SEM coefficient β (95% CI) for harmful drinking at the age of 14 years predicting depressed mood 2 years later** Males: Total effect β=0.09 (0.03, 0.16) Indirect effect β=0.12 (0.07, 0.17) Direct effect β=−0.03 (−0.10, 0.05) Females: Total effect β=0.08 (0.03, 0.13) Indirect effect β=0.11 (0.08, 0.14) Direct effect β=−0.03 (−0.09, 0.03) Difference: Total effect β=−0.01 (−0.09, 0.07), p=0.8 Indirect effect β=−0.01 (−0.07, 0.05), p=0.8 Direct effect β=−0.002 (−0.10, 0.10), p=1.0
Powers et al. (2016) Australia Population-based Australian Longitudinal Study on	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:**	N=8,197 women randomly selected from the Medicare database, who completed the 1996 survey (aged 18−23 years) N=6,466 women completed all 3 surveys (1996, 2000 and 2009) In 1996: Retrospective HED frequency	**HED** was defined as ≥5 drinks on a single occasion for both men and women At the 2009 survey, women were asked to retrospectively recall their HED at each age between 16 and 21 by answering the question, 'How often did you have five or more drinks on one	**Logistic regression OR (95% CI) of depression in women aged 22−27 years according to level of HED at age 16−21 years for females** Never: OR=1.00 (Reference) Rarely OR=1.04 (0.84, 1.28) OR_{adj1}=1.02 (0.82, 1.26) OR_{adj2}=1.02 (0.82, 1.27) Monthly OR=0.99 (0.81, 1.22) OR_{adj1}=0.97 (0.78, 1.21)

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Women's Health (ALSWH) included women aged 18−23 years at entry	Low risk of bias **Follow-up from baseline**: Wave 2: 4 years Wave 3: 13 years	aged 16−21 years N=1,998 Never drank alcohol N=1,376 Rarely drank alcohol N=1,417 Drank alcohol monthly N=2,134 Drank alcohol weekly N= 1,272 Drank alcohol more often than weekly Women living in rural and remote areas of Australia were intentionally oversampled.	occasion.' Never answered 'never' Rarely answered 'less than once a month' Monthly answered 'about once a month' Weekly answered 'about once a week' >Weekly answered 'more than once a week' **Depression:** depressive symptoms were assessed using the MHI and CESD10: A MHI score of <53 was considered to be a valid indicator of depression A CESD10 cut point of ≥10 was used to indicate depression	OR_{adj2}=0.94 (0.75, 1.17) Weekly OR=0.99 (0.82, 1.20) OR_{adj1}=0.98 (0.81, 1.20) OR_{adj2}=0.93 (0.76, 1.14) >Weekly OR=1.70 (1.38, 2.08) OR_{adj1}=1.45 (1.17, 1.81) OR_{adj2}=1.30 (1.04, 1.63) **Logistic regression OR (95% CI) of depression in women aged 31−36 years according to level of HED at age 16−21 years** Never: OR=1.00 (Reference) Rarely OR=0.97 (0.79, 1.19) OR_{ad12}=0.97 (0.78, 1.20) OR_{adj2}=0.99 (0.80, 1.23) Monthly OR=0.91 (0.74, 1.12) OR_{adj1}=0.90 (0.73, 1.12) OR_{adj2}=0.92 (0.74, 1.15) Weekly OR=1.01 (0.84, 1.21) OR_{adj1}=1.01 (0.83, 1.22) OR_{adj2}=1.01 (0.83, 1.23) >Weekly OR=1.34 (1.09, 1.64) OR_{adj1}=1.25 (1.01, 1.54) OR_{adj2}=1.19 (0.96, 1.48) OR_{adj1}: adjusted for demographics (age group, urban, education, employment, monetary stress) OR_{adj2}: adjusted for demographics, relationships (relationship status and living with children) and experience of violence
Schuler et al. (2015) United States National Longitudinal Study of Adolescent to Adult Health (Add Health)	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 19 years	N=6,070 Individuals who provided substance use and depressive symptoms data during at least one wave of the Add Health study, aged 12-31. N=3,096 females (51%) N=2,974 males	**HED**: defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) Dichotomised into any/no regular HED. **Depressive symptoms:** during the past seven days were measured using the CES-D scale	**Multivariate time-varying effect modelling for HED associated with elevated depressive symptoms** (adjusting for daily smoking and marijuana use) Age-varying coefficients (95% CI) – from Fig. 4: Females: β~3.7 (2.1, 5.3) at age 12 years β~0.7 (0.3, 1.1) at age 17 years β~0.4 (0.0, 0.8) at age 18.5 years β~−0.9 (−1.6, −0.3) at age 31 years Males: β~2.1 (1.7, 4.4) at age 12 years β~0.3 (0.0, 0.3) at age 17 years

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
				β~0.0 (−0.3, 0.3) at age 18.5 years β~−0.4 (−0.9, 0.3) at age 31 years HED was associated with elevated depressive symptoms only during adolescence for both females (until age 18.5) and males (until age 17). Mean CES-D score: Females: 3.7 points higher than non-users (95%CI 2.1, 5.3) Males: 3.1 points higher than non-users (95%CI 1.7, 4.4)
Wilkinson et al. (2016) United States National Longitudinal Study of Adolescent to Adults Health (Add Health)	**Level:** II **Quality:** CPHE 31/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 13-14 years	N=12,107 participants from 2 large schools and 14 small schools who participated in the Add Health study (wave I, III and IV) N=6,521 females N=5,474 males	**HED**: defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) **Depressive symptoms:** nine items from the CES-D. Answers are scored from 0 to 3, indicating rarely to most of the time; the summed score ranges from 0 to 27	**Linear regression coefficient (SE) of relationship between HED frequency at an earlier wave and depressive symptoms at later wave** Females: β=0.01 (0.01) Males: β=−0.01 (0.01)
Wymbs et al. (2014) United States Developmental Pathways Project (DPP), same study as McCarty et al. (2012)	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up:** 4 years	N=512 6th graders from 4 Seattle-area public schools. This article uses data from 8th grade – 12th grade (age 14 at baseline). N=249 females N=272 males	**Alcohol consumption:** based on the Customary Drinking and Drug Use Record to assess frequency in past 6 months, from 0 (never used) to 7 (more than once per day) **Depressive symptoms** based on the Diagnostic Interview Schedule for Children (DISC)	**SEM inter-correlations for girls** Alcohol (8th grade)-Depression (8th grade): β=0.24, p<0.01 Alcohol (8th grade)-Depression (9th grade): β=0.10 Alcohol (8th grade)- Depression (12th grade): β=0.13 Alcohol (9th grade)- Depression (9th grade): β=0.04 Alcohol (9th grade)- Depression (12th grade): β=0.07 **SEM inter-correlations for boys** (n=272) Alcohol (8th grade)-Depression (8th grade): β=0.05 Alcohol (8th grade)- Depression (9th grade): β=0.10 Alcohol (8th grade)- Depression (12th grade): β=0.11 Alcohol (9th grade)- Depression (9th grade): β=0.16, p<0.05 Alcohol (9th grade)- Depression (12th grade): β=0.02

CES-D = Center for Epidemiological Studies Depression Scale; CESD10 = 10-item Center for Epidemiologic Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; ICD = International Classification of Diseases; MHI = Mental Health Index; NS = not significant; OR = odds ratio; SD = standard deviation; SEM = structural equation models

Table 20 Depression outcomes from studies that reported on young adults of both genders together

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Armeli et al. (2015) United States University of Connecticut college students	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: affect in subsequent month. Total follow-up 4 years.	N=522 Introductory Psychology students who had a mean 3.1±1.1 completed yearly assessments. 58% freshmen 33% sophomores Mean age 18.9±1.1 years 1,616 person-year reports were completed 91% completed while still an undergraduate 2.8% completed when in graduate school 6.2% completed when not a student.	**Alcohol consumption (baseline)**: participants reported their frequency of drinking occasions over the past 30 days on a 7-point scale (0=0, 1=1–2, 2=3–5, 3=6–9, 4=10–19, 5=20–39, 6=≥40), and the number of standard drinks they usually consumed per drinking occasion using a 10-point scale (0=no drinks, 1=1 drink, to 9=≥9 drinks). The frequency and quantity values were multiplied to create an overall drinking composite. **Depressive symptoms** based on daily survey on their current affect states (sad and/or dejected) on a 5-point scale (1=not at all to 5=extremely), averaged to get month-level scores.	**Multilevel linear regression predicting daily depressive symptoms (**unstandardized regression coefficient) Mean drinking level: *b*=0.001 (95%CI -0.003, 0.005), p=0.0.646, **Multilevel linear regression predicting daily anxiety symptoms (**unstandardized regression coefficient) Mean drinking level: *b*=0.00 (95%CI -0.005, 005), p=0.855 Adjusted for sex, age, and school status (undergraduate vs. graduate student or other).
Gustafson (2012) United States National Longitudinal Study of Adolescent to Adults Health (Add Health)	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 6 years between wave II and III and 6 years between wave III and IV	N=3,194/15,197 school students who participated in wave II (in 1996), III (in 2002) and IV (in 2008) of the Add Health study Mean age at wave II 15.41±0.83 years 55% female 32% college attendance at T2 73% no HED at T1 48% no HED at T2 47% no HED at T3 Did not control for other substances	**HED**: defined as how many days did you drink 5 or more drinks in a row: 0: none, 6: nearly every day (over the last 12 months) **Depressive symptoms:** 5 items of the CES-D scale recorded as a continuous average score ranging from 0-3.	**Pearson correlations for HED at T2 (age 21 years and:** depressive symptoms at T2: *r*=0.014 depressive symptoms at T3: *r*=−0.045, p<0.05 **Pearson correlations for HED at T3 (age 27 years) and:** depressive symptoms at T3: *r*=−0.004

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Mason et al. (2008) United States Project Family (some families in Preparing for the Drug Free Years)	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years and 6 years	N=429 adolescents followed up for 2 years (from 10th grade to 12th grade), including intervention arm participants in Project Family. Alcohol assessment at Wave 5 (age 16 years) and Wave 6 (age 18 years) Mean alcohol consumption at: Age 16 was 1.46 drinks/month Age 18 was 2.33 drinks/month N=71 participated in HED at age 16 N=126 participated in HED at age 18 MDD assessed at Wave 7 (age 22 years) N=24 met criteria for MDD	**Alcohol consumption:** based on question about how many times they had consumed beer, wine, wine coolers or distilled spirits in past month. Responses on a 5-point scale (1): "I don't drink alcohol" to (5): "more than 6 drinks". **HED:** by question about "In the past month, how many times have you had three or more drinks (beer, wine or other liquor) in a row?" Drinking quantity frequency and HED frequency were categorical variables **Depressed mood** on the 8-item Child Behaviour Checklist-Youth Self-Report. Depressed-mood scales were computed as the average response to all items. **MDD** on the Diagnostic Interview Schedule with reference to DSM-IV criteria. MDD was a dichotomous variable that was coded 1 for those who met criteria in the past year and 0 for those who did not.	**SEM correlations between alcohol variables (age 18) and depressive symptoms (age 18)** Alcohol quantity: β=0.10 Alcohol frequency: β =0.07 HED: β =0.05 **SEM correlations between alcohol variables (age 18) and MDD (age 22)** Alcohol quantity: β=0.06 Alcohol frequency: β=0.03 HED: β=0.00 **SEM correlations among first-order alcohol dimensions (age 16−18 years) and MDD (age 22 years)** Adolescent alcohol frequency: β=0.08 Adolescent alcohol quantity: β=0.19, $p<0.01$ Adolescent frequency of HED: β=0.10
Piasecki et al. (2017) United States Social and Emotional Contexts of Adolescent Smoking Patterns project	**Level:** II **Quality:** CPHE 21/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 1 year	N=986 young adults (aged 20.2 – 25.5 years) who participated in the Social and Emotional Contexts of Adolescent Smoking Patterns project Data from year 6 and year 7 were used in this study 60% female Mean age 22.4±0.8 years Mean HED frequency 2.58±2.15	**HED frequency** based on how many times in past 12 months, ≥5 drinks (males) or ≥4 drinks (females) were consumed in a 2-hour period. **Depressive symptoms** on the CES-D. A cut-off score of 16 was used to indicates the presence of clinically significant depressive symptomatology Descriptive analyses characterized mean levels of depression symptoms and HED frequency	**Bivariate correlation between HED frequency and depressive symptoms** HED age 22 – Depressive symptoms age 22 $r=-0.02$ HED age 22 – Depressive symptoms age 23 $r=-0.02$ HED age 23 – Depressive symptoms age 23 $r=0.01$ **Unstandardised (*B*) and standardized (β) SEM path coefficient from HED to depressive symptoms** HED age 22 – Depressive symptoms age 22 $B=-0.522$, β=−0.026, p=0.410 HED age 22 – Depressive symptoms age 23

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				B=−0.071, β=−0.016, p=0.559 HED age 23 – Depressive symptoms age 23 *B*=−0.112, β=−0.009, p=0.779
Sloan et al. (2011) United States National Longitudinal Study of Youth 1979 (NLSY79)	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up:** 25 years	N=7,386 young adults aged 17 – 25 (mean age 20.6 at baseline), from National Study in United States (low income oversampled) 1,221 Frequent HED 2,964 Occasional HED 3,201 Other drinkers and abstainers	**Alcohol consumption** based on how often they consumed ≥6 drinks/occasion in 30 days prior to interview (HED). **Frequent HED (FHED)**: ≥4 heavy drinking episodes (males) or ≥3 heavy drinking episodes (females) **Occasional HED (OHED)**: ≥6 drinks on 1-3 occasions (males) or ≥6 drinks on 1-2 occasions (females) **Other drinkers and abstainers (ODA)**: those who did not consume ≥6 drinks in one occasion in past 30 days. Drinking categories based on mean values of drinking reported in 1982-1984 interviews **Depressive symptoms** on CES-D. Scores can range from 0 to 69 (in this sample, range was 0 to 59)	**Propensity score matching of FHEDs and OHEDs (n=2,246 matched observations)** **Depressive symptoms at age 40**: Mean CES-D score for FHED: 34.3; OBD: 30.6 Difference in CES-D score: 3.7 (95%CI 0.41, 7.1) **Propensity score matching of FHEDs and ODAs (n=1,492 matched observations)** **Depressive symptoms at age 40**: Mean CES-D score for FHED: 34.9; ODA: 35.9 Difference in CES-D score: −1.0 (95%CI -5.3, 3.4) Individuals were matched on other substance use (tobacco and illicit drugs), baseline health, educational attainment, ability and labour force status, individual motivation and long-term expectations, educational aspirations, household income, religious services attendance and rural/urban setting, as well as gender, race/ethnicity and marital status.

CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; MDD = major depressive disorder; SEM = structural equation models

Table 21 Depression outcomes from studies that reported on young men and/or women separately

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Grazioli et al. (2018) Switzerland Army-based	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of	N=4,617 men, aged 19−20 years, who completed both waves of C-SURF and were not abstainers at baseline (mean age =19.95±1.19 years	**Total drinks per week** over the past 12 months were computed by multiplying the number of drinking days by the number of drinks per drinking day. Average number of drinking days and the	**Bivariate (Spearman rank-order) correlations between alcohol consumption at baseline and depressive symptoms at 15 months** Total drinks /week: Alcohol age 20, depr age 20 rho=0.08, p<0.001

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Cohort Study on Substance Use Risk Factors (C-SURF)	bias **External validity:** High risk of bias **Follow-up from baseline**: 15 months		number of standard drinks (a standard drink =10 g of ethanol) consumed per drinking day over the past 12 months were measured at baseline and at follow-up. **HED** was defined as consuming 60 g or more of pure alcohol quickly on a single, discrete occasion. Participants were asked to indicate how often they drank six or more alcoholic beverages (> 60 g of pure alcohol) on one occasion in the past 12 months with a Likert scale ranging from 0=never, to 5=every day or almost every day. Answers were dichotomized to yield a report of monthly HED frequency, where 0=reporting less than 1 HED session per month and, 1=reporting one or more HED sessions per month. **Depressive symptoms** measured on the Major Depression Inventory (MDI), a 10-item scale covering ICD-10 symptoms of depression. Participants asked how often they had been feeling each symptom in past 2 weeks (0=no time at all; 5=all the time).	Alcohol age 20, depr age 21 rho=0.03, p<0.05 Alcohol age 21, depr age 21 rho=0.06, p<0.001 <u>HED</u> Alcohol age 20, depr age 20 rho=0.07, p<0.001 Alcohol age 20, depr age 21 rho=0.03 Alcohol age 21, depr age 21 rho=0.04, p<0.05 **SEM path coefficients for full model:** Baseline alcohol use – follow-up depressive symptoms Total drinks /week: β=−0.100 [−0.145, −0.053] HED: β=−0.144 [−0.224, −0.065] Adjusted for demographic covariates on mediators and the main outcome (suicide attempt)
Mushquash et al. (2013) Canada Undergraduate women attending Dalhousie University	**Level:** II **Quality:** CPHE 19/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias	N=200 women who attended Dalhousie University Mean age 19.86±3.02 years	**HED frequency**: Participants were asked the: "During the past 7 days, how often did you have 4 or more drinks containing any kind of alcohol, within a 2 hour period?" Participants responded to this item on a 12-point scale from "0 times" to "10 or more times." **HED severity**: Participants were asked the open-ended question "What is the	**SEM cross-lagged path coefficients for HED leading to depressive symptoms within 1 week** Wave 1 HED → Wave 2 depressive symptoms: β=0.05 *B*=0.18 Wave 2 HED → Wave 3 depressive symptoms: β=0.02 *B*=0.07 Wave 3 HED → Wave 4 depressive symptoms: β=0.02 *B*=0.07

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
	Follow-up from baseline: Wave 2: 1 week Wave 3: 2 weeks Wave 4: 3 weeks		greatest number of drinks you consumed in a 2 hour period during the past 7 days?" All values less than 4 drinks in 2 hours (the standard definition of HED) were recorded as 0. 1 alcoholic drink was defined as a 355 ml can, glass or bottle of beer or cooler, a 150 ml glass of wine, or a drink containing 1 shot of liquor or spirits. **Depressive symptoms** were measured with short forms of the Profile of Mood States depression subscale (POMS-D-SF), Depression Adjective Checklist (DACL-SF), and Center for Epidemiological Studies Depression Scale (CES-D-SF). The 4-item POMS-D-SF and the 4-item DACL-SF were answered using a 5-point scale from 0 (not at all) to 4 (extremely). The 10-item CES-D-SF included items (e.g., "I felt lonely") on a 4-point scale from 1 (rarely) to 4 (most or all of the time).	Cross-lagged paths from HED to depressive symptoms were not significant. Therefore, HED does not influence future depressive symptoms over a 1 week period.
Zhang et al. (2018) Germany Dresden Predictor Study	**Level:** II **Quality:** CPHE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 17 months	N=1,196 women, aged 18−25 years, who completed both surveys and interviews Mean age = 21.03±1.73 years; 37.2% low SES; 64% middle SES; 8.5% high SES **N=1,118 no MDD at follow-up** Smoker=22% **N=78 with incident MDD at follow-up** Smoker=33%	**Alcohol consumption** based on Swiss Health survey (Frick et al 1996). Answers to 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. Low risk drinking ≤20g alcohol/day; medium-risk drinking 20 – 40g alcohol/day' high-risk drinking >40g alcohol/day **MDD** based on Diagnostic Interview for Mental Disorders – Research version	**Logistic regression OR (95%CI) of incident MDD in young women according to alcohol consumption level** Low risk: OR=1.0 (Reference) OR_{adj}=1.0 (Reference) Medium risk: OR=1.80 (0.69, 4.71) OR_{adj}=1.50 (0.56, 4.05) High risk: OR=3.66 (1.02, 13.18), p<0.05 OR_{adj}=1.73 (0.37, 8.18) OR_{adj}: adjusted for BMI smoking, physical activity and physical health

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
			(DSM-IV axis I disorders), The interview provided 7 days point and lifetime prevalence diagnoses. At follow-up, The diagnosis of MDD was for the past 7 days, lifetime (baseline interview) and interval (between baseline and follow-up)	
Wymbs et al. (2014) United States Developmental Pathways Project (DPP), same study as McCarty et al. (2012)	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up:** 4 years	N=512 12th graders (aged 18 years) from 4 Seattle-area public schools. This article uses data from 8th grade – 12th grade (age 14 at baseline). N=249 females N=272 males	**Alcohol consumption:** based on the Customary Drinking and Drug Use Record to assess frequency in past 6 months, from 0 (never used) to 7 (more than once per day) **Depressive symptoms** based on the Diagnostic Interview Schedule for Children (DISC)	**SEM inter-correlations for females** Alcohol (12th grade)- Depression (12th grade): β=0.18, $p<0.05$ **SEM inter-correlations for males** (n=272) Alcohol (12th grade)- Depression (12th grade): β=0.17, $p<0.05$

CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; DISC = Diagnostic Interview Schedule for Children; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; ICD-10 = International Classification of Diseases, 10th revision; MDD = major depressive disorder; OR = odds ratio; SEM = structural equation models; SES = socioeconomic status.

Adults

Table 22 Depression outcomes from studies that reported on adults of both genders together

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Bell and Britton (2015) United Kingdom The Whitehall II prospective cohort study of British civil servants aged	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias	N=7,478 British civil servants who met inclusion criteria Maximum drinking session N=5,218 Non-HED N=1,948 HED N=312 Abstainers Usual drinking session N=6,044 Moderate drinker	**Drinking patterns**: At baseline participants were asked about the usual (fixed responses of: none, 1–2, 3–4 and 5 or more) and maximum (open response) number of drinks they consumed in a single drinking session. The number of UK alcohol units consumed was calculated by converting the number of drinks participants reported	**HR (95% CI) for depression during 28 years of follow-up by drinking pattern at baseline** **Maximum drinking session** Non-HED HR=1.0 (Reference) HED HR_{adj1}=1.05 (0.94,1.18) HR_{adj2}=1.03 (0.91,1.15) HR_{adj3}=1.03 (0.91,1.15) Abstainer HR_{adj1}=1.30 (1.04,1.61), p=0.02

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
35−55 years.	**Follow-up from baseline**: Wave 2: 4 years Wave 3: 6 years Wave 5: 12 years Wave 6: 16 years Wave 7: 17 years Wave 8: 21 years Wave 9: 22 years Wave 11: 27−28 years Median 22.7 years	N=1,122 Hazardous drinker N=312 Abstainer Hazardous drinking (alcohol intake in previous week) N=5,138 Within limits N=1,156 Exceeds limits N=1,184 Abstainer Frequency of drinking in year before baseline N=2,211 Daily N=3,119 Weekly N=956 Monthly N=875 Special occasions N= 317 Never	consuming using a conservative estimate of one UK unit of alcohol for each measure of spirits and glass of wine and two UK units for each pint of beer (1 UK unit = 8 g ethanol) HED: ≥8/6 UK units for men/women in a single drinking session Hazardous drinker: ≥5 UK units/session. Moderate drinker: 1−4 UK units/session Abstainers: 0 UK units Exceeding weekly harmful drinking: Exceeding UK weekly drinking guidelines of ≤21/14 UK units for men/women in past week at baseline **Depression** was dichotomised into case(scores ≥4) or no-case using the depression subscale of the 30-item GHQ-30	HR_{adj2}=1.26 (1.01,1.57), p=0.04 HR_{adj3}=1.23 (0.98,1.53), p=0.07 **Usual drinking session** Non-hazardous drinker HR=1.0 (Reference) Hazardous drinker HR_{adj1}=1.15 (1.00,1.31), p=0.04 HR_{adj2}=1.08 (0.95,1.24) HR_{adj3}=1.08 (0.94,1.24) Abstainer HR_{adj1}=1.30 (1.05,1.62), p=0.02 HR_{adj2}=1.26 (1.01,1.57), p=0.04 HR_{adj3}=1.23 (0.99,1.53) **Harmful weekly drinking** Drinking within limits HR=1.0 (Reference) Drinking exceeds limits HR_{adj1}=1.05 (0.92,1.20) HR_{adj2}=1.03 (0.90,1.18) HR_{adj3}=1.05 (0.91,1.20) Abstainer (0 in past week) HR_{adj1}=1.07 (0.94,1.22) HR_{adj2}=1.04 (0.91,1.18) HR_{adj3}=1.02 (0.89,1.16) **Drinking frequency** Weekly drinker HR=1.0 (Reference) Daily drinker HR_{adj1}=1.17 (1.04,1.31), p=0.01 HR_{adj2}=1.17 (1.04,1.31), p=0.01 HR_{adj3}=1.17 (1.05,1.32), p=0.01 Monthly drinker HR_{adj1}=1.09 (0.94,1.27]) HR_{adj2}=1.08 (0.93,1.26) HR_{adj3}=1.07 (0.92,1.25) Special occasion drinker HR_{adj1}=1.04 (0.89,1.23) HR_{adj2}=0.99 (0.84,1.17) HR_{adj3}=0.97 (0.83,1.15) Never drinker HR_{adj1}=1.34 (1.07,1.67), p=0.01 HR_{adj2}=1.28 (1.02,1.61), p=0.03

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				HR_{adj3}=1.24 (0.99,1.56) HR_{adj1}: age and gender HR_{adj2}: age, gender, socioeconomic position, marital status, smoking status, diet and physical activity HR_{adj3}: age, gender, socioeconomic position, marital status, smoking status, diet, physical activity and self-rated health.
Gea et al. (2012) Spain Professional-based "Seguimiento Universidad de Navarra" (SUN) Project which included adult university graduates	**Level:** II **Quality:** CPHE 22/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: every 2 years for at least 4 years and up to 10 years	N=13,619 participants without baseline or early incident depression Mean age 38 years 42% males N=628 male abstainers N=2,141 female abstainers N=3,017 males drinking <10 g/day N=4,904 females drinking <10 g/day N=1,462 males drinking 10−25 g/day N=778 females drinking 10−25 g/day N=594 males drinking >25 g/day N=95 females drinking >25 g/day	**Alcohol consumption level** was assessed at baseline with a semi-quantitative FFQ that included questions on alcoholic beverage consumption during the past year. Participants were divided into four groups according to their baseline alcohol intake: abstainers (0 g/day) <10 g/day of alcohol (spline analysis <5 g) 10−25 g/day (spline analysis 5−15 g) >25 g/day (spline analysis >15 g) **Depression** were defined as a positive answer to the question 'Have you ever been diagnosed of depression by a medical doctor?' or a positive report of habitual use of antidepressant drugs. This approach was validated by a Psychiatrist in a sub-sample using the SCID-I as a gold standard.	**HR (95% CI) for incident depression according to pre-determined categories of daily alcohol intake** **Total population** Abstainers: 114/16,921 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <10 g/day: 255/48,206 cases/person-years HR_{adj1}=0.84 (0.67, 1.05); HR_{adj2}=0.83 (0.66, 1.04) 10−25 g/day: 68/13,711 cases/person-years HR_{adj1}=0.83 (0.61, 1.14); HR_{adj2}=0.81 (0.59, 1.11) >25 g/day: 22/4,088 cases/person-years HR_{adj1}=0.91 (0.56, 1.46); HR_{adj2}=0.86 (0.53, 1.39) **HR (95% CI) for incident depression according to adapted spline categories of daily alcohol intake** **Total population** Abstainers: 114/16,921 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <5 g/day: 204/33,011 cases/person-years HR_{adj1}=0.96 (0.76, 1.21); HR_{adj2}=0.94 (0.75, 1.19) 5−15 g/day: 95/23,242 cases/person-years HR_{adj1}=0.66 (0.49, 0.87); HR_{adj2}=0.65 (0.49, 0.86) >15 g/day: 46/9,753 cases/person-years HR_{adj1}=0.77 (0.53, 1.10); HR_{adj2}=0.73 (0.50, 1.06) HR_{adj1}: adjusted for age (and gender for total population only) HR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity (MET-h/week), total energy intake (Kcal/day), baseline body mass index (kg/m^2), adherence to

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				the Mediterranean Dietary Pattern, marital status, and employment status
Paljärvi et al. (2009) Finland Community-based Health and Social Support (HSS) study of Finnish men and women of working age	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up from baseline**: 5 years	N=15,926 responded who completed Wave 1 and Wave 2 Alcohol intake (g/week) N=3,698 M1−37:W1−19 N=6,059 M38−110:W20−48 N=3,126 M111−168:W49−78 N=1,500 M169−255:W79−138 N=1,543 M≥256:W≥139 Number of intoxications N=2,946 none N=6,214 1−5 times/year N=1,531 6 times/year N=2,076 12 times/year N=3,123 ≥24 times/year No comparison of demographics between groups were reported	**Alcohol consumption** was measured according to answers to beverage-specific intake questions Alcohol intake refers to average total weekly intake in grams of absolute alcohol. For the estimation of alcohol intake, the beverage-specific average intake was asked and converted to the total weekly intake grams of absolute alcohol. Alcohol intake was categorized separately for men and women according to quintiles of their respective intake distributions (1–37; 38–110; 111–168; 169–255; and >255 g/week for men; 1–19; 20–48; 49–78; 79–138; and >138 g/week for women) Alcohol intoxication frequency was determined by the response options on a nine-point scale ranged from 'never' to 'at least twice weekly'. **Depressive symptoms** were assessed with the 21-item BDI scale. The sum score (range 0–63) of responses was categorized into six categories (0; 1–4; 5–9; 10–14; 15–19; and >19). A dichotomous measure, with a cut-off point score of ≥10, was selected to represent at least mild symptoms	**OR (95% CI) of BDI scores (0, 1−4, 5−9, 10−14, 15−19, ≥20) at Wave 2 and alcohol consumption at Wave 1** Alcohol intake (g/week) M1−37:W1−19: Reference M38−110:W20−48: OR_{adj1}=1.04 (0.97, 1.12) OR_{adj2}=1.02 (0.89, 1.04) M111−168:W49−78: OR_{adj1}=1.16 (1.06, 1.26) OR_{adj2}=1.11 (1.01, 1.21) M169−255:W79−138: OR_{adj1}=1.42 (1.27, 1.58) OR_{adj2}=1.16 (1.04, 1.30) M≥256:W≥139: OR_{adj1}=2.00 (1.80, 2.23) OR_{adj2}=1.43 (1.28, 1.60) Number of intoxications per year None: Reference 1−5 times/year: OR_{adj1}=1.36 (1.25, 1.58) OR_{adj2}=1.14 (1.05, 1.24) 6 times/year: OR_{adj1}=1.53 (1.36, 1.72) OR_{adj2}=1.22 (1.09, 1.38) 12 times/year: OR_{adj1}=1.59 (1.43, 1.78) OR_{adj2}=1.20 (1.08, 1.35) ≥24 times/year: OR_{adj1}=2.39 (2.16, 2.64) OR_{adj2}=1.49 (1.34, 1.65) OR_{adj1}: adjusted for gender and age OR_{adj2}: adjusted for gender, age and BDI scores at Wave 1 (categorized into six categories: 0, 1–4, 5–9, 10–14, 15–19, ≥20)

CI = confidence interval; BDI = Beck's Depression Inventory; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; FFQ = food-frequency questionnaire; GHQ-30 = General Health Questionnaire – 30 questions; HR = hazard ratio; MDD = major depressive disorder; PHQ = Patient Health Questionnaire; SCID-I = Structured Clinical Interview for DSM-IV

Table 23 Depression outcomes from studies that reported on men and/or women separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Augestad et al. (2008) Norway Population-based Health Survey in Nord-Trondelag (HUNT) included residents in the county aged ≥20 years	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: 9−12 years	N=6,661 participants, aged 21−40 years, who met the inclusion/exclusion criteria N=3,353 women 91.9% scored <8 on the HADS-D scale. N=666 aged 21−25 years N=871 aged 26−30 years N=954 aged 31−35 years N=862 aged 36−40 years N=3,308 men 91.1% scored <8 on the HADS-D scale. N=558 aged 21−25 years N=833 aged 26−30 years N=903 aged 31−35 years N=1,014 aged 36−40 years	**Alcohol consumption frequency** in the previous 2 weeks (at baseline) measure was NR but were defines as follows: Abstinent: does not drink alcohol No recent drinking: did not drink alcohol in the previous 2 weeks 1−4 times in the past 2 weeks 5−10 times in the last 2 weeks >10 times in the last 2 weeks **Depression** was defined using the Hospital Anxiety and Depression Scale depression subscale (HADS-D). Scores of <8 on the HADS-D subscale were considered as not depressed, and scores of ≥8 as depressed	**OR (95% CI) of depression based on HADS-D score at follow-up according to drinking frequency in the last 2 weeks at baseline for females** Abstinent OR=1.0 (Reference) No recent drinking: OR=1.17 (0.61, 2.24) Drank 1−4 times: OR=1.18 (0.61, 2.27) Drank 5−10 times: OR=1.02 (0.27, 3.88) Drank >10 times: OR=0.72 (0.15, 3.47) **OR (95% CI) of depression based on HADS-D score at follow-up according to drinking frequency in the last 2 weeks at baseline for males** Abstinent OR=1.0 (Reference) No recent drinking: OR=0.75 (0.38, 1.49) Drank 1−4 times: OR=0.62 (0.32, 1.21) Drank 5−10 times: OR=0.59 (0.24, 1.45) Drank >10 times: OR=0.47 (0.16, 1.38) ORs adjusted for age, smoking habits, BMI, alcohol consumption, education, and living arrangements.
Gea et al. (2012) Spain Professional-based "Seguimiento Universidad de Navarra" (SUN) Project which included adult university graduates	**Level:** II **Quality:** CPHE 22/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: every 2 years for at least 4 years and up to 10 years	N=13,619 participants without baseline or early incident depression Mean age 38 years 58% females N=7,082 N=2,141 female abstainers N=4,904 females drinking <10 g/day N=778 females drinking 10−25 g/day N=95 females drinking >25 g/day	**Alcohol consumption level** was assessed at baseline with a semi-quantitative food-frequency questionnaire (FFQ) that included questions on alcoholic beverage consumption during the past year. Participants were divided into four groups according to their baseline alcohol intake: abstainers (0 g/day) <10 g/day of alcohol (spline analysis <5 g) 10−25 g/day (spline analysis 5−15 g) >25 g/day (spline analysis >15 g)	**HR (95% CI) for incident depression according to pre-determined categories of daily alcohol intake for females** Abstainers: 92/13,107 cases/person-years HR_{adj1}=1.00 (Reference) HR_{adj2}=1.00 (Reference) <10 g/day: 179/29,552 cases/person-years HR_{adj1}=0.89 (0.69, 1.14) HR_{adj2}=0.87 (0.67, 1.13) 10−25 g/day: 27/4,582 cases/person-years HR_{adj1}=0.81 (0.52, 1.24) HR_{adj2}=0.78 (0.50, 1.21) >25 g/day: 5/575 cases/person-years

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		42% males N=6,537 N=628 male abstainers N=3,017 males drinking <10 g/day N=1,462 males drinking 10−25 g/day N=594 males drinking >25 g/day	**Depression** were defined as a positive answer to the question 'Have you ever been diagnosed of depression by a medical doctor?' or a positive report of habitual use of antidepressant drugs. This approach was validated by a Psychiatrist in a sub-sample using the Structured Clinical Interview for DSM-IV (SCID-I) as a gold standard.	HR_{adj1}=1.06 (0.43, 2.61) HR_{adj2}=1.06 (0.43, 2.63) **HR (95% CI) for incident depression according to pre-determined categories of daily alcohol intake for males** Abstainers: 22/3,814 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <10 g/day: 76/18,654 cases/person-years HR_{adj1}=0.68 (0.42, 1.10); HR_{adj2}=0.69 (0.43, 1.11) 10−25 g/day: 41/9,130 cases/person-years HR_{adj1}=0.75 (0.45, 1.26); HR_{adj2}=0.76 (0.45, 1.29) >25 g/day: 17/3,513 cases/person-years HR_{adj1}=0.77 (0.40, 1.45); HR_{adj2}=0.76 (0.40, 1.47) **HR (95% CI) for incident depression according to adapted spline categories of daily alcohol intake for females** Abstainers: 88/12,629 cases/person-years HR_{adj1}=1.0 (Reference) HR_{adj2}=1.0 (Reference) <5 g/day: 136/19,523 cases/person-years HR_{adj1}=1.01 (0.78, 1.31) HR_{adj2}=0.97 (0.75, 1.27) 5−15 g/day: 59/12,578 cases/person-years HR_{adj1}=0.62 (0.44, 0.89) HR_{adj2}=0.62 (0.43, 0.89) >15 g/day: 12/1,706 cases/person-years HR_{adj1}=0.86 (0.49, 1.51) HR_{adj2}=0.84 (0.47, 1.48) **HR (95% CI) for incident depression according to adapted spline categories of daily alcohol intake for males** Abstainers: 22/3,814 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				<u><5 g/day</u>: 53/10,911 cases/person-years HR_{adj1}=0.82 (0.49, 1.34); HR_{adj2}=0.82 (0.50, 1.36) <u>5−15 g/day</u>: 49/12,776 cases/person-years HR_{adj1}=0.64 (0.39, 1.07); HR_{adj2}=0.64 (0.39, 1.07) <u>>15 g/day</u>: 32/7,610 cases/person-years HR_{adj1}=0.68 (0.39, 1.17); HR_{adj2}=0.68 (0.39, 1.19) HR_{adj1}: adjusted for age (and gender for total population only) HR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity, total energy intake, baseline body mass index, adherence to the Meditteranean Dietary Pattern, marital status, and employment status
Otten et al. (2018) Netherlands Parents from the families included in the Family and Health study.	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 1 year Wave 3: 2 years Wave 4: 3 years Wave 5: 4 years	N=306 mothers with genetic information who completed all waves Mean age 43.8±3.55 years (range 35−56) N=288 fathers with genetic information who completed all waves Mean age 46.2±3.95 years (range 37−61)	**Alcohol use** was assessed using the answers to 4 questions on how many glasses of alcoholic beverages they had consumed in the previous week during weekdays, on the weekends, at home, and while not at home. <u>The mean number of alcoholic beverages consumed</u> was calculated from the summed answers. **Depressive symptoms** were assessed using a 6-item scale asking how often participants were bothered by negative feelings in the previous 12 months. Answers could be provided on a 5-point Likert scale, ranging from 1 (never) to 5 (always). It has been shown that this scale has high concurrent validity with other questionnaires. Cronbach's alpha was high for all fives waves and for both for males and females (α≥0.79).	**Linear regression analyses predicting depression at W5 by number of alcoholic beverages consumed at W1** Females: β=0.05, p=0.36 Males: β=0.01, p=0.87 **Latent growth curve analyses to determine if the intercept and slope of depressive symptoms were preceded alcohol use at W1** Females: Intercept=0.11, p<0.10 Slope=0.03 Males: Intercept=0.08 Slope=−0.02

BDI = Beck's Depression Inventory; CI = confidence interval; CIDI = Composite International Diagnostic Interview; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD = generalised anxiety disorder; HR = hazard ratio; MDD = major depressive disorder; NR = not reported; OR = odds ratio;

Older adults

Table 24 Depression outcomes from studies that reported on older adults of both genders together

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
An & Xiang (2015) United States Health and Retirement Study	**Level:** II **Quality:** CPHE 28/34 **Internal validity:** Low of bias **External validity:** High risk of bias (poor reporting on source population) **Follow-up**: 10 years (from 1992 to 2012)	N=24,759 adults aged ≥50 years, free from depression at baseline 27.38% had one or more depression onset during follow-up period 49% female Mean age 60.46 years 34% never drank Of those who ever drank: 18% heavy drinkers 82% not heavy drinkers	**Heavy drinking** defined as ≥1 drinks/day or ≥4 drinks on any occasion in past 3 months (women); or ≥2 drinks/day or ≥4 drinks on any occasion in past 3 months (men) **Depression** was defined as ≥3 on the CES-D	**Cox proportional HR (95% CI) for depression** No current heavy drinking: HR_{adj}=1.0 (Reference) Current heavy drinking: HR_{adj}=1.05 (95%CI 0.98, 1.13) Adjusted for gender, race/ethnicity, education, birth cohort, history of psychiatric problem, smoking, age, marital status, wealth, diagnosis of chronic condition, body weight status.
Brennan et al. (2016) United States Health and Retirement Study	**Level:** II **Quality:** CPHE 15/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up**: 10 years (from 1996 to 2006, with 6 waves)	N=7,939 adults aged 55 – 65 years at baseline (1996) 56% female Mean age 59.80±3.16 years N=3,133 Abstinent without history of drinking problems N=746 Abstinent with history of drinking problems N=1,352 Light drinkers N=1,586 Moderate drinkers N=1,122 Heavy drinkers N=439 HED	**Alcohol consumption**: number of drinks/day on days where alcohol was drink during prior 3 months. Abstinence: zero drinks/day Light drinkers: ≤2 drinks/day (men), less often than once/week; ≤1 drink/day (women), less often than once/week Moderate drinkers: ≤2 drinks/day (men) ≥ once/week; ≤1 drink/day ≥ once/week Heavy drinkers: >2 drinks/day (men), ≥ once/week; >1 drink/day (women), ≥ once/week **HED**: ≥4 drinks/day (men) or ≥3 drinks/day (women), ≥ once/week **Trajectories of depressive symptoms** on the CES-D scale reformatted to capture “yes” and “no” responses to five of the items (feeling depressed, having	**Multinomial logistic regressions: ORs for the effects of baseline drinking behaviour on depressive symptom trajectory:** Abstinence without history of drinking problems: Consistently elevated vs consistently low: OR=2.13, p<0.01 OR_{adj}=1.07 Increasing vs consistently low: OR=0.66, p<0.01 OR_{adj}=1.30 Decreasing vs consistently low: OR=1.63, p<0.01 OR_{adj}=1.13 Abstinence with a history of drinking problems Consistently elevated vs consistently low: OR=4.88, p<0.01 OR_{adj}=1.38 Increasing vs consistently low: OR=1.44 OR_{adj}=2.48, p<0.01 Decreasing vs consistently low:

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			restless sleep, inability to "get going," enjoying life [reverse scored], and feeling happy [reverse scored]).	OR=1.66 OR_{adj}=1.90, p<0.01 Light drinkers Consistently elevated vs consistently low: OR=1.51 OR_{adj}=0.80 Increasing vs consistently low: OR=0.34, p<0.01 OR_{adj}=0.76 Decreasing vs consistently low: OR=0.66 OR_{adj}=0.66 Moderate drinkers Consistently elevated vs consistently low: OR=1.09 OR_{adj}=0.40, p<0.01 Increasing vs consistently low: OR=0.46, p<0.01 OR_{adj}=0.59, p<0.01 Decreasing vs consistently low: OR=0.22, p<0.01 OR_{adj}=0.62 Heavy drinkers Consistently elevated vs consistently low: OR=1.76, p<0.01 OR_{adj}=1.14 Increasing vs consistently low: OR=0.43, p<0.01 OR_{adj}=0.95 Decreasing vs consistently low: OR=1.29 OR_{adj}=1.50 HED Consistently elevated vs consistently low: OR=2.71, p<0.01 OR_{adj}=1.84, p<0.01 Increasing vs consistently low: OR=0.75 OR_{adj}=1.54 Decreasing vs consistently low: OR=1.17 OR_{adj}=1.31 Adjusted for number of medical conditions. Being abstinent at baseline increased the likelihood of being

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				the consistently elevated depressive symptom class. Drinking heavily and HED elevated the risk of being in the 'consistently elevated' depressive symptom trajectory class. Being a heavy drinker doubled the risk of belonging to this class.
Cheng et al. (2016) China Population-based China Health and Retirement Longitudinal Study (CHARLS) included adults aged ≥45 years	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** High risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: 2 years	N=17,708 W1 participants aged ≥45 years Mean age 57.7±10.1 years N=4,383 current drinkers N=783 more than daily drinkers N=15,628 W2 participants	**Alcohol consumption** was defined by the answers to specific consumption questions. <u>Current drinkers</u> were defined as having drunk alcohol more than monthly in the last year <u>More than daily drinkers</u> were defined as those who reported drinking alcohol ≥2-times a day <u>Never drinkers</u> were defined as never having drunk more than once a month <u>Former drinkers</u> were defined as those who had previously drunk more than once a month. **Depressive symptoms** were measured using the CES-D short form and a cut-off score of 12 was used to define depression.	**Bivariate linear regression OR (95% CI) for incidence of depression in baseline drinkers** Never drinker: OR=1.0 (Reference) Former drinker: OR=0.8 (0.5, 1.1) Current drinker: OR=0.6 (0.5, 0.7), p<0.05 Among W1 current drinkers (n=2,295) More than daily drinking versus not: OR=1.2 (0.8, 1.7) **Bivariate linear regression OR (95% CI) for persistence of depression in baseline drinkers** Never drinker: OR=1.0 (Reference) Former drinker: OR=0.8 (0.6, 1.2) Current drinker: OR=0.6 (0.5, 0.8), p<0.05 Among W1 current drinkers (n=629) More than daily drinking versus not: OR=0.8 (0.5, 1.3)
Gea et al. (2013) Spain A large randomised controlled trial, the PREDIMED Study (Prevention with Mediterranean Diet) included	**Level:** II **Quality:** CPHE 21/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: annual	N=5,505 participants without baseline or early incident depression N=1,818 abstainers N=1,356 drinking <5 g/day N=1,279 drinking 5−15 g/day N=1,052 drinking >15 g/day	**Alcohol consumption level** was assessed at baseline with a semi-quantitative food-frequency questionnaire (FFQ) that included questions on alcoholic beverage consumption during the past year. Participants were divided into four groups according to their baseline alcohol intake: <u>abstainers</u> (0 g/day) <u><5 g/day</u> of alcohol (spline analysis <5 g) <u>5−15 g/day</u> (spline analysis 5−15 g)	**GEE RR (95% CI) for incident depression according to annually updated categories of daily alcohol intake** <u>Abstainers</u>: 195/7,777 cases/person-years RR=1.0 (Reference) RR_{adj1}=1.0 (Reference); RR_{adj2}=1.0 (Reference) <u><5 g/day</u>: 114/5,728 cases/person-years RR=0.63 (0.49, 0.81) RR_{adj1}=0.73 (0.56, 0.94); RR_{adj2}=0.73 (0.57, 0.95) <u>5−15 g/day</u>: 79/5,390 cases/person-years RR=0.49 (0.37, 0.66)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
adults aged ≥55 years	interviews for up to 7 years		>15 g/day (spline analysis >15 g) **Depression** were defined as a diagnosis of depression made by a physician and reported by participants in any of the follow-up interviews, or a positive report of habitual use of antidepressant drugs.	RR_{adj1}=0.71 (0.52, 0.97); RR_{adj2}=0.69 (0.50, 0.96) >15 g/day: 55/4,760 cases/person-years RR=0.37 (0.26, 0.52), p<0.001 for linear trend RR_{adj1}=0.71 (0.48, 1.05), p=0.727 for linear trend RR_{adj2}=0.69 (0.46, 1.04), p=0.773 for linear trend RR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity, total energy intake, baseline BMI, marital status, intervention group, recruiting centre, educational level and the number of persons living at home. **HR (95% CI) for incident depression according to baseline categories of daily alcohol intake** Abstainers: 195/7,777 cases/person-years HR=1.0 (Reference) HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <5 g/day: 114/5,728 cases/person-years HR=0.79 (o.63, 1.00) HR_{adj1}=0.91 (0.72, 1.15); HR_{adj2}=0.97 (0.75, 1.25) 5−15 g/day: 79/5,390 cases/person-years HR=0.59 (0.46, 0.77) HR_{adj1}=0.81 (0.62, 1.07); HR_{adj2}=0.72 (0.53, 0.98) >15 g/day: 55/4,760 cases/person-years HR=0.44 (0.33, 0.60), p<0.001 for linear trend HR_{adj1}=0.81 (0.58, 1.14), p=0.347 for linear trend HR_{adj2}=0.79 (0.53, 1.16), p=0.522 for linear trend HR_{adj1}: adjusted for age (and gender for total population only) HR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity, total energy intake, baseline BMI, marital status, intervention group, recruiting centre, educational level and the number of persons living at home.
Lang et al. (2007) United Kingdom	**Level:** II **Quality:** CPHE 23/34	N=7,286 participants in all 3 waves of ELSA who met inclusion criteria	**Alcohol consumption** was based on their answer to the question 'Do you ever drink alcohol nowadays, including drinks	**Linear regression z-scores (95% CI) for depressive symptoms by level of alcohol consumption** Ex-drinkers z=0.23 (0.06, 0.39), p<0.01

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Household-based Health Survey for England (HSE) included all members of households ≥1 member was aged ≥50 years English Longitudinal Study of Ageing (ELSA)	**Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 1 year Wave 3: 3 years	N=3,409 men aged ≥50 years N=87 ex-drinkers N=46 never drinkers N=1,735 >0−1 drinks/day N=799 >1−2 drinks/day N=739 >2 drinks/day N=3,877 women aged ≥50 years N=147 ex-drinkers N=153 never drinkers N=2,902 >0−1 drinks/day N=529 >1−2 drinks/day N=143 >2 drinks/day	you brew or make at home?' For various types of alcohol, respondents who drank were asked how often they drank and on average how much they drank over the last 12 months. Mean daily alcohol consumption was calculated and participants were categorised as: <u>Ex-drinkers</u>, non-drinkers who used to be drinkers <u>Never-drinkers</u>, non-drinkers who have never been drinkers <u>>0−1 drink/day</u>, those drinking up to one drink (14 g of alcohol) per day <u>>1−2 drinks/day</u>, those drinking up to two drinks (28 g of alcohol) per day <u>>2 drinks/day</u>, those drinking more than two drinks (28 g of alcohol) per day **Depressive symptoms** were measured using a version of the CES-D. A subset of eight items out of the original twenty were coded dichotomously (yes/no) to give a score out of 8. A higher CES-D score is not necessarily diagnostic of depression but indicates more depressive symptoms.	<u>Never-drinkers</u> z=0.27 (0.08, 0.46), p<0.01 <u>>0−1 drink/day</u> Reference <u>>1−2 drinks/day</u> z=−0.08 (−0.15, −0.02), p<0.05 <u>>2 drinks/day</u> z=0.02 (−0.06, 0.11) Analyses controlled for: age; gender; BMI; education level; smoking; co-morbidity; income; household wealth; participation in moderate or vigorous exercise; number of close family members; number of close friends. There was little difference between men and women. Compared to those drinking >0−1 drink/day, those who do not drink alcohol had significantly more depressive symptoms and those who drink >1−2 drinks/day had significantly fewer. There was no difference in depression between those who drink >2 drinks/day and those who drink >0−1 drink/day.
Luppa et al. (2012) Germany Population-based Leipzig Longitudinal Study of the Aged (LEILA75+)	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias	N=860 participants aged ≥75 years who were included. N=52 with at-risk alcohol consumption N=808 with no or normal alcohol consumption	**Alcohol consumption** was measured according to answers to a standardised questionnaire and recorded as g alcohol consumed/day: <u>No or normal alcohol consumption</u>: ≤20 g alcohol for women and ≤30 g alcohol for men <u>At-risk alcohol consumption</u>: >20 g alcohol for women and >30 g alcohol for	**HR (95% CI) of incident depressive symptoms during follow-up in participants without depressive symptoms at baseline** No or normal alcohol consumption: Reference At-risk alcohol consumption: HR=2.33 (1.09, 4.96), p<0.05 Fully adjusted for all variables

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
included older adults aged 75 years and over	**Follow-up from baseline**: every 1.5 years for 8 years		men **Depressive symptoms** were measured using the 20-item CES-D questionnaire. A CES-D score of ≥23 points was used to define the presence of depressive symptoms.	
Paulson et al. (2018) United States Health and Retirement Study	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 8 years	N=3,177 adults aged >65 years at baseline (2006) from HRS, who drink >14 drinks/week and >4 drinks/sitting. Mean age 74.3±7.0 years 57% female N=2,257 abstinent N=920 moderate drinkers	**Alcohol consumption** defined as average number of drinks per week <u>Moderate drinkers</u>: 1-14 drinks/week <u>Abstainers</u>: 0 drinks/week **Depressive symptoms** on CES-D Participants answered "yes" or "no" to each item with respect to how they were feeling "much of the time" in the past week. Scores ranged from 0 to 8, with higher scores suggesting higher levels of depression	**Slope-intercept model predicting depressive symptomatology** Reference: abstainers **Intercept:** Moderate use: β (SE)=-0.493 (0.07), p<0.001 **Linear slope:** Moderate use: β (SE)=0.151 (0.06), p=0.013 **Quadratic:** Moderate use: β (SE)=-0.030 (0.015), p=0.045 Moderate drinkers endorsed fewer depressive symptoms at baseline β (SE)=0.49 (0.07), but the rate of change in depressive symptoms over time was greater β (SE)=0.15 (0.06). Baseline differences in depressive symptoms between moderate drinkers and abstainers narrowed over time (benefits of moderate drinking eroded by passage of time).
Tsai et al. (2013) Taiwan Population-based Taiwan Longitudinal Study on Aging (TLSA) included subjects aged ≥60 years in 1989	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: 8 years	N=3,273 participants who completed the 2007 survey of the TLSA study N=849 with depressive symptoms at baseline who were excluded from longitudinal analysis. N=2,145 included in logistic regression analysis Those with depression at baseline were significantly older,	**Alcohol consumption level** was classified according to the frequency and amount consumed as disclosed during an in-home in-person interview by a trained interviewer: <u>Non/occasional drinkers</u> (<1 time/week) <u>Moderate drinkers</u> (≥1 time/week, <2 drinks/time) <u>Heavy drinkers</u> (≥1 time/week, ≥2 drinks/time) **Depressive symptoms** "during the past	**OR (95% CI) of the association between baseline alcohol use (times/week) and new onset depressive symptoms 8 years later** Non/occasional drinkers: OR_{adj}=1.0 (Reference) Moderate drinkers: OR_{adj}=0.89 (0.63, 1.26), NS Heavy drinkers: OR_{adj}=0.70 (0.30, 1.64), NS OR_{adj}: adjusted for gender, age, level of education, psychological stress, diabetes, heart disease, Instrumental Activities of Daily Living status, family support, and audio acuity.

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		more likely to be female, less educated, less likely to smoke, less likely to drink moderately, less likely to exercise and more likely to drink tea.	week" were rated with the 10-item CES-D10 form. Individuals who scored ≥10 on a scale of 0–30 were considered as having depressive symptoms.	
Weyerer et al. (2013) Germany German Study on Ageing, Cognition, Dementia in Primary Care Patients (AgeCoDe Study) involving patients aged ≥75 years	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: 1.5 years and 3 years	N=2,512 elderly patients aged ≥75 years who completed both follow-ups Alcohol consumption at baseline N=1,191 were abstinent N=654 drank <1 drink/day N=328 drank 1−2 drinks/day N=324 drank >2 drinks/day	**Alcohol consumption level** was determined by a self-reported measure and was differentiated according to their average daily level of consumption: abstinent; <1 drink; 1–2 drinks; 2+ drinks. One drink is the equivalent of 10 g of pure alcohol. **Depressive symptoms** were ascertained using the 15-item version of the Geriatric Depression Scale (GDS). A score of ≥6 was used to diagnose depressive symptoms.	**HR (95% CI) to predict incident depression (GDS-15: 0–5 points at baseline and 6+ points at either follow-up** Abstinent: 155/1,191 incident cases HR=1.0 (Reference) HR_{adj}=1.0 (Reference) <1 drink/day 66/654 incident cases HR=0.75 (0.56, 1.00), p=0.055 HR_{adj}=0.84 (0.62, 1.14), p=0.271 1−2 drinks/day: 31/328 incidence cases HR=0.70 (0.47, 1.03), p=0.073 HR_{adj}=0.90 (0.60, 1.35), p=0.638 >2 drinks/day: 40/324 incident cases HR=0.75 (0.66, 1.34), p=0.757 HR_{adj}=1.18 (0.79, 1.76), p=0.405 HR_{adj}: fully adjusted for age, gender, living alone, marital status, level of education, mobility impairment, vision impairment, hearing impairment, functional impairment, somatic co-morbidity, mild cognitive impairment, subjective memory impairment, baseline smoking, apoE4.

BMI = body mass index; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; GEE = general estimating equation; HR = hazard ratio; OR = odds ratio; RR = relative risk;

Table 25 Depression outcomes from studies that reported on older men and/or women separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
An & Xiang (2015)	**Level:** II **Quality:**	N=24,759 adults aged ≥50 years, free from depression at baseline	**Heavy drinking** defined as ≥1 drinks/day or ≥4 drinks on any occasion in past 3 months (women); or ≥2 drinks/day or ≥4	**Cox proportional hazards regressions for depression for females**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
United States Health and Retirement Study	CPHE 28/34 **Internal validity:** Low of bias **External validity:** High risk of bias (poor reporting on source population) **Follow-up**: 10 years (from 1992 to 2012)	27.38% had one or more depression onset during follow-up period 49% female (n=12,132) Mean age 60.46 years 34% never drank Of those who ever drank: 18% heavy drinkers 82% not heavy drinkers 51% male (n=12,627) Mean age 60.46 years 34% never drank Of those who ever drank: 18% heavy drinkers 82% not heavy drinkers	drinks on any occasion in past 3 months (men) **Depression** was defined as ≥3 on the CES-D	No current heavy drinking: HR_{adj}=1.0 (Reference) Current heavy drinking: HR_{adj}=1.09 (95%CI 0.98, 1.20) **Cox proportional HR (95% CI) for depression for males** No current heavy drinking: HR_{adj}=1.0 (Reference) Current heavy drinking: HR_{adj}=1.05 (95%CI 0.95, 1.17) Adjusted for gender, race/ethnicity, education, birth cohort, history of psychiatric problem, smoking, age, marital status, wealth, diagnosis of chronic condition, body weight status.
Bots et al. (2008) Finland, Italy and the Netherlands Elderly (FINE) study	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up:** 5 years	N=826 elderly males, excluding those classified with depression at baseline Mean age 75.2 years at baseline	**Alcohol intake:** categorised into no intake (<1g/day), moderate intake (1-31g/day) and high intake >31g/day). **Depression** assessed on the 20-item Zung Self-rating Depression Scale (ZSDS). Those scoring 48/80 defined as depressed.	**OR (95%CI) for predictors of depression** No intake (<1g/day): OR=1.0 (Reference) Moderate (1-31g/day): OR=0.24 (0.22, 0.86), p=0.018 OR_{adj}=0.36 (0.15, 0.90), p=0.028 High (>31g.day): OR=0.78 (0.36, 1.66), p=0.513 OR_{adj}=0.64 (0.23, 1.80), p=0.401 OR: adjusted for age OR_{adj}: adjusted for baseline depressive symptoms (ZSDS score), physical activity, change in cholesterol
Byers et al. (2012) United States Study of Osteoporotic Fractures	**Level:** II **Quality:** CPHE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias	N=7,240 elderly females, aged ≥65 years. Mean age 72.8±4.7 years	**Alcohol consumption** based on number of drinks consumed per week. Frequent use defined as ≥7 drinks/week. **Depressive symptoms** measured using the Geriatric Depression Scale short form (GDS). A score of ≥6 indicates depression. Depressive symptoms were grouped into 4 latent classes: Persistently	**OR (95%CI) for persistently low depressive symptoms (compared to minimal depressive symptoms)** Infrequent alcohol consumption: OR_{adj}=1.0 (reference) Frequent alcohol consumption: OR_{adj}=1.02 (0.77, 1.35) **OR (95%CI) for increasing depressive symptoms (compared to minimal depressive symptoms)** Infrequent alcohol consumption: OR_{adj}=1.0 (reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	Follow-up: Mean 12.2 years (20 years for study)		high; Increasing; Persistently low; and Minimal.	Frequent alcohol consumption: OR_{adj}=0.99 (0.69, 1.43) **OR (95%CI) for persistently high depressive symptoms (compared to minimal depressive symptoms)** Infrequent alcohol consumption: OR_{adj}=1.0 (reference) Frequent alcohol consumption: OR_{adj}=0.85 (0.44, 1.63) Models adjusted for education, married, living alone. Frequent alcohol consumption (≥7drinks/week) had inverse relationship. Group with persistently high depressive symptoms had lowest prevalence of frequent drinking (8.1%), compared to prevalence for other groups (10.2 – 12.7%; p=0.02 for trend).
Chang et al (2016) United States Nurses' Health Study	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**:10 years	N=21,728 elderly women, aged ≥65 years without depression or history of depression at baseline Mean age 71.4±4.1 years 41% had no drinks on any single day 49% had a maximum of 1–2 drinks on any single day 10% had ≥3 drinks on any single day	**Largest number of drinks in a single day** categorised as none, 1–2 and ≥3 drinks/day **Heavy drinking/HED** defined as ≥3 drinks/day **Late life depression** (onset ≥65 years) on Mental Health Index-5 (MHI-5) subscale of SF-36 in 2000, the CESD-10 in 2004 and Geriatric Depression Scale-15 (GDS-15) in 2008 using validated cut-points for clinical depression.	**HR (95% CI) for late-life depression** (n=21,728) Largest number of drinks in a single day: No drinks: 1,695 cases/73,540 person-years HR=1.0 (Reference) 1-2 drinks: 1,838 cases/88,951 person-years HR=0.93 (95%CI 0.87, 1.00) HR_{adj}=1.00 (955CI 0.94, 1.08) ≥3 drinks: 412 cases/17,650 person-years HR=1.13 (95%CI 1.01, 1.26), p<0.05 HR_{adj}=1.03 (95%CI 1.03, 1.29) HR: adjusted for age (years) only HR_{adj}: adjusted for age, and time-varying covariates (education, race, social network, body mass index, diet, cigarette smoking, vigorous activity, co-morbidities, hours of sleep per day) **HR (95% CI) for incident late-life depression** (n=21,728) No heavy drinking/HED: HR=1.0 (Reference) Heavy drinking/HED: HR=1.20 (1.08, 1.33) population attributable risk=1.7 (95%CI 0.7, 2.7) <u>In subgroup without physical/functional limitation</u> No heavy drinking/HED: HR=1.0 (Reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Heavy drinking/HED: HR=1.40 (95%CI 1.15, 1.71) population attributable risk=4.3 (95%CI 1.6, 7.0) In subgroup with physical/functional limitation No heavy drinking/HED: HR=1.0 (Reference) Heavy drinking/HED: HR=1.13 (95%CI 1.01, 1.28) population attributable risk=1.1 (95%CI 0, 2.2)
Cheng et al. (2016) China Population-based China Health and Retirement Longitudinal Study (CHARLS) included adults aged ≥45 years	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: 2 years	N=17,708 W1 participants aged ≥45 years Mean age 57.7±10.1 years N=4,383 current drinkers N=783 more than daily drinkers N=15,628 W2 participants N=8,175 females N=7,449 males	**Alcohol consumption** was defined by the answers to specific consumption questions. Current drinkers were defined as having drunk alcohol more than monthly in the last year More than daily drinkers were defined as those who reported drinking alcohol ≥2-times a day Never drinkers were defined as never having drunk more than once a month Former drinkers were defined as those who had previously drunk more than once a month. **Depressive symptoms** were measured using the CES-D short form and a cut-off score of 12 was used to define depression.	**OR (95% CI) for incidence of depression in baseline drinkers for females** Never drinker: OR_{adj}=1.0 (Reference) Current drinker: OR_{adj1}=0.9 (0.5, 1.4) OR_{adj2}=0.8 (0.5, 1.3) Former drinker: OR_{adj}=1.0 (Reference) Current drinker: OR_{adj1}=1.2 (0.4, 3.3) OR_{adj2}=1.3 (0.5, 3.8) **OR (95% CI) for incidence of depression in baseline drinkers for males** Never drinker: OR=1.0 (Reference) Current drinker: OR_{adj1}=0.8 (0.6, 1.0), p=0.05 OR_{adj2}=0.7 (0.5, 0.9), p<0.05 Former drinker: OR=1.0 (Reference) Current drinker: OR_{adj1}=0.7 (0.5, 1.1) OR_{adj2}=0.8 (0.6, 1.3) **OR (95% CI) for persistence of depression in baseline drinkers for females** Never drinker: OR_{adj}=1.0 (Reference) Current drinker: OR_{adj1}=0.8 (0.6, 1.2) OR_{adj2}=0.7 (0.5, 1.1) Former drinker: OR_{adj}=1.0 (Reference) Current drinker: OR_{adj1}=1.6 (0.8, 3.2) OR_{adj2}=1.9 (0.9, 4.0) **OR (95% CI) for persistence of depression in baseline drinkers for males**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Never drinker: OR=1.0 (Reference) Current drinker: OR_{adj1}=0.7 (0.5, 1.0) OR_{adj2}=0.7 (0.5, 1.0) Former drinker: OR=1.0 (Reference) Current drinker: Male: OR_{adj1}=0.6 (0.4, 1.0), p=0.05 OR_{adj2}=0.7 (0.5, 1.1) OR_{adj1} were adjusted for age and baseline tobacco use or drinking status (never, current, or past). OR_{adj2} were adjusted for age, baseline tobacco use or drinking status, baseline health status and changes in marital status (i.e., divorced or widowed).
Chou et al. (2011) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 3 years	N=13,489 middle aged and older adults in the United States (aged ≥50 years) N=7,981 females 4,302 non-drinkers 3,223 current drinkers but no past year HED 223 past year HED <1 per month 233 past year HED ≥1 per month N=5,461 males 1,987 non-drinkers 2,616 current drinkers but no past year HED 310 past year HED <1 per month 548 past year HED ≥1 per month	**HED**: defined as 5 drinks or more (men) or 4 drinks or more (women) in one occasion. **MDD** by AUDADIS-IV	**OR (95% CI) of MDD at Wave 2 based on HED status wave 1 for females** Non-drinkers: OR_{adj}=1.07 (0.86, 1.33) Current non-HED: OR_{adj}=1.0 (reference) Past-year HED <1 per month: OR_{adj}=0.89 (0.52, 1.51) Past-year HED ≥1 per month: OR_{adj}=0.79 (0.40, 1.55) **OR (95% CI) of MDD at Wave 2 based on HED status wave 1 for males** Current non-HED: OR_{adj}=1.0 (Reference) Non-drinkers: OR_{adj}=1.61 (1.09, 2.38) Past-year HED <1 per month: OR_{adj}=1.27 (0.56, 2.86) Past-year HED ≥1 per month: OR_{adj}=0.94 (0.44, 2.03) Adjusted for age, marital status, education, race, household income, employment status, lifetime history of row-defined psychiatric disorder prior to Wave 1 assessment, and lifetime history of alcohol use disorder prior to Wave 1 assessment.
Gea et al. (2013) Spain A large randomised	**Level:** II **Quality:** CPHE 21/34 **Internal validity:** Moderate risk of	N=5,505 participants without baseline or early incident depression N=1,818 abstainers N=1,356 drinking <5 g/day	**Alcohol consumption level** was assessed at baseline with a semi-quantitative food-frequency questionnaire (FFQ) that included questions on alcoholic beverage consumption during	**GEE RR (95% CI) for incident depression according to annually updated categories of daily alcohol intake** **Females** Abstainers: 173/6,069 cases/person-years RR_{adj1}=1.0 (Reference); RR_{adj2}=1.0 (Reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
controlled trial, the PREDIMED Study (Prevention with Mediterranean Diet) included adults aged ≥55 years	bias **External validity:** High risk of bias **Follow-up from baseline**: annual interviews for up to 7 years	N=1,279 drinking 5−15 g/day N=1,052 drinking >15 g/day N=2,822 females N=1,418 abstainers N=800 drinking <5 g/day N=486 drinking 5−15 g/day N=126 drinking >15 g/day N=2,683 males N=400 abstainers N=556 drinking <5 g/day N=793 drinking 5−15 g/day N=926 drinking >15 g/day	the past year. Participants were divided into four groups according to their baseline alcohol intake: abstainers (0 g/day) <5 g/day of alcohol (spline analysis <5 g) 5−15 g/day (spline analysis 5−15 g) >15 g/day (spline analysis >15 g) **Depression** were defined as a diagnosis of depression made by a physician and reported by participants in any of the follow-up interviews, or a positive report of habitual use of antidepressant drugs.	<5 g/day: 88/3,376 cases/person-years RR_{adj1}=0.76 (0.58, 1.00); RR_{adj2}=0.77 (0.58, 1.01) 5−15 g/day: 51/2,042 cases/person-years RR_{adj1}=0.70 (0.48, 1.00); RR_{adj2}=0.69 (0.47, 1.01) >15 g/day: 10/550 cases/person-years RR_{adj1}=0.62 (0.31, 1.23), p=0.216 for trend RR_{adj2}=0.64 (0.32, 1.28), p=0.275 for trend **Males** Abstainers: 22/1,708 cases/person-years RR_{adj1}=1.0 (Reference); RR_{adj2}=1.0 (Reference) <5 g/day: 26/2,352 cases/person-years RR_{adj1}=0.60 (0.30, 1.23); RR_{adj2}=0.60 (0.29, 1.23) 5−15 g/day: 28/3,348 cases/person-years RR_{adj1}=0.71 (0.36, 1.23); RR_{adj2}=0.68 (0.34, 1.35) >15 g/day: 45/4,210 cases/person-years RR_{adj1}=0.71 (0.37, 1.39), p=0.677 for trend RR_{adj2}=0.65 (0.33, 1.29), p=0.828 for trend RR_{adj1}: adjusted for age (and gender for total population only) RR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity, total energy intake, baseline BMI, marital status, intervention group, recruiting centre, educational level and the number of persons living at home. **HR (95% CI) for incident depression according to baseline categories of daily alcohol intake** **Females** Abstainers: 173/6,069 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <5 g/day: 88/3,376 cases/person-years HR_{adj1}=0.92 (0.71, 1.19); HR_{adj2}=0.99 (0.74, 1.31) 5−15 g/day: 51/2,042 cases/person-years HR_{adj1}=0.89 (0.65, 1.224); HR_{adj2}=0.83 (0.58, 1.18)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				>15 g/day: 10/550 cases/person-years HR_{adj1}=0.62 (0.33, 1.18), p=0.169 for trend HR_{adj2}=0.61 (0.30, 1.27), p=0.192 for trend **Males** Abstainers: 22/1,708 cases/person-years HR_{adj1}=1.0 (Reference); HR_{adj2}=1.0 (Reference) <5 g/day: 26/2,352 cases/person-years HR_{adj1}=0.86 (0.48, 1.53); HR_{adj2}=0.84 (0.42, 1.66) 5−15 g/day: 28/3,348 cases/person-years HR_{adj1}=0.68 (0.39, 1.21); HR_{adj2}=0.51 (0.26, 1.00) >15 g/day: 45/4,210 cases/person-years HR_{adj1}=0.84 (0.50, 1.43), p=0.868 for trend HR_{adj2}=0.75 (0.39, 1.43), p=0.909 for trend HR_{adj1}: adjusted for age (and gender for total population only) HR_{adj2}: Adjusted for age, gender (for total population only), smoking, physical activity, total energy intake, baseline BMI, marital status, intervention group, recruiting centre, educational level and the number of persons living at home.
Hiles et al. (2015) Australia Hunter Community Study	**Level:** II **Quality:** CPHE 33/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up:** 3.5 – 5.5 years	N=1,410 older adults (aged 55−85 at baseline) from Hunter Community Study Mean age 65.6±7.1 years N=711 females N=699 males	**Alcohol consumption** based on number of days when alcohol was consumed, and number of standard drinks consumed in past month. Hazardous use classified as those who drink over Australian alcohol guidelines (>4 standard drinks per day for men, >2 standard drinks per day for women). Safe use classified as those who drank within guidelines. **Depressive symptoms** on the CES-D, providing scores in range of 0 – 60 Depression categorised as ≥16 on the CES-D, reflecting at least mild depressive symptomatology and possible depression	**Unstandardised (b) and standardised (β) coefficients for variation in follow-up depressive symptoms not explained by baseline CES-D scores and age for females** Unadjusted (except for age and CES-D) No alcohol: Reference Safe use: b(SE)=-1.09(0.89); β=-0.06, p=0.224 Hazardous use: b(SE)=1.06(2.77); β=0.02, p=0.703 Use at unknown quantity: b(SE)=1.93(1.65); β=0.06, p=0.241 Lifestyle adjusted No alcohol: Reference Safe use: b(SE)=-1.63(0.99); β=-0.09, p=0.101; *r*=-0.08 Hazardous use: b(SE)=-0.83(2.77); β -0.02, p=0.764; *r*=-0.02

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Use at unknown quantity: b(SE)=0.30(1.81); β 0.01, p=0.870; *r*=0.01 <u>Fully adjusted</u> No alcohol: Reference Safe use: b(SE)=-1.71(1.02); β -0.09, p=0.951; *r*=-0.08 Hazardous use: b(SE)=-1.26(2.68); β=-0.02, p=0.639; *r*=-0.02 Use at unknown quantity: b(SE)=0.58(1.91); β=0.02, p=0.760; *r*=0.02 **Unstandardised (b) and standardised (β) coefficients for variation in follow-up depressive symptoms not explained by baseline CES-D scores and age for males** No alcohol: Reference Safe use: b(SE)=-0.02(0.85); β=-0.002, p=0.978 Hazardous use: b(SE)=-0.12(1.02); β=-0.006, p=0.910 Use at unknown quantity: b(SE)=0.11(1.18); β=0.004, p=0.924 <u>Lifestyle adjusted</u> No alcohol: Reference Safe use: b(SE)=0.64(0.65); β=0.04, p=0.327; *r*=0.03 Hazardous use: b(SE)=-0.10(0.89); β=-0.01, p=0.907; *r*=0.004 Use at unknown quantity: b(SE)=0.36(1.11); β=0.01, p=0.748; *r*=0.01 <u>Fully adjusted</u> No alcohol: Reference Safe use: b(SE)=0.58(0.65); β=0.04, p=0.377; *r*=0.03 Hazardous use: b(SE)=-0.12(0.97); β=-0.01, p=0.901; *r*=-0.004 Use at unknown quantity: b(SE)=-0.35(0.24); β=-0.06, p=0.155; *r*=-0.05 **OR (95%CI) after multivariate adjustment for depression, excluding those with depression at baseline for females**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Age adjusted No alcohol: OR=1.0 (Reference) Safe use: OR=0.70 (0.37, 1.32), p=0.271 Hazardous use: OR=1.03 (0.21, 5.09), p=0.974 Use at unknown quantity: OR=1.50 (0.63, 3.61), p=0.362 Lifestyle adjusted No alcohol: OR=1.0 (Reference) Safe use: OR=0.58 (0.29, 1.16), p=0.125 Hazardous use: OR=0.44 (0.05, 3.75), p=0.452 Use at unknown quantity: OR=1.10 (0.39, 3.11), p=0.851 Fully adjusted No alcohol: OR=1.0 (Reference) Safe use: OR=0.70 (0.33, 1.49), p=0.358 Hazardous use: OR=0.36 (0.04, 3.43), p=0.376 Use at unknown quantity: OR=1.05 (0.82, 1.34), p=0.525 **OR (95%CI) after multivariate adjustment for depression, excluding those with depression at baseline for males** Age adjusted No alcohol: OR=1.0 (Reference) Safe use: OR=0.82 (0.40, 2.10), p=0.842 Hazardous use: OR=0.88 (0.30, 2.62), p=0.824 Use at unknown quantity: OR=0.54 (0.11, 2.68), p=0.449 Lifestyle adjusted No alcohol: OR=1.0 (Reference) Safe use: OR+1.28 (0.46, 3.55), p=0.631 Hazardous use: OR=0.77 (0.20, 2.96), p=0.709 Use at unknown quantity: OR=0.84 (0.15, 4.72), p=0.842 Fully adjusted No alcohol: OR=1.0 (Reference) Safe use: OR=1.35 (0.45, 4.08), p=0.594 Hazardous use: OR=0.83 (0.20, 3.43), p=0.797

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Use at unknown quantity: OR=0.81 (0.13, 5.22), p=0.824 Adjusted for age, CES-D score, IL-6 level, CRP, waist-to-hip ratio, BMI, Steps per day, % energy intake from saturated fat, physical health problems, Quality of Life score; independent living, relationships, coping and pain
Lang et al. (2007) United Kingdom Household-based Health Survey for England (HSE) included all members of households ≥1 member was aged ≥50 years English Longitudinal Study of Ageing (ELSA)	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 1 year Wave 3: 3 years	N=7,286 participants in all 3 waves of ELSA who met inclusion criteria N=3,877 women aged ≥50 years N=147 ex-drinkers N=153 never drinkers N=2,902 >0−1 drinks/day N=529 >1−2 drinks/day N=143 >2 drinks/day N=3,409 men aged ≥50 years N=87 ex-drinkers N=46 never drinkers N=1,735 >0−1 drinks/day N=799 >1−2 drinks/day N=739 >2 drinks/day	**Alcohol consumption** was based on their answer to the question 'Do you ever drink alcohol nowadays, including drinks you brew or make at home?' For various types of alcohol, respondents who drank were asked how often they drank and on average how much they drank over the last 12 months. Mean daily alcohol consumption was calculated and participants were categorised as: <u>Ex-drinkers</u>, non-drinkers who used to be drinkers <u>Never-drinkers</u>, non-drinkers who have never been drinkers <u>>0−1 drink/day</u>, those drinking up to one drink (14 g of alcohol) per day <u>>1−2 drinks/day</u>, those drinking up to two drinks (28 g of alcohol) per day <u>>2 drinks/day</u>, those drinking more than two drinks (28 g of alcohol) per day **Depressive symptoms** were measured using a version of the CES-D. A subset of eight items out of the original twenty were coded dichotomously (yes/no) to give a score out of 8. A higher CES-D score is not necessarily diagnostic of depression but indicates more depressive symptoms.	**Linear regression z-scores (95% CI) for depressive symptoms by level of alcohol consumption for females** <u>Ex-drinkers</u> z=0.20 (−0.02, 0.42) <u>Never-drinkers</u> z=0.31 (0.08, 0.54), p<0.01 <u>>0−1 drink/day</u> Reference <u>>1−2 drinks/day</u> z=−0.02 (−0.13, 0.09) <u>>2 drinks/day</u> z=0.00 (−0.21, 0.22) **Linear regression z-scores (95% CI) for depressive symptoms by level of alcohol consumption for males** <u>Ex-drinkers</u> z=0.26 (0.02, 0.51), p<0.05 <u>Never-drinkers</u> z=0.12 (−0.13, 0.37) <u>>0−1 drink/day</u> Reference <u>>1−2 drinks/day</u> z=−0.13 (−0.21, −0.05), p<0.01 <u>>2 drinks/day</u> z=0.00 (−0.09, 0.10) Analyses controlled for: age; gender; BMI; education level; smoking; co-morbidity; income; household wealth; participation in moderate or vigorous exercise; number of close family members; number of close friends. There was little difference between men and women. Compared to those drinking >0−1 drink/day, those who do not drink alcohol had significantly more depressive symptoms and those who drink >1−2 drinks/day had significantly fewer. There was no difference in depression between those who drink >2 drinks/day and those who drink >0−1 drink/day.
Tait et al. (2012)	**Level:** II	N=39,104 participants contributed	**Alcohol consumption** was calculated	**GEE OR (95% CI) for depression according to level of**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Australia Population-based Dynamic Analyses to Optimise Ageing (DYNOPTA) included adults aged ≥45 years	**Quality:** CPHE 23/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: The median length of follow-up was 4 years (IQR 0–7.8) with the median number of interviews being three (IQR 1–3)	data N=17,668 aged 45−54 years N=5,255 aged 55−64 years N=13,060 aged 65−74 years N=2,620 aged 75−84 years N=501 aged ≥85 years N=7,526 abstinent N=28,112 low risk N=2,271 long-term risk N=1,195 short-term risk N=31,202 females N=7,902 males	from questions included in all the studies on the frequency and quantity of alcohol typically consumed, similar to the format in the AUDIT survey. Consumption was classified according to the Australian guidelines using standard drinks (10 g alcohol)/day <u>Abstinent</u> 0 standard drinks/day <u>Low risk</u> >0–≤2 standard drinks/day <u>Long-term risk</u> >2–≤4 standard drinks/day <u>Short-term risk</u> >4 standard drinks/day **Depression** was assessed using a range of established screening tools: CES-D in ALSA; SF-36 in ALSWH, AusDiab, and HILDA; MHC Summary score from SF-12 in PATH and PAS in MELSHA The scores were standardised using the recommended cut points and equating them to 1.0, 1.2, 1.6 and 1.8 standard deviations (SD) above the mean on the new binary harmonized variable. A cut-off of 1.5 SD above the mean was selected as an indicator of “probable depression.” The resultant prevalence by age and gender validated against national Australian data.	**alcohol consumption for females** Low risk: OR=1.0 (Reference) Abstinent: OR=1.23 (1.14, 1.32), p<0.001 Long-term risk: OR=1.22 (1.08, 1.38), p<0.05 Short-term risk: OR=1.54 (1.22, 1.95), p<0.001 **GEE OR (95% CI) for depression according to level of alcohol consumption for males** Low risk: OR=1.0 (Reference) Abstinent: OR=1.47 (1.22, 1.78), p<0.05 Long-term risk: OR=0.99 (0.82, 1.19) Short-term risk: OR=1.30 (1.06, 1.59), p<0.05 **GEE OR (95% CI) for depression participants who were always abstinent compared with those who were always low risk for females** Always Low risk (n=16,319): OR=1.0 (Reference) Always abstinent (n=18,320): OR=1.20 (1.08, 1.34), p<0.05 **GEE OR (95% CI) for depression participants who were always abstinent compared with those who were always low risk for males** Always Low risk: OR=1.0 (Reference) Always abstinent: OR=1.61 (1.01, 2.21), p<0.05
Tanaka et al. (2011) Japan Population-based Komo-Ise study included middle-	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:**	N=9,201 participants in the Komo-Ise study of middle-aged and elderly persons (aged 40-69 years) who were included in the analysis. N=4,875 women N=4,326 men	**Alcohol consumption** was assessed by asking, “Do you drink a lot of alcoholic beverages?” with possible answers of “yes,” “only a little,” or “never drink.” **Depression** was assessed using the 12-item DSM-12D self-administered questionnaire. The probe statement inquired as to whether the respondent	**OR (95% CI) for depression in 2000 according to alcohol consumption level in 1993 for females** <u>Never consumed alcohol</u> OR=1.00 (Reference) OR_{adj}=1.00 (Reference) <u>Light alcohol drinker</u> OR=0.79 (0.49, 1.28) OR_{adj}=0.67 (0.37, 1.19) <u>Heavy alcohol drinker</u>

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
aged and elderly persons living in the village of Komochi and the downtown area of the city of Isesaki.	Moderate risk of bias **Follow-up from baseline**: 7 years		had experienced a particular symptom of depression nearly every day for the past two weeks. Subjects reporting five or more symptoms of depression (including depressed mood or anhedonia) during their usual activities, were diagnosed with a MDE.	OR=1.01 (0.24, 4.24) OR_{adj}=0.39 (0.05, 3.08) **OR (95% CI) for depression in 2000 according to alcohol consumption level in 1993 for males** Never consumed alcohol OR=1.00 (Reference) OR_{adj}=1.00 (Reference) Light alcohol drinker OR=0.46 (0.25, 0.86),$p<0.05$ OR_{adj}=0.54 (0.26, 1.13) Heavy alcohol drinker OR=0.81 (0.42, 1.55) OR_{adj}=0.99 (0.46, 2.11) OR: adjusted for age OR_{adj}: adjusted for age, area, education, occupation, social network (marriage, household, neighbourhood, participation, and friends

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; AUDIT = Alcohol Use Disorder Identification Test; BMI = body mass index; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GEE = general estimating equation; HR = hazard ratio; MDD = major depressive disorder; MDE = major depressive episode; MHC = Mental Health Components Summary score; OR = odds ratio; PAS = Psychogeriatric Assessment Scales; RR = relative risk; SF-36 = Short-Form Health Survey-36

The effect of alcohol consumption on bipolar disorder (general population)

Table 26 Incident bipolar episode outcomes from studies that reported on population-based cohorts of mixed gender

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Chou et al. (2011) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 3 years	N=13,489 middle aged and older adults in the United States (aged ≥50 years) N=5,461 males 1,987 non-drinkers 2,616 current drinkers but no past year HED 310 past year HED <1 per month 548 past year HED ≥1 per month	**HED**: defined as 5 drinks or more (men) or 4 drinks or more (women) in one occasion. **Bipolar disorder** by AUDADIS-IV	**OR (95% CI) of Bipolar disorder at Wave 2 based on HED status at wave 1 in men** Non-drinkers: OR_{adj}=1.16 (0.58, 2.32) Current non-HED: OR_{adj}=1.0 (Reference) Past-year HED <1 per month: OR_{adj}=2.05 (0.83, 5.03) Past-year HED ≥1 per month: OR_{adj}=1.80 (0.67, 4.86) Adjusted for age, marital status, education, race, household income, employment status, lifetime history of row-defined psychiatric disorder prior to Wave 1 assessment, and lifetime

		N=7,981 females: 4,302 non drinkers 3,223 current drinkers but no past year HED 223 past year HED <1 per month 233 past year HED ≥1 per month		history of alcohol use disorder prior to Wave 1 assessment. **OR (95% CI) of Bipolar disorder at Wave 2 based on HED status at wave 1 in females** Non-drinkers: OR_{adj}=1.22 (0.78, 1.91) Current non-HED: OR_{adj}=1,0 (Reference) Past-year HED <1 per month: OR_{adj}=0.78 (0.25, 2.44) Past-year HED ≥1 per month: OR_{adj}=1.69 (0.62, 4.74) Adjusted for age, marital status, education, race, household income, employment status, lifetime history of row-defined psychiatric disorder prior to Wave 1 assessment, and lifetime history of alcohol use disorder prior to Wave 1 assessment.
Cougle et al. (2015) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** Unknown risk of bias (poor reporting on population) **Follow-up**: 3 years Wave 1: 2001-2002 Wave 2: 2004-2005	N=34,653 adults (nationally representative survey of non-institutionalised US citizens)	**Weekly alcohol consumption** by AUDADIS-IV (dose not stated) **Bipolar disorder** by AUDADIS-IV	**OR (95%CI) for incident bipolar disorder at wave 2** Reference: not stated (assume consumption of alcohol less than weekly) Weekly alcohol: OR_{adj}= 0.79 (0.73, 0.86), p<0.001 Adjusted for age, income, marital status, gender, ethnicity, education, and psychiatric comorbidity.

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; OR = odds ratio

The effect of alcohol consumption on suicidal ideation, attempts and completed suicides (general population)

All ages

Table 27 Suicide outcomes from studies that reported on older men and/or women from population-based cohorts, separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Glasheen et al. (2015) United States National Survey on Drug Use and Health data (NSDUH)	**Level** IV aetiological evidence **Quality**: CHPE 22/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias	N=136,500 adults (≥18 years) who had had at least one drink in past month from 2008 and 2012 surveys, with and without MDE as defined by DSM-IV	**Past month HED** (≥ 5 standard drinks at same time or within a couple hours) in the past 30 days **Suicidal ideation**: thoughts of trying to kill yourself in past 12 months **Suicide attempts:** trying to kill yourself in past 12 month	**Females** **OR (95%CI) of Suicidal ideation** No HED in past 30 days: OR=1.00 (reference) HED in past 30 days: OR=1.94 (1.74, 2.16) **OR (95%CI) of Suicide attempt** No HED in past 30 days: OR=1.00 (reference) HED in past 30 days: OR=2.77 (2.12, 3.61) **Adjusted OR (95%CI) of suicidal ideation** No HED: No MDE: OR_{adj}=1.00 (reference) MDE: OR_{adj}=14.91 (12.48, 17.81) HED: No MDE: OR_{adj}=1.51 (1.28, 1.79) MDE: OR_{adj}=14.53 (12.06, 17.50) **Adjusted OR (95%CI) of suicide attempt** No HED: No MDE: OR_{adj}=1.00 (reference) MDE: OR_{adj}=17.46 (11.10, 27.46) HED: No MDE: OR_{adj}=2.57 (1.74, 3.79) MDE: OR_{adj}=16.41 (11.28, 23.88) OR_{adj}: Adjusted for age, race/ethnicity, marital status, education, employment, income, illicit drug abuse/dependence. **MDE*HED interaction** Tests for an interaction of HED and MDE on the odds of suicide attempts indicated that the association between HED and suicide attempts was not equal in females with and without MDE (females: adjusted Wald χ^2=14.58(1), p<0.001). **Males** **Suicidal ideation** No HED in past 30 days: OR=1.00 (reference) HED in past 30 days: OR=1.73 (1.34, 2.23) **Suicide attempt** No HED in past 30 days: OR=1.00 (reference) HED in past 30 days: OR=2.64 (1.76, 3.95)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
				Adjusted OR (95%CI) of suicidal ideation No HED: No MDE: OR_{adj}=1.00 (reference) MDE: OR_{adj}=19.67 (15.21, 25.44) HED: No MDE: OR_{adj}=1.25 (1.04, 1.49) MDE: OR_{adj}=16.77 (13.55, 20.74) **Adjusted OR (95%CI) of suicide attempt** No hed: No MDE: OR_{adj}=1.00 (reference) MDE: OR_{adj}=11.38 (5.39, 24.05) HED: No MDE: OR_{adj}=1.52 (0.91, 2.52) MDE: OR_{adj}=17.66 (10.36, 30.10) OR_{adj}: Adjusted for age, race/ethnicity, marital status, education, employment, income, illicit drug abuse/dependence. **MDE*HED interaction** Tests for an interaction of HED and MDE on the odds of suicide attempts indicated that the association between HED and suicide attempts was not significant among males (adjusted Wald χ^2=0.01(1), p=0.989).

AUDIT = Alcohol Use Disorder Identification Test; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; HED= heavy episodic drinking; MDE= major depressive episode; OR = odds ratio

Adolescents

Table 28 Suicide outcomes from studies that reported on population-based cohorts of mixed gender

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Gart & Kelly (2015) United States Youth Risk Behavior Survey	**Level** IV aetiological evidence **Quality**: CHPE 20/34 **Internal validity:** High risk of bias (no	N=15,363 adolescents (grades 9 to 12) aged 16±1.2 years	**Frequency of heavy drinking** defined as no. of days drinking more than 5 drinks in a row (within a couple hours) in the past 30 days **Suicidal ideation** as a dichotomous outcome, whether they had ever considered suicide in past 12 months	**Bivariate correlation:** Days of 5 or more drinks - considered suicide: *r*=0.11, p<0.001 Days of 5 or more drinks - attempted suicide: *r*=0.15, p<0.001 Days of 5 or more drinks – suicide attempt with injury: *r*=0.12, p<0.001 **Multiple regression analysis of predictors of suicidal ideation (n=12,456):**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	controlling for other factors) **External validity:** High risk of bias		**Suicide attempt** – whether they had injured themselves from a suicide attempt in past 12 months, and no. of times they had attempted suicide in past 12 months.	Alcohol use: *B*=0.02, β=0.02, p=0.027 **Multiple regression analysis of predictors of suicide attempt (n=11,159):** Alcohol use: *B*=0.03, β=0.05, p<0.001
Peltzer & Pengpid (2015) Kiribati, Samoa, Solomon Islands and Vanuatu Global School-Based Health Survey (GSHS)	**Level** IV aetiological evidence **Quality**: CHPE 27/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias	N=6,540 adolescents from Pacific Island countries, predominantly aged 13 to 16 years old.	**Early alcohol initiation** based on question "How old were you when you had your first drink of alcohol other than a few sips?" with ordered categorical responses. **Suicidal ideation** based on question "During the past 12 months, did you plan about how you would attempt suicide?" as dichotomous yes, no answer. **Suicide attempts** based on question "During the past 12 months, how many times did you attempt suicide?" with ordered categorical responses.	**Total sample** **OR (95%CI) for suicidal ideation** Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=4.14 (3.52, 4.86) OR_{adj}=3.39 (2.44, 4.71) Alcohol initiated ≥12 years: OR=2.48 (2.01, 3.06) OR_{adj}=1.95 (1.32, 2.89) Current alcohol use: OR=2.69 (2.3, 3.12) **OR (95%CI) for suicide attempt** Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=8.48 (6.51, 11.06) OR_{adj}=4.55 (3.34, 6.21) Alcohol initiated ≥12 years: OR=2.89 (2.26, 3.70) OR_{adj}=1.64 (1.16, 2.32) Current alcohol use: OR=4.16 (3.44, 5.03) Adjusted for age, psychological distress and current alcohol use.
Schilling et al. (2009) United states Signs of Suicide program 2001-2002	**Level** IV aetiological evidence **Quality**: CHPE 26/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias	N=31,953 adolescents from 225 schools, predominantly aged 14 to 17 years old. 8.8% of those who participated in HED attempted suicide 3.3% of those who did not participate in HED attempted suicide	**Heavy episodic drinking** measured by question "In the past year, has there been a time when you had 5 or more alcohol drinks in a row". **Drinking while down** measured by "In the past year, have you used alcohol because you were feeling down?" (yes or no). **Suicidal ideation** measure by question "Has there been a time (in the past year) when you thought seriously about	**Multivariate logistic regression model predicting suicide attempts (95%CI)** HED: *B*=0.20 (0.06, 0.34), p<0.05 Drinking while down: *B*=0.56 (0.42, 0.69), p<0.05 Suicidal ideation: *B*=3.64 (3.39, 3.90), p<0.05 OR=38.2 (29.6, 48.3) Depressive symptoms: *B*=0.13 (0.10, 0.15), p<0.05 Drinking while down with prior ideation: OR=1.68 (1.46, 1.93) Drinking while down without prior ideation: OR=3.02 (2.03, 4.49) **Interaction: drinking while down * Ideation:**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			killing yourself?" (yes or no). **Suicide attempt** measured by question "Have you tried to kill yourself in the last year" (yes or no).	*B*=−0.59, SE=0.21 (−1.01, −0.18), p<0.05 Coefficient for interaction of suicidal ideation and drinking alcohol while down was significant and negative, indicating that drinking alcohol while down was associated with a higher risk of suicide attempts among those who did not report suicidal ideation. **Interaction: HED * Ideation:** *B*=−0.40, (−0.80, 0.01), NS Relationship between HED and suicide attempt did not differ between those who had suicidal ideation, and those who did not. (Although HED was a predictor of suicide attempt). Other factors in the logistic regression model: sex, age, race
Souza et al. (2010) Brazil	**Level** IV aetiological evidence **Quality**: CHPE 29/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias	N=1,039 adolescents from urban Brazil 225 had consumed alcohol in last month, 815 had not 40 had got drunk in last month, 814 had not	**Alcohol consumption** in previous month **Drunkenness** in previous month **Suicidal ideation** measured by item 9 of the Children's Depression Inventory, combining answers "I think of killing myself but I would not do it" and "I want to kill myself".	**OR (95%CI) for suicidal ideation** No alcohol consumption: OR=1.00 (reference) Alcohol consumption: OR=2.67 (1.84, 3.87), p<0.001 OR_{adj}=1.64 (1.04, 2.58), p=0.033 Did not get drunk: OR=1.00 (reference) Got drunk: OR=4.46 (2.31, 8.61), p<0.001 OR_{adj}=1.94 (0.86, 4.36) Adjusted for gender, age and socioeconomic status, sexual intercourse, alcohol consumption, drunkenness, tobacco use, and use of illicit drugs in previous month, symptoms of conduct disorder and high depressive symptoms.

CI = confidence interval; CPHE = Centre for Public Health Excellence; OR = odds ratio

Table 29 Suicide outcomes from studies that reported on males and females from population-based cohorts, seperately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Kim & Kim (2010) Korea 2006 Korean Youth Risk Behavior Survey	**Level** IV aetiological evidence **Quality**: CHPE 28/34 **Internal validity:**	N=63,884 adolescents, grades 7 – 12 (age 13 – 19 years) Males: 12,356 non-initiators; 13,595 teen initiators; 6,466 preteen initiators	**Age of drinking initiation** in three categories: non-initiation, preteen initiation, teen initiation **Suicidal ideation** based on whether participants had seriously considered attempting suicide during past 12	**Females** **OR (95%CI) of suicidal ideation** Non-initiators: OR=1.00 (reference) (20.1%); Teen initiators: OR=1.63 (1.54, 1.72) (29.1%); OR_{adj}=1.21 (1.12, 1.30) Preteen initiators: OR=2.33 (2.16, 2.50) (37.0%);

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
	Low risk of bias **External validity:** Low risk of bias	Females: 12,251 non-initiators; 14,442 teen initiators; 4,774 preteen initiators	months **Suicide attempts** based on whether participants had made a suicide attempt during past 12 months	OR_{adj}=1.45 (1.33, 1.59) **OR (95%CI) of suicide attempts** Non-initiators: OR=1.00 (reference) (3.3%); Teen initiators: OR=1.81 (1.61, 2.05) (5.8%); OR_{adj}=1.23 (1.05, 1.43) Preteen initiators: OR=3.36 (2.93, 3.85) (10.2%); OR_{adj}=1.61 (1.37, 1.89) adjusted for age, family living structure, household economic status, academic performance, perceived body weight, unhealthy weight control behaviour, current alcohol drinking, current cigarette smoking, current butane gas or glue sniffing, subjective sleep satisfaction, and depressed mood. **Males** **OR (95%CI) of suicidal ideation** Non-initiators: OR=1.00 (reference) (13.4%) Teen initiators: OR=1.60 (1.50, 1.71) (19.9%) OR_{adj}=1.11 (1.01, 1.22) Preteen initiators: OR=1.98 (1.83, 2.14) (23.4%) OR_{adj}=1.28 (1.16, 1.41) **OR (95%CI) of suicide attempts** Non-initiators: OR=1.00 (reference) (2.7%) Teen initiators: OR=1.58 (1.38, 1.82) (4.2%) OR_{adj}=1.06 (0.89, 1.27) Preteen initiators: OR=2.44 (2.11, 2.83) (6.4%) OR_{adj}=1.27 (1.06, 1.52) adjusted for age, family living structure, household economic status, academic performance, perceived body weight, unhealthy weight control behaviour, current alcohol drinking, current cigarette smoking, current butane gas or glue sniffing, subjective sleep satisfaction, and depressed mood.
Peltzer & Pengpid (2015)	**Level** IV aetiological	N=6,540 adolescents from Pacific Island countries, predominantly	**Early alcohol initiation** based on question “How old were you when you	**Females** **OR (95%CI) for suicidal ideation**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Kiribati, Samoa, Solomon Islands and Vanuatu Global School-Based Health Survey (GSHS)	evidence **Quality**: CHPE 27/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias	aged 13 to 16 years old.	had your first drink of alcohol other than a few sips?" with ordered categorical responses. **Suicidal ideation** based on question "During the past 12 months, did you plan about how you would attempt suicide?" as dichotomous yes, no answer. **Suicide attempts** based on question "During the past 12 months, how many times did you attempt suicide?" with ordered categorical responses.	Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=4.89 (3.63, 6.59) OR_{adj}= Alcohol initiated ≥12 years: OR=3.14 (2.41, 4.09) OR_{adj}= Current alcohol use: OR=3.20 (2.54, 4.03) **OR (95%CI) for suicide attempt** Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=10.36 (7.68, 13.97) OR_{adj}= Alcohol initiated ≥12 years: OR=3.75 (2.71, 5.19) OR_{adj}= Current alcohol use: OR=4.98 (3.60, 6.88) Adjusted for age, psychological distress and current alcohol use. **Males** **OR (95%CI) for suicidal ideation** Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=3.55 (2.6, 4.74) OR_{adj}=3.37 (2.16, 5.27) Alcohol initiated ≥12 years: OR=2.12 (1.5, 2.92) OR_{adj}=1.88 (1.14, 3.10) Current alcohol use: OR=2.37 (1.9, 2.87) **OR (95%CI) for suicide attempt** Alcohol non-initiators: OR=1.00 (reference) Alcohol initiated <12 years: OR=7.63 (5.18, 11.23) OR_{adj}= Alcohol initiated ≥12 years: OR=2.37 (1.75, 3.20) OR_{adj}= Current alcohol use: OR=4.54 (2.85, 4.41) Adjusted for age, psychological distress and current alcohol use.

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results

CI = confidence interval; CPHE = Centre for Public Health Excellence; OR = odds ratio

Young Adults

Table 30 Suicide outcomes from the study that reported on young adult men

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Grazioli et al. (2018) Switzerland Army-based Cohort Study on Substance Use Risk Factors (C-SURF)	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up from baseline**: 15 months	N=4,617 young men, aged 19−20 years, who completed both waves of C-SURF and were not abstainers at baseline (mean age =19.95±1.19 years	**Total drinks per week** over the past 12 months were computed by multiplying the number of drinking days by the number of drinks per drinking day. Average number of drinking days and the number of standard drinks (a standard drink =10 g of ethanol) consumed per drinking day over the past 12 months were measured at baseline and at follow-up. **HED** was defined as consuming 60 g or more of pure alcohol quickly on a single, discrete occasion. Participants were asked to indicate how often they drank six or more alcoholic beverages (> 60 g of pure alcohol) on one occasion in the past 12 months with a Likert scale ranging from 0=never, to 5=every day or almost every day. Answers were dichotomized to yield a report of monthly HED, where 0=reporting less than once per month and, 1=reporting one or more per month. **Suicide attempts** at follow-up were measured with one item. Participants were asked to indicate how often they	**SEM path coefficients for full model (Model 3):** **Total association between alcohol consumption at baseline and suicide attempt at 15-months** Total drinks /week: β=−0.049 (−0.266, 0.148); *B*=−0.063 (0.104) HED: β=−0.049 (−0.443, 0.212); *B*=−0.124 (0.167) **Direct effect: alcohol on suicide** Total drinks /week: β=−0.019 (−0.289, 0.260) HED: β=0.119 (−0.408, 0.665) **Indirect effect: alcohol through baseline depression on suicide** Total drinks /week β=−0.042 (−0.097, −0.024); *B*=−0.054 (0.019) HED β=−0.030 (−0.143, −0.029); *B*=−0.077 (0.031) Adjusted for demographic covariates on mediators and the main outcome (suicide attempt) The total prospective associations between alcohol use at baseline and suicide attempts at follow-up were not significant for either total drinks/week or HED. The indirect associations through depressive symptoms were significant and positive: baseline alcohol use was positively related to baseline depressive symptoms, which in turn increased the risk for follow-up suicide attempt **Bivariate correlations between alcohol consumption at**

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
			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 with 0=no suicide attempt, 1=at least one suicide attempt.	**baseline and suicide attempt at 12 months** Total drinks /week: rho=0.01 HED rho=0.00

CPHE = Centre for Public Health Excellence; SEM = structural equation models

Adults

Table 31 Suicide outcomes from studies that reported on adults (mostly men)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Conner et al. (2017) United states Individuals in New Mexico ages 18−54 years that died in 2012 by suicide or motor vehicle collisions	**Level:** III-3 **Quality:** CPHE 26/24 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias	N=185/264 (70%) suicide victims 34 excluded due to missing or out-of-range data 45 excluded due to poisoning 5 Asian/Pacific Islanders 4 African Americans 18% women N=161/195 (83%) comparator (motor vehicle accident victims) 34 excluded due to missing or out-of-range data 3 Asian/Pacific Islanders 4 African Americans 29% women	**Alcohol and drug use** were determined by toxicology reports The presence of alcohol was based on blood alcohol concentrations ≥ 0.001 g/dl (below legal limit) The presence of 1 or more drugs including cocaine, opiate, amphetamine or methamphetamine was determined by a positive result Victims were grouped into 4 categories: Alcohol + Drug Alcohol (without drug) Drug (without alcohol) Neither **Suicide**: individuals that died in 2012 by suicide were compared to those who dies in a motor vehicle accident	**OR (95% CI) of dying by suicide compared with motor vehicle accident if blood toxicology shows the presence of alcohol alone or in combination with another drug.** Alcohol alone OR=1.02 (0.64, 1.60) OR_{adj}=1.22 (0.74, 2.00) Alcohol plus drug OR=3.34 (1.36, 8.21), p<0.05 OR_{adj}=4.33 (1.70, 11.03), p<0.05 Drug alone OR=1.22 (0.46, 3.25) OR_{adj}=1.03 (0.37, 2.88) Neither 1.0 (Reference) OR_{adj}: adjusted for gender, age (18−34, 35−54), and race/ethnicity (Hispanic, American Indian/Alaskan Native [AI/AN], white non-Hispanic).
Herberman et al. (2016) United States	**Level** IV aetiological evidence	N=3,813 soldiers who completed all relevant survey items and were lifetime alcohol users.	**Average daily alcohol use** based on past 30 days (typical volumes of alcohol of beer, wine and liquor, converted to	**OR (95%CI) of suicidality** Light/moderate alcohol use: OR=1.00 (reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Department of Defense Survey of Health-Related Behaviors among Active Duty Military Personnel (DoD HRB)	**Quality**: CHPE 27/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias	43% were aged 17 to 25 (n=1,600) 87% male (n=2,840) 67% non-Hispanic White 31% had high school education or less 43% unmarried 80% enlisted 32% heavy drinkers 5% light/moderate drinkers were suicidal 8% of heavy drinkers were suicidal	ounces of ethanol). **Heavy alcohol use** defined as average daily ethanol consumption of ≥1.72 ounces (48.8 g) for men and ≥0.86 ounces (24.4 g) for women **Suicidality** based on "have you seriously considered suicide" and "have you ever attempted suicide" in past year.	Heavy alcohol use: OR=1.65 (1.15, 2.38), χ^2=7.40, p=0.007 OR_{adj}=1.05 (0.67, 1.65), χ^2=0.05, p=0.822 adjusted for age, gender, race, education, marital status, enlistment status, average daily alcohol use, depression, PTSD, avoid rejection/"fit in" motive, and pleasure-seeking./enjoyment motive. Heavy drinkers much more likely to be suicidal, however, this was no longer significant after adjustments for confounding factors such as level of depression and motives for drinking. Those drinking to "fit in" had 1.78 the odds of being suicidal than those drinking for other reasons. There was no association between drinking for pleasure-seeking/enjoyment and suicidality.

AUDIT = Alcohol Use Disorder Identification Test; CI = confidence interval; CPHE = Centre for Public Health Excellence; OR = odds ratio

The effect of alcohol consumption on anxiety and symptoms of anxiety (general population)

All ages

Table 32 Anxiety outcomes from studies that reported on population-based cohorts of mixed gender and with a broad age range

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Cougle et al. (2015) United States National Epidemiologic Survey on Alcohol and Related Conditions	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias (poor reporting on	N=34,653 adults, aged 18 years and older, (nationally representative survey of non-institutionalised US citizens)	**Weekly alcohol consumption** by AUDADIS-IV (dose not stated) **GAD** by AUDADIS-IV	**Odds ratio (95%CI) for incident GAD at wave 2** Reference: not stated (assume consumption of alcohol less than weekly) Weekly alcohol: OR_{adj}=0.88 (0.82, 0.95), p<0.01 Adjusted for age, income, marital status, gender, ethnicity, education, and psychiatric comorbidity.

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
(NESARC)	population) **Follow-up**: 3 years Wave 1: 2001-2002 Wave 2: 2004-2005			
Dawson et al (2008) United States National Epidemiological Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 31/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up:** 3 years	N=22,122 adults ≥18 years old who had at least one drink in year preceding Wave 1 interview, from a nationally representative study in the United States.	**Frequency of risk drinking** defined as the frequency of drinking ≥5 drinks/day; and ≥2.7 ounces (≥5.5 standard drinks) of ethanol in a single day for men. Defined as the frequency of drinking ≥4 drinks/day; and ≥2.1 ounces (≥4.5 standard drinks) of ethanol in a single day for women. Frequencies reflect number of risk drinking days in year preceding Wave 1 interviews. **Any anxiety disorder** on the Wave 2 interview (derivation not described).	**Adjusted OR (95%CI) for association between frequency of risk drinking at Wave 1 and incidence of any anxiety disorder** Never: 1.00 (Reference) <1/month: 1.03 (0.81, 1.31) 1-3/month: 1.13 (0.85, 1.51) 1-2/week: 1.09 (0.80, 1.48) 3-4/week: 1.43 (0.95, 2.13) Daily/near daily: 1.31 (0.92, 1.88) Adjusted for age, sex, race/ethnicity, whether married, whether employed, whether attended/completed college, health status, body mass index, tobacco use, drug use, any mood or anxiety disorder, any personality disorder, family history of alcoholism, volume of ethanol intake consumed on non-risk drinking days and mean quantity of drinks consumed on risk drinking days, and years since first drink.

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD = generalised anxiety disorder; OR = odds ratio

Table 33 Anxiety outcomes from studies that reported on males and/or females with a broad age range separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Adults and elderly adults				
Flensborg-Madsen et al. (2011) Denmark	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias	N=18,146 adults aged ≥20 years who completed at least one of the three questionnaires in CCHS waves I–III	**Alcohol consumption** was obtained from all 3 waves where participants were asked in multiple-choice format to describe their alcohol habits. The average weekly intake of beer, wine	**HR (95% CI) of incident anxiety disorders for women who reported drinking above the sensible drinking 15−21 drinks per week in the previous survey compared to non-drinkers** 0 drinks/week 1.0 (Reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Population-based Copenhagen City Heart Study (CCHS) enrolled adults aged ≥20 years	**External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 5 years from baseline Wave 3: 15 years from baseline		and spirits was summed to the total alcohol intake (with one bottle of beer being approximately equivalent to the alcohol contents of one glass of wine or one glass of spirits, assuming each drink contains 12 g of alcohol) Participants were divided into those drinking below and those drinking above the sensible drinking guidelines of 14 drinks per week for women and 21 drinks per week for men. **Anxiety** was diagnosed from Danish psychiatric hospital admissions and discharge registers.	>0−14 drinks/week <1.0 (from graph) 15−21 drinks/week 1.92 (1.10–3.33), p<0.05 >21 drinks/week 1.74 (from graph) **HR (95% CI) of incident anxiety disorders for women who reported drinking above the sensible drinking limit of 14 drinks per week in the previous survey** 0−14 drinks/week 1.0 (Reference) >14 drinks/week 2.00 (1.31, 3.04), p<0.05 **HR (95% CI) of incident anxiety disorders for men who reported drinking above the sensible drinking limit of 21 drinks per week in the previous survey** 0−21 drinks/week 1.0 (Reference) >21 drinks/week 0.79 (0.42, 1.50) HRs are Adjusted for smoking, co-habitation status, education, and income.
Johnson et al. (2013) United States Chicago Health and Life Experiences of Women (CHLEW) study	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 4 years	N=382 adult women who identify as lesbian (aged 18-83 years)	**Hazardous drinking** by combining indicators of heavier drinking and adverse consequences. HED: ≥1 occasions of drinking ≥6 drinks/day Subjective intoxification: ≥1 or more occasions of having consumed "enough to feel drunk – that is, when drinking noticeably affected your thinking, talking and behaviour" based on past 12-month reports. Adverse drinking consequences (e.g. driving while drunk, complaints about drinking by partner) and symptoms of potential alcohol dependence (e.g. memory lapses, inability to stop or reduce consumption). **Anxiety** assessed on 5-point Likert scale,	**Longitudinal effects of hazardous drinking and anxiety on one another.** No significant relationship between hazardous drinking (wave 1) and anxiety (wave 2), after adjusting for baseline anxiety (although wave 1 anxiety was associated with wave 2 hazardous drinking).

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
			with items adapted from the neuroticism scale of the Eysenck Personality Questionnaire.	

CI = confidence interval; CPHE = Centre for Public Health Excellence; HR = hazard ratio

Adolescents

Table 34 Anxiety outcomes from studies that reported on adolescents of both genders together

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Fröjd et al. (2011) Finland School-based Adolescent Mental Health Cohort Study (AMHCS) included adolescents aged 15−16 years	**Level:** II **Quality:** CPHE 24/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**:2 years	N=2,070 ninth grade students, aged 15−16 years Those with an intact family and those with better educated parents responded to the follow-up more frequently. General anxiety and higher levels of alcohol use were associated with a lower probability of responding	**Frequency of drinking alcohol** was elicited by the question: 'How often do you use alcoholic beverages?' **Frequency of drunkenness** was elicited by the question: 'How often do you drink alcohol until you are really drunk?' Response options were once a week or more often, approximately once or twice a month, less often and never. <u>Frequently drink alcohol</u> was defined as 'Once a week or more often'. <u>Frequently drunk</u> was defined as 'Once a week or more often'. **General anxiety** was measured by a single question: 'I don't easily lose my nerve or get anxious' (=0)/'I don't feel anxious or nervous' (=0); 'I get anxious and nervous rather easily' (=1); 'I get very easily distressed, anxious or nervous' (=2); 'I am constantly anxious and distressed, my nerves are always on edge' (=3). Scores of 2–3 were taken as symptomatic of significant anxiety.	**OR (95% CI) for the incidence of anxiety at 2 years in students who frequently drink alcohol (n=78) compared to those who do not** OR_{adj1}=1.6 (0.78, 3.4) OR_{adj2}=1.3 (0.6, 2.8) **OR (95% CI) for the incidence of anxiety at 2 years in students who are frequently drunk (n=62) compared to those who do not** OR_{adj1}=1.2 (0.3, 5.0) OR_{adj2}=0.8 (0.2, 3.6) OR_{adj1}: adjusted for gender, family structure and parental education OR_{adj2}: additionally adjusted for depression

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Mackie et al. (2011) United Kingdom London secondary school-based study	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up from baseline**: Wave 2: 6 months Wave 3: 12 months Wave 4: 18 months	N=393 students met inclusion criteria N=61 low risk for substance abuse N=73 scored high for hopelessness N=89 scored high for anxiety sensitivity N=81 scored high for impulsivity N=89 scored high for sensation seeking Mean age 13 years, 9 months at W1 Slightly more boys (53.5%) than girls (47.5%) reported consuming alcohol at W1. Students who scored higher in H and IMP were more likely to be consuming alcohol and HED at T1.	**Alcohol Use** was assessed using a quantity by frequency (Q×F) composite score as a continuous variable. Quantity was assessed by asking participants how many alcoholic drinks they would consume on a typical day in which they drank (none to ≥10). Frequency was assessed by asking participants how often they have an alcoholic drink (never to almost daily). HED was assessed by asking participants whether they had consumed ≥5 (for males) or ≥4 (for girls) drinks on one occasion in the past 6 months. The Q×F measure demonstrated a positive skew as some participants reported little or no alcohol use, so a natural log transformation was used for analyses. **Anxiety** was assessed using the Brief Symptom Inventory (BSI). Anxiety symptoms were assessed by five items (i.e. feeling tense, fearful, restless, scared for no reason, nervousness or shakiness). Participants were asked to rate the frequency of each item occurrence on a five-point scale (not at all, a little bit, moderately, quite a bit, often) in the previous 6 months. A 6-month time frame was used instead of the standard 7 days to fit in with the 6-month follow-up periods.	**Bivariate Correlations of Q×F Alcohol Use with Anxiety** Wave 1 Q×F: anxiety at: W1 *r*=0.26, p<0.001 W2 *r*=0.16, p<0.05 W3 *r*=−0.02 W4 *r*=0.05 Wave 2 Q×F: anxiety at W2 *r*=0.08 W3 *r*=0.01 W4 *r*=0.13. p<0.05 Wave 3 Q×F: anxiety at W3 *r*=−0.01 W4 *r*=0.10 Wave 4 Q×F: depression at W4 *r*=0.23, p<0.001 Q×F and anxiety were weakly correlated **Parameter Estimates for Unconditional Linear Growth Models** Q×F: Intercept β=0.42, p<0.01 Slope β=0.02, p<0.05 Intercept-Slope covariance β=−0.001 Anxiety Intercept β=10.03, p<0.01 Slope β=−0.21, p<0.01 Intercept-Slope covariance β=−0.003, p<0.05 Q×F significantly increased over time Anxiety showed a significant decrease over time **SEM regression analysis of causal relationship between alcohol use and anxiety** There was no significant directional effects between Q×F and anxiety (p>0.39).
Pardee et al.	**Level:** II	N=387 adolescents (aged 11 –	**Alcohol consumption** assessed using 2 items from the National Youth Survey on	**Parallel process growth curve model, unstandardized**

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
(2014) United States	**Quality:** CPHE 21/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 3 years	13 years at baseline) Mean age 12.09 years 55% female	quantity and frequency of past year alcohol use. Quantity x frequency index computed and converted into a 3-level ordinal variable (no use in past year; 1-5 drinks in past year; ≥5 drinks in past year) **Generalised anxiety** assessed on Youth Self Report, scored using Lengua's system that distinguishes DSM categories of anxiety.	**parameter estimates** Alcohol intercept to general anxiety slope: Unstandardised covariance *B*=0.001 High initial alcohol use has no association with changes in general anxiety. Alcohol slope to general anxiety slope: Unstandardised covariance *B*=0.012, $p<0.05$ Standardised *r*=0.14 Slower than average declines in general anxiety symptoms were associated with more rapid increases in alcohol use (slope covariance). (Although high initial social or general anxiety associated with increasing amounts of alcohol).
Parrish et al. (2016) United States California Families Project	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years	N=620 Mexican-origin youth living in California, age 14 at baseline 50% female 16% of participants at age 14 had tried alcohol at least once in the last 3 months. Mean=1.12±0.34, range 1.00–3.67 23% of participants at age 16 had tried alcohol at least once in the last 3 months. Mean=1.19±0.45, range 1.00–4.00	**Frequency of alcohol use:** how many times in past 3 months they had used or tried (more than just a few sips) beer, wine or wine coolers, or liquor using a 5-point scale (1="Never"; 5="Almost every day or every day"). Frequency of alcohol use was computed as a continuous variable by taking the mean of the three drink types **Anxiety symptoms** using the 3-item Anxiety subscale of the Mini-Mood and Anxiety Symptom Questionnaire Participants rated how much they "felt or experienced" each symptom "during the past week" using a 5-point scale at age 14 and a 4-point scale at age 16 (continuous variable).	**SEM cross-lagged latent variable regression models.** **Standardised estimates of structural coefficients in bivariate models:** Frequency of alcohol use (age 14) and Anxiety symptoms (age 16): Unadjusted β=0.03 Adjusted β=0.02 Adjusted for gender and generational status and delinquency

CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM = Diagnostic and Statistical Manual of Mental Disorders; OR = odds ratio; SEM = structural equation models

Table 35 Anxiety outcomes from studies that reported on male and/or female adolescents separately

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Cerda et al. (2016) United States Pittsburgh Youth Study (PYS)	**Level:** II **Quality:** CPHE 29/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 13 years (annually or semi-annually)	N=503 boys from public schools in Pittsburgh who participated in the PYS, data taken from Waves when aged 13−19 years Mean T-scores for alcohol frequency: Age 13 years, 5.66±30.60 Age 19 years 49.38±101.36 Mean T-scores for alcohol quantity: Age 13 years, 1.19±2.43 Age 19 years 4.25±4.03 Mean T-scores for anxiety: Age 13 years, 53.55±3.62 Age 19 years 51.52±3.87	**Alcohol use** measured by 16-item Substance Use Scale adapted from the National Youth Survey. Alcohol frequency: number of drinking occasions in past year. Alcohol quantity: average number of drinks per occasion in past year. **Anxiety:** DSM-IV diagnosis as determined by CBLC, TRF, YSR and YASR from Achenback system of assessment. Scores transformed to T scores based on age- and gender-specific national norms.	**Alcohol quantity predicting changes in anxiety T-scores (n=489)** Alcohol quantity: β=0.33 (95%CI 0.05, 0.61) $p<0.05$ Alcohol quantity * age 13-14: β=−0.36 (95%CI −0.62, −0.11) $p<0.05$ Alcohol quantity * age 15-16: β=−0.26 (95%CI −0.84, 0.32) Alcohol quantity * age 17-19: β=−0.20 (95%CI −0.38, −0.02) $p<0.05$ The effect of quantity of alcohol on anxiety was strongest in early adolescence (13-14 years) and although the effect size was smallest in late adolescence (17-19 years) the effect was statistically significant. **Changes in anxiety problem T scores with lagged changes in alcohol frequency and quantity** Alcohol frequency: β=−0.00002 (95%CI −0.003, 0.003) Alcohol quantity: β=0.12 (95%CI 0.05, 0.19), $p<0.05$ Controlling for age trends. Results were similar when also controlling for prior SES, psychiatric problem domains not modelled as the outcome, and substance use measures not the exposure of interest. During years in which adolescents experienced a one-unit increase in alcohol consumed when drinking, their anxiety T-score increased in the following year by 0.12 (95%CI 0.05, 0.19)
Edwards et al. (2014) United Kingdom Population-based Avon Longitudinal Study of Parents	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias	N=7,100 adolescents, aged 13−15 years, had data on frequency of alcohol use available N=3,630 females N=3,470 males N=4,292 adolescents has data	**Alcohol use:** participants attended clinics and answered questions related to their alcohol use via computerized questionnaires. Participants' reports of drinking frequency was classified into three categories (none, occasional, or weekly use). This measure (assessed at three ages) was	**Logistic regression OR (95% CI) for the impact of medium and high alcohol drinking on anxiety compared with low alcohol drinking** Low alcohol use: OR=1.00 (Reference) Medium alcohol use: Females OR=1.25 (0.88, 1.77) OR_{adj}=1.19 (0.80, 1.76) Males OR=1.13 (0.65, 1.95)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
and Children (ALSPAC), during adolescence	**Follow-up from baseline**: Median 2 years and 5 months	on depression and anxiety N=2,414 females N=1,878 males	subjected to longitudinal latent class analysis to capture drinking frequency over time (ages 13–15), yielding three categories (low, medium, and high). **Anxiety-dependent variables:** The Clinical Interview Schedule–Revised (CIS-R) was self-administered via computer. Last-month mild, moderate, and severe anxiety disorders (generalized anxiety disorder, phobias, obsessive–compulsive disorder, and panic disorder) were assessed and Individuals who met ICD criteria for an anxiety disorder were coded 1, otherwise they were coded 0.	High alcohol use Females OR=1.78 (1.13, 2.81), p<0.05 OR_{adj}=1.41 (0.84, 2.36) Males OR=1.20 (0.55, 2.62) OR_{adj}: adjusted for housing tenure (mortgaged/owned/ rented/subsidised rental), conduct problems at age 11, maternal depression factor score

CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD = generalised anxiety disorder; ICD = International Classification of Diseases; OR = odds ratio; SEM = structural equation models; SES = socioeconomic status.

Older adults

Table 36 Anxiety outcomes from the study that reported on older males

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Chou et al. (2011) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 3 years	N=13,489 middle aged and older adults in the United States (aged ≥50 years) N=7,981 females 4,302 non-drinkers 3,223 current drinkers but no past year HED 223 past year HED <1 per month 233 past year HED ≥1 per month N=5,461 males	**HED**: defined as 5 drinks or more (men) or 4 drinks or more (women) in one occasion. **GAD** by AUDADIS-IV	**OR (95% CI) of GAD at Wave 2 based on HED status wave 1 for women** Non-drinkers: OR_{adj}=1.20 (0.88, 1.64) Current non-HED: OR_{adj}=1.0 (Reference) Past-year HED <1 per month: OR_{adj}=1.28 (0.58, 2.82) Past-year HED ≥1 per month: OR_{adj}=0.50 (0.18, 1.39) **OR (95% CI) of GAD at Wave 2 based on HED status wave 1 for men** Non-drinkers: OR_{adj}=0.85 (0.49, 1.48) Current non-HED: OR_{adj}=1.0 (Reference)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
		1,987 non-drinkers 2,616 current drinkers but no past year HED 310 past year HED <1 per month 548 past year HED ≥1 per month		Past-year HED <1 per month: OR_{adj}=2.25 (0.87, 5.80) Past-year HED ≥1 per month: OR_{adj}=0.88 (0.32, 2.42) Adjusted for age, marital status, education, race, household income, employment status, lifetime history of row-defined psychiatric disorder prior to Wave 1 assessment, and lifetime history of alcohol use disorder prior to Wave 1 assessment.

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD = generalised anxiety disorder; OR = odds ratio

The effect of alcohol consumption on PTSD

Table 37 PTSD outcomes from studies that reported cohorts from the general population (with and without exposure to trauma)

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Cisler et al (2012) United States National Survey of Adolescents – Replication (NSA-R)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 15.3±4.6 months between wave 1 and 2 14.4±2.7 months between wave 2 and 3 29.0±4.5 between wave 1 and 3	N=3,614 adolescents aged 12−17 years residing in the United States who participated in Wave 1 of the National Survey of Adolescents-Replication (NSA-R). N=2,511 participated in Wave 2 N=1,653 participated in Wave 3	**HED frequency** defined as how many days in past 12 months, had they consumed ≥5 alcoholic drinks **PTSD symptoms** defined by PTSD module of the NSA survey (assessing DSM-IV symptoms	**Multiple regression analyses predicting PTSD at wave 2 (from wave 1 HED)** Original data (n=2,511) β=0.01, t=0.74 Multiple imputation (n=3,614) β=0.02, t=1.01 Adjusted for ethnicity, sex, age, interpersonal violence, baseline PTSD, delinquency, baseline depression. **Multiple regression analyses predicting PTSD at wave 3 from wave 1 HED** Original data (n=1,653) β=0.03, t=1.15 Multiple imputation (n=3,614) β=0.14, t=2.20, p<0.05 Adjusted for ethnicity, sex, age, interpersonal violence, baseline PTSD, delinquency, baseline depression.

Chou et al. (2011) United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 3 years	N=13,489 middle aged and older adults in the United States (aged ≥50 years) N=7,981 females 4,302 non-drinkers 3,223 current drinkers but no past year HED 223 past year HED <1 per month 233 past year HED ≥1 per month N=5,461 males 1,987 non-drinkers 2,616 current drinkers but no past year HED 310 past year HED <1 per month 548 past year HED ≥1 per month	**HED**: defined as 5 drinks or more (men) or 4 drinks or more (women) in one occasion. **PTSD** by AUDADIS-IV	**OR (95% CI) of PTSD at Wave 2 based on HED status wave 1 for females** Non-drinkers: OR_{adj}=1.21 (0.80, 1.85) Current non-HED: OR_{adj}=1.0 (Reference) Past-year HED <1 per month: OR_{adj}=2.67 (1.05, 6.84) Past-year HED ≥1 per month: OR_{adj}=1.45 (0.80, 2.62) **OR (95% CI) of PTSD at Wave 2 based on HED status wave 1 for males** Non-drinkers: OR_{adj}=0.89 (0.49, 1.62) Current non-HED: OR_{adj}=1.0 (Reference) Past-year HED <1 per month: OR_{adj}=0.63 (0.13, 2.99) Past-year HED ≥1 per month: OR_{adj}=1.36 (0.61, 3.04) Adjusted for age, marital status, education, race, household income, employment status, lifetime history of row-defined psychiatric disorder prior to Wave 1 assessment, and lifetime history of alcohol use disorder prior to Wave 1 assessment.
Read et al. (2016) United States	**Level:** II **Quality:** CPHE 11/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up**: T1 to T2: 3 months T2 to T3: 4 months	N=944 first-year college students who either did or did not meet trauma criteria at baseline. 65% female Mean age 18.11±0.44 years N=597 T1 (September) drinkers with mean 4.63±2.35 drinks/occasion N=665 T2 (December) drinkers with a mean 3.84±2.45 drinks/occasion N=605 T3 (April) drinkers with mean 4.39±2.48 drinks/occasion	**Alcohol consumption** based on past month alcohol use, dichotomised into drinkers and non-drinkers (no alcohol in the past month) **PTSD symptoms** on the PCL-C. Divided into 3 classes: Severe PTSD symptoms: symptom class 1 Moderate PTSD symptoms: symptom class 2 No PTSD symptoms: symptom class 3	**Latent transition analysis with covariate effect of drinker status on PTSD transitions (n=904)** T1 to T2 / T2 to T3 Continuing with severe PTSD: Reference Transition from severe to moderate PTSD: OR=0.97 / OR=0.82 Transition from severe to no PTSD: OR=1.20 / OR=1.10 Continuing with moderate PTSD: Reference Transition from moderate to severe PTSD: OR=1.28 / OR=1.51 Transition from moderate to no PTSD: OR=1.34 / OR=1.12 Continuing with no PTSD: Reference: Transition from no to severe PTSD: OR=0.68 / OR=0.83 Transition from no to moderate PTSD: OR=1.35 / OR=0.76 No 95%CI or p-values provided. Significance of odds therefore unknown.

AUDADIS-IV = National Institute on Alcohol and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; OR = odds ratio; PCL-C = PTSD Checklist Civilian Version; PTSD = post-traumatic stress disorder

The effect of alcohol consumption on depression and suicidal behaviour in people with existing mental and physical illnesses

People with unipolar depressive mood disorders

Table 38 Depression and suicidal behaviour outcomes from studies that reported on people diagnosed with depressive disorders at baseline

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
Adolescents				
Meririnne et al. (2010) Finland Adolescent Depression Study	**Level:** II **Quality:** CPHE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up:** 1 year	N=197 adolescents with unipolar depression at baseline (scoring ≥10 on BDI and ≥4 on General Health Questionnaire) in a naturalistic treatment setting.	**Alcohol consumption** on the K-SADS-PL interview and AUDIT questionnaire**.** Categorised into: **Excessive use**: weekly drunkenness, or consuming typically more than 7 (females) or 10 (males) drinks/session; **Regular use**: monthly use, not weekly use, and not excessive use; N**o/occasional use:** abstinence/ less than monthly use. **Depression** on the BDI. Remission defined as a score <10. Diagnostic recovery defined as remission without relapse based on diagnostic interview.	**Univariate HR (95% CI) for remission on BDI at follow-up** No/occasional use: HR=1.00 (Reference) Regular users: HR=0.86 (0.61, 1.23); p=0.411 Excessive users: HR=0.43 (0.24, 0.75), p=0.003 **Multivariate HR (95% CI) for remission on BDI at follow-up** No/occasional use: HR=1.00 (Reference) Regular users: HR=1.02 (0.71, 1.47), p=0.904 Excessive users: HR=0.49 (0.27, 0.89), p=0.020 Adjusted for sex, age, depression diagnosis and BDI scores at baseline, comorbidity, personality disorder, and GAF scores at baseline. **Univariate OR (95% CI) for recovery of depression at follow-up** No/occasional use: OR=1.00 (Reference) Regular users: OR=1.22 (0.62, 2.40), p=0.559 Excessive users: OR=0.69 (0.26, 1.78), p=0.440 **Multivariate OR (95% CI) for recovery of depression at follow-up** No/occasional use: OR=1.00 (Reference) Regular users: OR=1.28 (0.63, 2.59), p=0.500 Excessive users: OR=0.96 (0.35, 2.66), p=0.942 Adjusted for sex, age, depression diagnosis and BDI scores at

Study / Location / Setting	Level of evidence / Quality / Follow-up	Population	Variable definitions	Results
				baseline, comorbidity, personality disorder, and GAF scores at baseline. Alcohol did not predict sustained recovery, however, excessive alcohol use predicted poorer likelihood for remission from depressive symptoms.

AUDIT = Alcohol Use Disorder Identification Test; BDI = Beck's Depression Inventory; CI = confidence interval; CPHE = Centre for Public Health Excellence; HR = hazard ratio; K-SADS-PL Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; OR = odds ratio

People with bipolar disorder

Table 39 Depression and suicidal behaviour outcomes from studies that reported on people diagnosed with bipolar disorder at baseline

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Baethge et al. (2008) United States McLean-Harvard First-Episode Project	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Low risk of bias **External validity:** Moderate risk of bias **Follow-up**: mean 4.7±2.6 years	N=166 first-episode BD I patients aged 18–72 years, median age=28 years. 46% female	**Consumption of alcohol**: defined as present or absent regardless of volume. Weeks of substance use assessed with Longitudinal Interval Follow-up Evaluation (LIFE) **DSM-IV major affective episodes and subsyndromal mania or hypomania, and depression-dysthymia**. Weeks in specific morbid states assessed using LIFE	**GEE-based, population-averaged, regression models of temporal sequencing of alcohol and affective state** Manic or hypomanic morbidity unrelated to alcohol use at any time β=−0.014 to 0.011; z-scores −0.74 to 0.64, p=0.046−0.59 Depressive morbidity significantly associated with alcohol abuse in the preceding quarter β=0.058; 95%CI 0.015, 0.100; z-score 2.67, p=0.007 Adjusted for age, sex and exposure-time
Jaffee et al. (2009) United States	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias	N=115 patients with bipolar disorder and substance dependence other than nicotine Aged 39.9±10.9 years 46.1% female Mean 7.6±8.6 days of alcohol use per month Mean 3.96 days of heavy drinking per month	**Days of alcohol use** by ASI, which assesses alcohol use by: days of any alcohol use in the most recent 30 days and days of heavy alcohol use (≥3 drinks/day) in the most recent 30 days. **Change in days of alcohol use from prior month to current month** by ASI *Post hoc* **Days of heavy alcohol use** (≥3	**Generalised estimating equation OR (95% CI) for predicting depression in subsequent month** (OR is exp(β)) Days of alcohol use (per day): OR=1.036 (1.010, 1.062) z=2.71, p=0.007 Days of alcohol use (per 10 days): OR=1.421 (1.102, 1.832) Increase in days of alcohol use (per day): OR=1.088 (1.033, 1.146) z=3.17, p=0.002 Increase in days of alcohol use (per 10 days):

	Follow-up: 8 months (but results are for prediction of outcomes in following month)	Mean 1.44 days of non-heavy drinking per month	drinks/day) by ASI **Change in days of heavy alcohol use** by ASI **Depressive episode** based on Longitudinal Interval Follow-up Evaluation (LIFE), which is combination of HAM-D and YMRS, and a SCID-based interview	OR=2.326 (1.380, 3.921) Days heavy alcohol use (per day): OR=1.042 (1.010, 1.078) Days of heavy alcohol use (per 10 days): OR=1.527 (1.100, 2.119) Increase in days of heavy alcohol use (per 10 days): OR=1.073 (1.003, 1.148) z=2.04, p=0.04 Increase in days of heavy alcohol use (per 10 days): OR=2.022 (1.028, 3.975) Days of non-heavy alcohol use: NS. For each day of alcohol use in current month significantly increased odds of a depressive episode in subsequent month by 3.6%. Ten days of use increased odds ratio to 42.1%
van Zaane et al. (2014) Netherlands Outpatient-based study of adult BP patients	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: every 2 months for up to 1 year	N=137 BP patients with follow-up data for at least two months. N=60 with lifetime diagnosis of AUD 8 had AA, 52 had AD N=77 no lifetime diagnosis of AUD	**Alcohol intake:** The number of standard alcoholic drinks was reported daily using the National Institute of Mental Health self-rated prospective Life Chart Method (LCM). One unit of alcohol was defined as 12 mL (about10 g) pure alcohol, equivalent to 100 mL wine (12% alcohol), 250 mL beer (5% alcohol), or 35 mL spirits (35% alcohol **BP:** During the full year of the study, patients rated their mood with the LCM at the end of every day.	**HR (95% CI) for the time to transition from one mood state to another, associated with an increase in weekly consumption of alcohol by one standard unit/day** From → To / Males / Females Depression → Euthymia 0.95 (0.90, 1.01) 1.18 (1.03, 1.36)* Euthymia → Mania 0.81 (0.71, 0.92)* 1.01 (0.85, 1.18) Mania → Euthymia 0.94 (0.84, 1.05) 1.12 (0.94, 1.34) Euthymia → Depression 1.03 (0.97, 1.11) 0.97 (0.82, 1.14) *p<0.05 For women in a depressive state, higher alcohol use was significantly associated with shorter times to enter a euthymic state For men in an euthymic state, higher alcohol use was significantly associated with longer times to enter a manic state

AD = alcohol dependence; ASI = Addiction Severity Index; AUD = alcohol use disorder; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GEE = general estimating equation; HAM-D = Hamilton Depression Rating Scale; NS = not significant; OR = odds ratio; SCID = Structured Clinical Interview for DSM-IV; YMRS = Young Mania Rating Scale.

Table 40 Depression outcomes from studies that reported on people diagnosed with HIV at baseline

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Lawrence et al. (2010) United states HIV/AIDS Clinic Cohort Observational Database project	**Level** IV aetiological evidence **Quality**: CHPE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias	N=1,216 People attending routine primary care visit in HIV/AIDS clinic. No risk: n=471 Lower risk: n=528 At risk: n=175	**Alcohol consumption** on the AUDIT-C. Categorised into no risk (0), low risk (1-4), or at risk for abuse (≥5). **Suicidal ideation** using a single question in the 9-item Patient Health Questionnaire (PHQ-9) "Please indicate how often over the last 2 weeks you have thought you would be better off dead or hurting yourself in some way" with response options "not at all", "several days", and "more than half of the days" and "nearly every day". Any level of suicidal ideation was modelled as being suicidal.	**OR (95%CI) for suicidal ideation (% reporting suicidal ideation)** No risk: OR=1.00 (reference), (32.3%) Lower risk: OR=1.21 (0.84, 1.77) (42.9%), OR_{adj}=1.43 (0.86, 2.38) At risk: OR=1.96 (1.23, 3.11) (21.2%), OR_{adj}=1.14 (0.61, 2.14) Adjusted for age, sex, race, insurance status, location, CD4 cell count, level of depression and substance abuse
Sullivan et al. (2011) United States Veterans Aging Cohort Study (VACS)	**Level:** II **Quality:** CPHE 30/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 6 years	N=2,446 Veterans with or without HIV, aged 22 to 87 years, either low risk drinkers or unhealthy drinkers (complete abstainers were excluded) 95% male Mean age 50.2±9.7 years N=1,339 with HIV N=1,677 low-risk drinkers N=769 unhealthy drinkers	**HED** defined as consuming 6 or more drinks on one occasion 3 or more times during past year. **Non-hazardous drinking** defined as consuming alcohol in previous year but not a HED or hazardous drinker. **MDD** defined as score of PHQ-9 >9	**GEE model to assess association of baseline alcohol use and MDD over time in those who are HIV positive compared with those who are HIV negative** Reference: non-hazardous drinkers Estimate (standard error), OR (95% CI), p-value: <u>HED</u> β=0.76 (0.19) OR_{adj}=2.14 (1.49, 3.07), p<0.001 <u>Interaction HED × HIV+:</u> β=−0.46 (0.25), 0.63 (0.38, 1.03), p=0.07 <u>Past alcohol use</u> β=0.26 (0.21) OR=1.15 (0.93, 1.42) OR_{adj}=1.30 (0.86, 1.96), p=0.21 <u>Interaction past alcohol use × HIV+:</u> β=−0.11 (0.27), 0.90 (0.52, 1.53), p=0.68 GEE model adjusted for correlated outcome data, gender, race, and age

				3-way interaction of the association of alcohol-related category with depressive symptoms by HIV status: OR = 0.99 (95% CI 0.83, 1.18), p = .88 HIV-infected and HIV-uninfected participants og HED have depressive symptoms more severe than non-hazardous drinkers
Sullivan et al. (2008) United States HIV – Longitudinal Interrelationships of Viruses and Ethanol (HIV-LIVE)	**Level:** II **Quality:** CPHE 26/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up**: Median 23.6 months (IQR 16.7, 30.3)	N=400 people with HIV and current or past alcohol problems. Mean age 43±7.4 years (range 21 – 71 31% reported heavy drinking 11% reported moderate drinking 58% reported no alcohol consumption)	**Heavy drinking** defined as >4 drinks on 1 day or >14 drinks/week (men); or >3 drinks on 1 day or >7 drinks/week (women) in past month **Not heavy drinking:** either abstinence or drinking less than heavy drinking. **Non-drinkers**: no alcohol consumption **Moderate:** (any alcohol consumption but not heavy drinking) **Very heavy drinking:** >4 separate days of more than 4 drinks on 1 day (men); >4 days of more than 3 drinks on 1 day (women) **Depressive symptoms** on the CES-D with scores ranging from 0 to 60	**Unadjusted mean depressive symptom scores (SE)** (n=400, from 1726 observations) Not heavy drinking: 21 (0.58) Current heavy drinking: 23 (0.75) Mean difference: 1.76 (0.53, 2.98), p=0.005 **Adjusted mean depressive symptom scores (SE)** (n=391, from 1514 observations) Not heavy drinking: 21 (0.77) Current heavy drinking: 22 (0.90) Mean difference: 1.04 (-0.24, 2.32), p=0.11 Adjusted for gender, age, race/ethnicity, homelessness, hepatitis C virus antibody status, CD$ cell counts, human immunodeficiency virus log RNA measurements and time in months since study enrolment. While unadjusted mean CES-D scores were significantly higher for heavy drinkers compared to those who were not current heavy drinkers, the differences decreased after adjustments. **Adjusted mean depressive symptom scores (SE)** Non-drinkers: 21 (0.81) Moderate drinkers: 21 (1.01) Heavy drinkers: 22 (0.93) Very heavy drinkers: 23 (1.15) Depressive symptoms appeared to increase as drinking levels increased but the differences were not statistically significant.

AUDIT = Alcohol Use Disorder Identification Test; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; GEE = general estimating equation; HIV = human immunodeficiency virus; MDD = major depressive disorder; OR = odds ratio; PHQ = Patient Health Questionnaire; SE = standard error

The effect of alcohol consumption on depression and anxiety in people on medicines or other drugs

Table 41 Depression and anxiety outcomes from studies that reported on people on other drugs

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Bahorik et al. (2016) United States	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Low risk of bias **External validity:** High risk of bias **Follow-up**: 6 months	N=307 participants with serious alcohol or drugs problems referred to a dependency recovery unit Aged 37.0±13.8 years 70% female N=182 hazardous drinking at baseline N=111 hazardous drinking at 3 months N=101 hazardous drinking at 6 months	**Hazardous drinking:** defined as 4 drinks/day (women) or 5 drinks/day (men) **Depressive symptoms** on PHQ-9, which measured depression in the 2 weeks prior to each interview; scores ranged from 0–27; with a score >5 being at least mild depression. **Anxiety symptoms** on GAD-7 scale, which measured anxiety in the 2 weeks prior to each interview; scores ranged from 0–21 with a score >5 being at least mild anxiety.	**Hazardous drinking as longitudinal predictor of depressive symptoms** Reference: No hazardous drinking Hazardous drinking: β(SE)=0.10 (0.03), t=2.84, p=0.004 Reductions in hazardous drinking: β(SE)=-0.10 (0.04), t=2.44, p=0.015 **Hazardous drinking as longitudinal predictor of anxiety symptoms** Hazardous drinking: β(SE)=0.09 (0.03), t=2.79, p=0.005 Reductions in hazardous drinking: β(SE)=-0.09 (0.03), t=-2.56, p=0.010 Unconditional growth model showed participants anxiety and depression reduced. Hazardous drinking was associated with slower improvements (conversely, reductions in hazardous drinking were associated with faster improvements in anxiety and depression).
Brook et al. (2016) United States Children and Adults in the Community study	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 23 years	N=806 adolescents randomly selected from 2 counties in New York who participated in the Harlem Longitudinal Development Study (HLDS) Mean age at baseline 14.1±2.8 years Followed up until mean age 36.6±2.8 years N=105 HHH (Chronic, moderate-to-heavy cigarette, alcohol, and marijuana use) N=189 DDD (Delayed/late-	**Alcohol consumption** based on question "How often did you drink beer, wine, or hard liquor in the past year?" The possible responses were: 0 (none), 1 (≤3 times per month, 2 (once a week or several times per week), 3 (1 or 2 drinks/day), 4 (≥3 every day) **Cigarette use** based on question "How many cigarettes a day did you smoke in the past year?" The possible responses were: none (0), less than daily (1), 1–5 cigarettes a day (2), about half a pack a day (3), about a pack a day (4), and about 1.5 packs a day or more (5) **Marijuana use** based on question **"**How	**OR (95% CI) for triple trajectory of cigarette, alcohol and marijuana as predictors of MDE (n=607)** NON: OR_{adj}=1.0 (Reference) HHH: OR_{adj}=2.67 (1.14, 6.26), p<0.05 DDD: OR_{adj}=0.85 (0.41, 1.76) LML: OR_{adj}=1.92 (0.84, 4.41) HMN: OR_{adj}=1.10 (0.45, 2.69) **OR (95% CI) for triple trajectory of cigarette, alcohol and marijuana as predictors of GAD (n=607)** Occasional drinking: OR_{adj}=1.0 (Reference) HHH: OR_{adj}=6.39 (2.62, 15.56), p<0.001 DDD: OR_{adj}=2.64 (1.22, 5.75), p<0.05 LML: OR_{adj}=3.71 (1.51, 9.10), p<0.001

		starting, moderate cigarette, alcohol, and marijuana use) N=143 LML (Little to no tobacco use, moderate alcohol use, and occasional marijuana use) N=121 HMN (Chronic heavy smoking, moderate alcohol use but no marijuana use) N=248 NON (Occasional alcohol use only)	often have you used marijuana in the past year?" The possible responses were: none (0), a few times a year or less (1), once a month (2), several times a month (3), once a week (4), several times a week (5), and daily (6). **MDE** assessed on the University of Michigan Composite International Diagnostic Interview (UM-CIDI) MDE was diagnosed if the participant had at least 5 of the 9 symptoms, including A (consistently depressed or down most of the day, nearly every day) and/or B (markedly diminished interest or pleasure in all, or almost all, activities) during a period in the past 5 years.	HMN: OR_{adj}=1.70 (0.64, 4.55) OR_{adj}: adjusted for gender, age at T2, original residency in Albany county, T2 parental education level and T2 family income
Brook et al. (2014) United States Harlem Longitudinal Development Study (HLDS)	**Level:** II **Quality:** CPHE 17/34 **Internal validity:** High risk of bias **External validity:** High risk of bias **Follow-up**: 13 years	N=816 urban African American (52%) and Puerto Rican (48%) participants in the HLDS Mean age at baseline (T2) was 19.2±1.5 years. Mean age at last follow-up (T5) was 32.3±1.3 years N=188 (23%) use of all 3 substances (tobacco, alcohol, and marijuana) N=114 (14%) marijuana and alcohol use N=131 (16%) tobacco and alcohol use N=310 (38%) alcohol use only N=73 (9%) no substance use	**Alcohol consumption** based on question "How often did you drink beer, wine, or hard liquor in the past year?" The possible responses ranged from: 0 (none) to 4 (≥3 every day) **Tobacco use** based on question "How many cigarettes a day did you smoke in the past year?" The possible responses ranged from: 0 (none) to 4 (about 1.5 packs a day) **Marijuana use** based on question **"**How often have you used marijuana in the past year?" The possible responses ranged from: 0 (none) to 4 (≥once a week). **GAD** on Michigan Composite International Diagnostic Interview for Generalized Anxiety Disorder. If participants answered "yes" to the first 3 questions and "yes" to 3 or more of the last 6 questions, then the participant was	**OR (95% CI) for triple trajectory of tobacco, alcohol and marijuana as predictors of GAD** All 3 substances vs alcohol only: OR_{adj}=2.22 (1.33, 3.70), p<0.01 All 3 substances vs no substance use: OR_{adj}=4.35 (1.63, 11.63), p<0.001 All 3 substances vs alcohol and tobacco use: ORadj=1.53 (0.83, 2.80) All 3 substances vs alcohol and marijuana use: ORadj=1.01 (0.56, 1.83) OR_{adj}: Adjusted for gender, race/ethnicity, self-deviance (T1), depressed mood (T1), poverty (T5), and educational level (T5) Membership in the comorbid triple trajectory highly predictive of GAD.

			considered to have GAD	

CI = confidence interval; CIDI = Composite International Diagnostic Interview; CPHE = Centre for Public Health Excellence; GAD = generalised anxiety disorder; MDE = major depressive episode; OR = odds ratio; PHQ = Patient Health Questionnaire; SE = standard error

The effect of alcohol consumption on PTSD in people exposed to trauma

People with traumatic injuries

Table 42 PTSD outcomes from studies that reported on people with traumatic injuries

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Powers et al. (2014) United States	**Level:** II **Quality:** CPHE 28/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 3 months	N=227 adult patients at a Level I Trauma Center Cause of injury: 11% gunshot; 24% motor vehicle; 6% aggravated assault; 12% motorcycle; 10% pedestrian/bike; 29% fall; 10% other Mean age 46±18 years 36% female Mean blood alcohol level in those who were tested (n=90) 64.6±104.0 N=89 had a positive AUDIT-C	**Blood alcohol level at admission** Thresholds not defined **PTSD symptoms** on the PC-PTSD. A score of ≥3 considered PTSD.	**Logistic regression OR (95% CI) for being in PTSD group compared to being in PTSD absent group (step-wise analyses)** Positive alcohol screen: OR=1.11 (0.23, 5.37) OR_{adj}=0.65 (0.11, 3.97) Blood alcohol level: OR=1.00 (0.99, 1.01) OR_{adj}=1.00 (0.99, 1.01) OR_{adj}: adjusted for baseline PTSD symptoms
Hruska et al. (2017) United States	**Level:** II **Quality:** CPHE 18/34 **Internal validity:** Moderate risk of bias **External validity:** High risk of bias **Follow-up**: 7-day sampling period	N = 36 adult patients at a Level I Trauma Center. Cause of injury: motor vehicle/cycle accident: 33.3%; assault: 33.3% Mean age 34.0±10.8 years 25% female	**Alcohol consumption** defined as the number of drinks containing alcohol they consumed since the last signal (from 0 to 10 or more). This was adapted from the AUDIT. **PTSD symptoms** on the SF-PCL. Symptoms and impairment were categorized as endorsed if they were rated as a 3 (Moderately) or higher, and participants were classified as meeting probable PTSD if they endorsed at least	**Generalised linear mixed model using a gamma error distribution and log link** (for positively skewed and continuous data) **for predicting PTSD symptoms** Alcohol consumption: *B*=0.01 (95%CI −0.01, 0.02) The coefficient indicates the log value of the outcome when the predictor changes by 1 unit

			1 re-experiencing, 3 avoidance, and 2 hyperarousal symptoms, plus functional impairment from endorsed symptoms.	

AUDIT = Alcohol Use Disorder Identification Test; CAPS = Clinically Administered PTSD Scale; CI = confidence interval; CPHE = Centre for Public Health Excellence; OR = odds ratio; PC-PTSD = Primary Care Post-Traumatic Stress Disorder Screen; PTSD = post-traumatic stress disorder; SF-PCL = Short Form PTSD Checklist

People exposed to terrorism

Table 43 PTSD outcomes from studies that reported on people exposed to terrorism

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Boscarino et al. (2011) United States	**Level:** II **Quality:** CPHE 23/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 1 year	N=1,681 adults who were living in New York City at the time of the World Trade Center (WTC) attack. Female 54% N=587 HED N=134 PTSD at 24 months	**Alcohol consumption**: based on the number of drinks/day they had in the past month on days they drank, as well as how many days in the past month they drank. **HED**: asked about the previous year, and the 12 months prior to the attacks. HED defined as ≥6 drinks. **PTSD** was based on a scale initially developed for telephone administration. To be coded as having PTSD, subjects had to meet DSM-IV criteria A through F, but the time frame was based on the past 12-month period, both at baseline and at follow-up. <u>PTSD at 24 months</u>, was defines as respondents who met the full PTSD criteria (A through F) at follow-up, while having been PTSD negative for the full criteria at baseline.	**Unadjusted generalised estimating equation coefficients of alcohol use at 3 time points and PTSD at 24 months post WTC attack** **(PTSD X Time)** HED: β(SE)=0.09 (0.04), p=0.018 Drinks/drinking day: β(SE)=0.29 (0.13), p=0.023 Drinks/month: β(SE)=0.13 (0.07), p=0.066 **GEE coefficients for likelihood of high levels of drinks per drinking day, drinks per month and HED among patients with delayed PTSD onset at 24 months compared with those without** HED: β(SE)=1.03(0.12), p<0.001 Drinks/drinking day: β(SE)=1.18(0.22), p<0.001 Drinks/month: β(SE)=0.69(0.15), p<0.001 β coefficients were positive indicated that each respective alcohol outcome assessed increased over time for those with delayed-onset PTSD, compared to those without.

CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; PTSD = post-traumatic stress disorder; SE = standard error

Table 44 PTSD outcomes from studies that reported on defence force personnel and veterans

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Goodwin et al. (2017) United Kingdom A random sample of serving personnel from the UK Royal Navy, Army and Royal Air Force	**Level:** II **Quality:** CPHE 25/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up from baseline**: at 2−4 years and 5−7 years	N=667 serving personnel from the Royal Navy, Army and Royal Air Force who completed a full questionnaire and 2 follow-up assessments N=368 average drinkers N=29 abstainers N=125 low level drinkers N=18 decreasing drinkers N=127 heavy drinkers There were significant differences in the number of personnel: aged ≥35 years, in the RAF, females, in an Officer rank, of single status, smokers and childhood antisocial behaviour between drinking groups	**Average units of alcohol consumed** per week was assessed using the 3-item Alcohol Use Disorders Identification Test – Consumption (AUDIT-C). The average units per drinking session was calculated by multiplying the average number of units with frequency per week. Alcohol units were defined as: a pint of standard beer/lager=2 units, a single measure of spirit/small glass of wine=1 unit. Class 1: average drinkers who consumed on average 12 units per week Class 2: abstainers who drank no alcohol across the three phases Class 3: low level drinkers, drinking 2 units per week across all phases Class 4: decreasing drinkers with average consumption of 11 units at baseline. decreasing to 1 unit by follow-up 2 Class 5: heavy drinkers, who drank on average 28−29 units/week across all three phases **Symptoms of PTSD** were assessed using DSM-IV criteria by the National Centre for PTSD Checklist – Civilian version (PCL-C). Probable PTSD was defined as individuals with a score of 50 or above.	**OR (95% CI) for probable PTSD at baseline in British military personnel by drinking level** Class 1: average drinkers 2/368 cases OR=1.0 (Reference) Class 2: abstainers 2/29 cases OR=14.89 (1.98, 111.62) Class 3: low level drinkers 3/125 cases OR=4.59 (0.75, 28.02) Class 4: decreasing drinkers 1/18 cases OR=10.02 (0.85, 117,98) Class 5: heavy drinkers 6/127 cases OR=9.31 (1.77, 48.96) **OR (95% CI) for probable PTSD at follow-up 1 in British military personnel by drinking level** Class 1: average drinkers 12/368 cases OR=1.0 (Reference) Class 2: abstainers 2/29 cases OR=4.69 (0.70, 31.21) Class 3: low level drinkers 5/125 cases OR=1.54 (0.47, 5.06) Class 4: decreasing drinkers 0/18 cases - Class 5: heavy drinkers 11/127 cases OR=1.60 (0.62, 4.14) ORs adjusted for age and gender**OR (95% CI) for probable PTSD at follow-up 2 in British military personnel by drinking level** Class 1: average drinkers

				9/366 cases OR=1.0 (Reference) Class 2: abstainers 1/29 cases OR=1.58 (0.19, 13.06) Class 3: low level drinkers 5/124 cases OR=1.76 (0.57, 5.41) Class 4: decreasing drinkers 1/18 cases OR=2.15 (0.26, 18.20) Class 5: heavy drinkers 8/124 cases OR=2.68 (0.98, 7.33) ORs adjusted for age and gender
Schultz et al. (2014) United States	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Low risk of bias **Follow-up**: 6 months	N=512 veterans returned from deployment in Iraq or Afghanistan 56.8% Army; 17.8% Navy; 21.5% Air force; 3.9% Marines 60% female Mean age 31.1 years Surveyed between 3 and 12 months after returning from deployment (T1)	**Alcohol consumption**: on the AUDIT-C, a 3-item version of the AUDIT measure, designed to identify individuals who are experiencing problems with alcohol. A cut-off of 3 out of 12 possible points was used to identify patients with alcohol abuse, alcohol dependence or heavy drinking. (binary variable) **PTSD** on the PTSD checklist (PCL) Military version (binary variable)	**Logistic regression for the prediction of PTSD** Alcohol use at T1: estimate(SE): -0.04 (0.13), NS Adjusted for gender, age, ethnicity, education level, marital status, income, military status and branch, length of deployment, physical health, mental health, chronic pain, deployment risk factors and resilience factors Alcohol use 2−12 months after deployment did not predict a worsening of PTSD symptom severity over the next 6 months.

AUDIT-C = Alcohol Use Disorder Identification Test - Consumption; CI = confidence interval; CPHE = Centre for Public Health Excellence; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; OR = odds ratio; PCL-C = PTSD Checklist Civilian Version; PTSD = post-traumatic stress disorder; SE = standard error;

People exposed to mixed traumas

Table 45 PTSD outcomes from studies that reported on people exposed to mixed trauma

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Kaysen et al. (2011) United States	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of	N=64 female sexual or physical assault victims (aged 19-53 years) Mean number of drinks on a peak drinking occasion during the 30 days prior to the assault=3.8±5.5	**Peak drinking level:** greatest amount of alcohol consumed in the 30 days prior to the trauma, from the TLFB **PTSD symptoms** on the CAPS, a clinician-administered diagnostic interview that measures PTSD in two	**Hierarchical linear modelling for course of PTSD symptoms over time** Peak drinking intercept: β=95.10 (95% CI 80.89, 109.30) p<0.05 Peak drinking: β=−5.34 (95% CI −19.52, 8.85)

	bias **External validity:** High risk of bias **Follow-up**: 6 months post-assault		separate dimensions—frequency and intensity of symptoms—on a scale ranging from 0–4. In order for a symptom to be considered clinically significant, it must score at least a "1" on frequency and a "2" on intensity. The scale yields both a PTSD diagnosis and a continuous measure of PTSD severity	Peak drinking x time: β=1.65 (95%CI −1.63, 4.93) There was no main effect or interaction of peak drinking and time. Thus, peak drinking over the 30 days prior to the assault was not a significant predictor either of initial PTSD symptoms or change in symptoms over time.
Read et al. (2014) United States	**Level:** II **Quality:** CPHE 27/34 **Internal validity:** Moderate risk of bias **External validity:** Moderate risk of bias **Follow-up**: 2 years	N=734 trauma exposed students entering college	**Alcohol consumption:** typical past month consumption on the Daily drinking Questionnaire was used to calculate a typical, past month weekly quantity score as a continuous variable ranging from 0 to 60. **PTSD symptoms** on the PCL-C. Responses to this 17-item measure were re-coded so that symptoms were identified as either present (1) or absent (0). Thus, the possible range of PCL scores (0–17) were used as a continuous variable.	**Mean±SD for alcohol quantity and PTSD at relevant time-points** Alcohol quantity (time 1): 6.39±9.39 Alcohol quantity (time 2) 6.52±9.45 PTSD symptoms score (time 2) 2.79±3.81 PTSD symptoms score (time 3) 2.45±3.77 **Bivariate correlations between alcohol quantity and PTSD symptoms:** Alcohol quantity (time1) - PTSD symptoms (time2): r=0.09, p<0.05 Alcohol quantity (time 1) – PTSD symptoms (time 3): r=0.00 Alcohol quantity (time 2) - PTSD symptoms (time 3): r=0.01 **Cross-lagged structural equation (path) model including alcohol use, PTSD symptoms, coping and alcohol consequences** Alcohol use did not have any significant direct or indirect associations with PTSD symptoms.

CAPS = Clinically Administered PTSD Scale; CPHE = Centre for Public Health Excellence; PCL-C = PTSD Checklist – Civilian version; PTSD = post-traumatic stress disorder; SD = standard deviation; TLFB = timeline follow-back interview

The effect of alcohol consumption on depression in people exposed to trauma

Table 46 Depression outcomes from studies that reported on people exposed to trauma

Study / Location / Setting	Level of evidence / Quality	Population	Variable definitions	Results
Hoffman et al. (2011)	**Level:** II	N=1,035 participants with spinal cord injuries, who completed 1-	**Unsafe alcohol use**: more than 7 drinks per week (women), more than 14 drinks	**Logistic regression: change in unsafe alcohol use as a predictor of improvement in depression from year 1 to 5**

United States Spinal Cord Injury (SCI) Model System Longitudinal data set	**Quality:** CPHE 31/34 **Internal validity:** Low risk of bias **External validity:** Low risk of bias **Follow-up**: 5 years	and 5- year follow-up questionnaires. Mean age 37.1±14.8 years 25% female	per week (men), or reported any episode of HED (≥5 drinks/occasion) in past month. **MDD** defined as score of ≥10 on PHQ-9	β=not stated, p=0.59 **Logistic regression: prediction of becoming depressed at year 5 if not depressed at year 1:** No unsafe use of alcohol: OR=1.0 (Reference) Reducing unsafe use: β(SE)=1.08 (0.43), p=0.011 OR=2.95 (95%CI 1.28, 6.79) Beginning unsafe use: β(SE)=0.39 (0.43), p=0.385 OR=1.47 (95%CI 0.62, 3.50) Continued unsafe use: β(SE)=-1.26 (1.04), p=0.24 OR=0.28 (95%CI 0.04, 2.18)

CI = confidence interval; CPHE = Centre for Public Health Excellence; MDD = major depressive disorder; OR = odds ratio; PHQ = Patient Health Questionnaire;

Appendix D Quality appraisal

Table 47 AMSTAR 2 Checklist for appraising the quality of systematic reviews

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:	Optional (recommended)	
☐ Population	☐ Timeframe for follow-up	☐ Yes
☐ Intervention		☐ No
☐ Comparator group		
☐ Outcome		

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:	For Yes:	
The authors state that they had a written protocol or guide that included ALL the following:	As for partial yes, plus the protocol should be registered and should also have specified:	
☐ review question(s)	☐ a meta-analysis/synthesis plan, if appropriate, *and*	☐ Yes
☐ a search strategy	☐ a plan for investigating causes of heterogeneity	☐ Partial Yes
☐ inclusion/exclusion criteria	☐ justification for any deviations from the protocol	☐ No
☐ a risk of bias assessment		

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review satisfy ONE of the following:	
☐ *Explanation for* including only RCTs	☐ Yes
☐ OR *Explanation for* including only NRSI	☐ No
☐ OR *Explanation for* including both RCTs and NRSI	

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):	For Yes, should also have (all the following):	
☐ searched at least 2 databases (relevant to research question)	☐ searched the reference lists/bibliographies of included studies	☐ Yes
☐ provided key word and/or search strategy	☐ searched trial/study registries	☐ Partial Yes
☐ justified publication restrictions (eg, language)	☐ included/consulted content experts in the field	☐ No
	☐ where relevant, searched for grey literature	
	☐ conducted search within 24 months of completion of the review	

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:	
☐ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include	☐ Yes
☐ OR two reviewers selected a sample of eligible studies <u>and</u> achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer	☐ No

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:

☐ at least two reviewers achieved consensus on which data to extract from included studies ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder extracted by one reviewer	☐ Yes ☐ No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:	For Yes, must also have:	
☐ provided a list of all potentially relevant studies that were read in full text form but excluded from the review	☐ Justified the exclusion from the review of each potentially relevant study	☐ Yes ☐ Partial Yes ☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):	For Yes, should also have ALL the following:	
☐ described populations ☐ described interventions ☐ described comparators ☐ described outcomes ☐ described research designs	☐ described population in detail ☐ described intervention and comparator in detail (including doses where relevant) ☐ described study's setting ☐ timeframe for follow-up	☐ Yes ☐ Partial Yes ☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs

For Partial Yes, must have assessed RoB from	For Yes, must also have assessed RoB from	
☐ unconcealed allocation, *and* ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)	☐ allocation sequence that was not truly random, *and* ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome	☐ Yes ☐ Partial Yes ☐ No ☐ Includes only NRSI

NRSI

For Partial Yes, must have assessed RoB:	For Yes, must also have assessed RoB:	
☐ from confounding, *and* ☐ from selection bias	☐ methods used to ascertain exposures and outcomes, *and* ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome	☐ Yes ☐ Partial Yes ☐ No ☐ Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes:

☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	☐ Yes ☐ No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs

For Yes:

☐	The authors justified combining the data in a meta-analysis	☐	Yes
☐	AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present	☐	No
☐	AND investigated the causes of any heterogeneity	☐	No meta-analysis conducted

NRSI

For Yes:

☐	The authors justified combining the data in a meta-analysis	☐	Yes
☐	AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present	☐	No
☐	AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available	☐	No meta-analysis conducted
☐	AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review		

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

☐	included only low risk of bias RCTs	☐	Yes
☐	OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect	☐	No
		☐	No meta-analysis conduced

13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?

For Yes:

☐	included only low risk of bias RCTs	☐	Yes
☐	OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results	☐	No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

☐	There was no significant heterogeneity in the results	☐	Yes
☐	OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	☐	No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

☐	performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	☐	Yes
		☐	No
		☐	No meta-analysis conduced

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

For Yes:

☐	The authors reported no competing interests OR	☐	Yes
☐	The authors described their funding sources and how they managed potential conflicts of interest	☐	No

Source: Shea et al. 2017

Table 48 CPHE Quality appraisal checklist – quantitative studies reporting correlations and associations

Questions	Response	Comments
Section 1: Population		
1.1 Is the source population or source area well described? *Was the country (e.g. developed or non-developed, type of health care system), setting (primary schools, community centres etc), location (urban, rural), population demographics etc adequately described?*	++ / + / - / NR / NA	
1.2 Is the eligible population or area representative of the source population or area? *Was the recruitment of individuals, clusters or areas well defined (e.g. advertisement, birth register)?* *Was the eligible population representative of the source? Were important groups underrepresented?*	++ / + / - / NR / NA	
1.3 Do the selected participants or areas represent the eligible population or area? Was the method of selection of participants from the eligible population well described? What % of selected individuals or clusters agreed to participate? Were there any sources of bias? Were the inclusion or exclusion criteria explicit and appropriate?	++ / + / - / NR / NA	
Section 2: Method of selection of exposure (or comparison) group		
2.1 Selection of exposure (and comparison) group. How was selection bias minimised? How was selection bias minimised?	++ / + / - / NR / NA	
2.2 Was the selection of explanatory variables based on a sound theoretical basis? How sound was the theoretical basis for selecting the explanatory variables?	++ / + / - / NR / NA	
2.3 Was the contamination acceptably low? Did any in the comparison group receive the exposure? If so, was it sufficient to cause important bias?	++ / + / - / NR / NA	
2.4 How well were likely confounding factors identified and controlled? Were there likely to be other confounding factors not considered or appropriately adjusted for? Was this sufficient to cause important bias?	++ / + / - / NR / NA	
2.5 Is the setting applicable to Australia? Did the setting differ significantly from Australia?	++ / + / - / NR / NA	
Section 3: Outcomes		
3.1 Were the outcome measures and procedures reliable? Were outcome measures subjective or objective (e.g. biochemically validated nicotine levels ++ vs self-reported smoking −)? How reliable were outcome measures (e.g. inter- or intra-rater reliability scores)? Was there any indication that measures had been validated (e.g. validated against a gold standard measure or assessed for content validity)?	++ / + / - / NR / NA	
3.2 Were the outcome measurements complete? Were all or most of the study participants who met the defined study outcome definitions likely to have been identified?	++ / + / - / NR / NA	
3.3 Were all the important outcomes assessed? Were all the important benefits and harms assessed? Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?	++ / + / - / NR / NA	
3.4 Was there a similar follow-up time in exposure and comparison groups? If groups are followed for different lengths of time, then more events are likely to occur	++ / + / - / NR / NA	

Questions	Response	Comments
in the group followed-up for longer distorting the comparison. Analyses can be adjusted to allow for differences in length of follow-up (e.g. using person-years).		
3.5 Was follow-up time meaningful? Was follow-up long enough to assess long-term benefits and harms? Was it too long, e.g. participants lost to follow-up?	++ / + / - / NR / NA	
Section 4: Analyses		
4.1 Was the study sufficiently powered to detect an intervention effect (if one exists)? A power of 0.8 (i.e. it is likely to see an effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?	++ / + / - / NR / NA	
4.2 Were multiple explanatory variables considered in the analyses? Were there sufficient explanatory variables considered in the analysis?	++ / + / - / NR / NA	
4.3 Were the analytical methods appropriate? Were important differences in follow-up time and likely confounders adjusted for?	++ / + / - / NR / NA	
4.6 Was the precision of association given or calculable? Is association meaningful? Were confidence intervals or p values for effect estimates given or possible to calculate? Were CIs wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?	++ / + / - / NR / NA	
4.1 Was the study sufficiently powered to detect an intervention effect (if one exists)? A power of 0.8 (i.e. it is likely to see an effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?	++ / + / - / NR / NA	
4.2 Were multiple explanatory variables considered in the analyses? Were there sufficient explanatory variables considered in the analysis?	++ / + / - / NR / NA	
4.3 Were the analytical methods appropriate? Were important differences in follow-up time and likely confounders adjusted for?	++ / + / - / NR / NA	
4.6 Was the precision of association given or calculable? Is association meaningful? Were confidence intervals or p values for effect estimates given or possible to calculate? Were CIs wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?	++ / + / - / NR / NA	
Section 5: Summary		
5.1 Are the study results internally valid (i.e. unbiased)? How well did the study minimise sources of bias (i.e. adjusting for potential confounders)? Were there significant flaws in the study design?	++ / + / - / NR / NA	
5.2 Are the findings generalisable to the source population (i.e. externally valid)? Are there sufficient details given about the study to determine if the findings are generalisable to the source population? Consider: participants, interventions and comparisons, outcomes, resource and policy implications.	++ / + / - / NR / NA	

Questions	Response	Comments

Source: (Centre for Public Health Excellence 2012)
++ Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias
+ Indicates the either the answer to the checklist question is not clear from the way the study is reported or that the study may not have addressed all potential sources of bias for that particular aspect of study design
- Should be reserved for those aspects of the study design in which significant sources of bias may persist
Not Reported (NR) Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.
Not applicable (NA) Should be reserved for those study designs that are not applicable given the study design under review (for sample, allocation concealment would not be applicable for case-control studies)

Table 49 Cochrane Collaboration's tool for assessing risk of bias (for randomised-controlled trials)

Bias domain	Source of bias	Support for judgment	Review authors' judgment (assess as low, unclear or high risk of bias)
Selection bias	Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
	Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment
Performance bias	Blinding of participants and personnel*	Describe all measures used, if any, to blind trial participants and researchers from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Detection bias	Blinding of outcome assessment*	Describe all measures used, if any, to blind outcome assessment from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessment
Attrition bias	Incomplete outcome data*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions where reported, and any reinclusions in analyses for the review	Attrition bias due to amount, nature, or handling of incomplete outcome data
Reporting bias	Selective reporting	State how selective outcome reporting was examined and what was found	Reporting bias due to selective outcome reporting
Other bias	Anything else, ideally prespecified	State any important concerns about bias not covered in the other domains in the tool	Bias due to problems not covered elsewhere

Source: Higgins et al. 2011

Table 50 Summary of risk of bias assessments for included cohort and case-control studies, according to CPHE Quality appraisal checklist

Author	Population	Exposure/ control	Outcomes	Analyses	Overall	Internal validity	Generalisability
An & Xiang (2015)	0	10	10	8	28	Low risk of bias	High risk of bias
Armeli et al. (2015)	3	8	9	6	26	Low risk of bias	Moderate risk of bias
Augestad et al. (2008)	3	7	9	5	27	Moderate risk of bias	High risk of bias
Baethge et al. (2008)	3	9	10	6	26	Low risk of bias	Moderate risk of bias
Bahorik et al. (2016)	0	7	10	6	23	Low risk of bias	High risk of bias
Bell & Britton (2015)	3	7	8	6	24	Moderate risk of bias	High risk of bias
Birkley et al. (2015)	1	6	8	1	16	Moderate risk of bias	High risk of bias
Boscarino et al. (2011)	5	5	9	4	23	Moderate risk of bias	Low risk of bias
Bots et al. (2008)	0	9	10	7	26	Low risk of bias	High risk of bias
Brennan et al. (2016)	0	5	8	2	15	High risk of bias	High risk of bias
Brook et al. (2014)	0	3	9	5	17	High risk of bias	High risk of bias
Brook et al. (2016)	5	9	7	6	27	Moderate risk of bias	Low risk of bias
Bulloch et al. (2012)	3	7	9	7	26	Moderate risk of bias	High risk of bias
Byers et al. (2012)	4	9	10	7	30	Low risk of bias	Low risk of bias
Cabello et al. (2017)	2	7	9	8	26	Low risk of bias	Moderate risk of bias
Cerda et al. (2016)	5	9	9	6	29	Low risk of bias	Low risk of bias
Chan et al. (2013)	4	6	10	3	23	High risk of bias	Moderate risk of bias
Chang et al. (2016)	4	9	8	8	29	Low risk of bias	Moderate risk of bias
Cheng et al. (2016)	5	5	9	7	26	Moderate risk of bias	Moderate risk of bias
Choi et al. (2011)	0	8	10	7	25	Low risk of bias	High risk of bias
Cisler et al. (2012)	4	9	7	6	26	Moderate risk of bias	Moderate risk of bias
Conner et al. (2017)	4	7	10	5	26	Moderate risk of bias	Moderate risk of bias
Cougle et al. (2015)	4	3	9	8	24	Moderate risk of bias	Moderate risk of bias
Danzo et al. (2017)	4	9	9	6	28	Low risk of bias	Low risk of bias
Dawson et al. (2008)	6	9	8	8	31	Low risk of bias	Low risk of bias
Edwards et al. (2014)	4	7	9	7	27	Moderate risk of bias	Moderate risk of bias
Fleming et al. (2008)	4	5	9	2	20	Moderate risk of bias	Moderate risk of bias
Flensborg-	2	7	8	7	24	Moderate risk	High risk of bias

Author	Population	Exposure/ control	Outcomes	Analyses	Overall	Internal validity	Generalisability
Madsen et al. (2011)						of bias	
Frojd et al. (2011)	4	7	7	6	24	Moderate risk of bias	Moderate risk of bias
Gea et al. (2012)	2	6	8	6	22	Moderate risk of bias	High risk of bias
Gea et al. (2013)	1	6	8	6	21	Moderate risk of bias	High risk of bias
Goodwin et al. (2017)	4	7	9	5	25	Moderate risk of bias	Moderate risk of bias
Grazioli et al. (2018)	3	6	9	5	23	Moderate risk of bias	High risk of bias
Gustafson (2012)	4	8	10	5	27	Low risk of bias	Low risk of bias
Hiles et al. (2015)	6	9	10	8	33	Low risk of bias	Low risk of bias
Hoffman et al. (2011)	4	9	10	8	31	Low risk of bias	Low risk of bias
Hooshmand et al. (2012)	5	9	10	5	29	Low risk of bias	Low risk of bias
Hruska et al. (2017)	3	5	7	3	18	Moderate risk of bias	High risk of bias
Jaffee et al. (2009)	3	8	8	7	26	Moderate risk of bias	Moderate risk of bias
Johnson et al. (2013)	4	9	10	2	25	Moderate risk of bias	Low risk of bias
Kaysen et al. (2011)	3	8	10	3	24	Moderate risk of bias	High risk of bias
Lang et al. (2007)	2	7	8	6	23	Moderate risk of bias	High risk of bias
Luppa et al. (2012)	4	9	10	6	29	Low risk of bias	Moderate risk of bias
Mackie et al. (2011)	1	6	8	3	18	High risk of bias	High risk of bias
Magnusson Hanson et al. (2016)	3	7	7	4	21	High risk of bias	High risk of bias
Marmonstein (2009)	6	6	9	4	25	Moderate risk of bias	Low risk of bias
Mason et al. (2008)	2	7	9	0	18	High risk of bias	Moderate risk of bias
Mason & Spoth (2011)	4	5	9	0	18	High risk of bias	Moderate risk of bias
McCarty et al. (2012)	4	8	10	1	23	Moderate risk of bias	Low risk of bias
Meng (2017)	4	8	9	8	29	Low risk of bias	Low risk of bias
Meng et al. (2017)	5	9	9	7	30	Low risk of bias	Low risk of bias
Meririnne et al. (2010)	5	9	10	6	30	Low risk of bias	Low risk of bias
Mushquash et al. (2013)	4	6	6	3	19	High risk of bias	Moderate risk of bias
Needham (2007)	6	7	10	3	26	Moderate risk of bias	Low risk of bias
Onwuameze et al. (2013)	4	4	4	2	16	High risk of bias	Moderate risk of bias

Author	Population	Exposure/ control	Outcomes	Analyses	Overall	Internal validity	Generalisability
Otten et al. (2018)	2	5	8	3	18	High risk of bias	High risk of bias
Paljarvi et al. (2009)	5	8	9	7	29	Moderate risk of bias	Low risk of bias
Pardee et al. (2014)	2	8	9	2	21	Moderate risk of bias	Moderate risk of bias
Parrish et al. (2016)	5	6	10	6	27	Low risk of bias	Moderate risk of bias
Patwardhan et al. (2017)	3	8	9	6	26	Low risk of bias	High risk of bias
Paulson et al. (2018)	3	7	8	6	24	Moderate risk of bias	Moderate risk of bias
Pesola et al. (2015)	4	8	9	6	27	Moderate risk of bias	Moderate risk of bias
Piasecki et al. (2017)	3	7	10	1	21	Moderate risk of bias	Moderate risk of bias
Powers et al. (2012)	3	8	10	5	28	Moderate risk of bias	Moderate risk of bias
Powers et al. (2016)	4	6	10	7	27	Moderate risk of bias	Low risk of bias
Ruggles et al. (2014)	4	8	10	7	29	Low risk of bias	Moderate risk of bias
Read et al. (2016)	3	3	4	1	11	High risk of bias	High risk of bias
Read et al. (2014)	4	8	10	5	27	Moderate risk of bias	Moderate risk of bias
Scholes-Balog et al. (2015)	3	7	9	4	23	High risk of bias	High risk of bias
Schuler et al. (2015)	0	9	10	5	24	Low risk of bias	High risk of bias
Schulz et al. (2014)	5	9	9	4	27	Moderate risk of bias	Low risk of bias
Skogen et al. (2016)	2	5	9	4	20	High risk of bias	High risk of bias
Sloan et al. (2011)	5	9	9	4	27	Moderate risk of bias	Low risk of bias
Sui et al. (2009)	3	8	9	6	26	Low risk of bias	Moderate risk of bias
Sullivan et al. (2008)	3	9	9	5	26	Moderate risk of bias	High risk of bias
Sullivan et al. (2011)	6	7	10	7	30	Low risk of bias	Low risk of bias
Tait et al. (2012)	2	7	7	6	22	Moderate risk of bias	High risk of bias
Tanaka et al. (2011)	3	7	9	7	26	Moderate risk of bias	Moderate risk of bias
Tsai et al. (2013)	3	8	10	8	29	Low risk of bias	Moderate risk of bias
van Gool et al. (2007)	5	7	9	6	27	Moderate risk of bias	Low risk of bias
van Zaane et al. (2014)	4	9	6	4	23	Moderate risk of bias	Moderate risk of bias
Weyerer et al. (2013)	3	8	8	7	26	Low risk of bias	Moderate risk of bias
Wilkinson et al. (2017; 2016)	4	9	10	8	31	Low risk of bias	Low risk of bias

Author	Population	Exposure/ control	Outcomes	Analyses	Overall	Internal validity	Generalisability
Windle & Windle (2017)	5	7	10	4	26	Moderate risk of bias	Moderate risk of bias
Wymbs et al. (2014)	4	8	10	1	23	Moderate risk of bias	Low risk of bias
Zhang et al. (2018)	5	8	10	5	30	Low risk of bias	Low risk of bias

Table 51 Summary of risk of bias assessments for included large cross-sectional studies, according to CPHE Quality appraisal checklist

Author	Population	Exposure/ control	Outcomes	Analyses	Overall	Internal validity	Generalisability
Gart & Kelly (2015)	0	8	8	6	20	High risk of bias	High risk of bias
Glasheen et al. (2015)	3	7	6	6	22	Moderate risk of bias	High risk of bias
Herherman Mash et al. (2016)	4	10	7	8	27	Low risk of bias	Moderate risk of bias
Kim & Kim (2010)	6	7	5	8	28	Low risk of bias	Low risk of bias
Lawrence et al. (2010)	6	9	7	8	30	Low risk of bias	Low risk of bias
Peltzer & Pengpid (2015)	4	8	7	8	27	Low risk of bias	Moderate risk of bias
Schilling et al. (2009)	3	10	5	8	26	Low risk of bias	Moderate risk of bias
Souza et al. (2010)	6	8	7	8	29	Low risk of bias	Low risk of bias

Appendix E GRADE evidence profiles

GRADE evidence profiles for people of all ages

Question: What is the effect of alcohol on mental health outcomes (across ages)?
Patient or population: General population (across youth and adults, males and females)
Exposure: Heavy drinking/excessive drinking/ drinking to exceed guidelines
Reference group: Abstinence/ non-hazardous

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=22,151 K=3 prospective cohort studies (Bulloch et al. 2012; Magnusson Hanson et al. 2016; Van Gool et al. 2007)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Excessive drinking (exceeding guidelines) vs abstinence or drinking within guidelines: RR=2.48 (1.05, 5.69), p<0.05, HR=0.9 (0.7, 1.3) ß=0.92, p>0.05 (n=193)	*No reliable evidence of an association* One out of three studies reported a statistically signficiant association between excessive drinking and an increased risk of depression.	Critical
	N=11,523 K=3 prospective cohort studies (Cabello et al. 2017; Van Gool et al. 2007) (Sullivan et al. 2011)	Risk of bias: -1 Inconsistency: 0 Indirectness: -1 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Non-heavy drinkers or regular (non-excessive) drinkers vs abstinence: OR=0.93 (0.57, 3.67) RR=1.15 (0.68, 1.96) Non-hazardous drinkers vs former drinkers: OR=1.3 (0.86, 1.96)	*No reliable evidence of an association* No relationship between regular drinking (not at hazardous levels) and depression 5-8 years later was found. Although these studies were consistent, a strong conclusion of no harm could not be made due to the risk of bias and the indirectness of the evidence (unclear how the drinking cultures in Ghana, Mexico, India and Russia differ from Australia).	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=27,630 K=3 prospective cohort studies (Bulloch et al. 2012; Cabello et al. 2017; Sullivan et al. 2011)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Heavy drinking on a given day and HED vs abstinent or drinking within guidelines: OR=1.59 (0.67, 3.75) HR=1.1 (0.9, 1.3) HED vs drinking within guidelines: OR=2.14 (1.49, 3.07), p<0.001	*No reliable evidence of an association* Only one out of three studies reported a significant relationship between HED (vs non-HED or abstinence) and a higher likelihood of depression or not after 5-8 years, although point estimates were in the same direction.	Critical
	N=37,092 K=3 prospective cohort studies (Cougle et al. 2015; Meng 2017a; Meng et al. 2017b)	Risk of bias: -1 Inconsistency: -2 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Occasional or monthly drinkers vs never drinkers: RR=1.28 (1.12, 1.45) RRs=0.51 (0.44, 0.58) to 1.56 (0.61, 0.76) Monthly drinkers vs never or occasional drinkers: HR=0.88 (0.78, 0.995) Weekly drinker vs <weekly drinker: ORs=0.88 (0.83, 0.94) RRs=0.51 (0.44, 0.58) to 1.56 (0.61, 0.76)	*No reliable evidence of an association* Drinking weekly or monthly (not at hazardous levels) was found to be beneficial in three studies. Occasional drinkers had significantly higher levels of depression than never drinkers. No conclusions can therefore be made.	Critical
Bipolar disorder	N=43,093 K=1 prospective cohort study (Cougle et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Weekly consumption vs less than weekly consumption: OR=0.79 (0.73, 0.86), p<0.001	*Limited evidence of an association* A single large study reported that those who drank less than weekly (or abstained), had higher levels of incident bipolar disease than those who drank alcohol on a weekly basis.	Critical
Anxiety	N=22,122 K=1 prospective cohort study	Risk of bias: 0 Inconsistency: N/A Indirectness: 0	⊕⊕⊕⊖	Frequency of HED <1/month vs never: OR=1.03 (0.81, 1.31)	*No evidence of an association* A single large study at low risk of bias found no significant differences in likelihood of developing anxiety by frequency of	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	(Dawson, Li & Grant 2008)	Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0		1-3/month vs never: OR=1.13 (0.85, 1.51) 1-2/week vs never: OR=1.09 (0.80, 1.48) 3-4/week vs never: OR=1.43 (0.95, 2.13) Daily/near daily vs never: OR=1.31 (0.92, 1.88)	HED.	
	N=43,093 K=1 prospective cohort study (Cougle et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Weekly consumption vs less than weekly consumption: OR=0.88 (0.82, 0.95), p<0.01	*Limited evidence of an association* A single large study reported that those who drank less than weekly (or abstained), had higher levels of anxiety than those who drank alcohol on a weekly basis.	Critical
Suicide	N=0 K=0				*No evidence for this outcome*	Important
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0				*No evidence for this outcome*	Important

Question: What is the effect of alcohol on mental health outcomes (across ages)?
Patient or population: Females, general population (across youth and adults or younger adults and older adults)
Exposure: 5 drinks or over per week, or being monthly or weekly drinker
Reference group: less than 5 drinks per week, or never drinker

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=3,085 K=1 prospective cohort study (Sui et al. 2009)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	≥5 vs <5 drinks per week (≥10 vs ≤10 grams per day): OR=1.00 (0.75, 1.33)	*The evidence shows no association* A single study at low risk of bias reported no difference in rates of depression between females who drank more or less than 10g of alcohol per day.	Critical.
	N=6,980 K=2 prospective cohort studies (Meng 2017a; Meng et al. 2017b)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Monthly drinker vs < monthly drinker: HR=0.92 (0.80, 1.05), Monthly drinker vs never drinker: RR=0.75 (0.63, 0.89) Occasional drinker vs never drinker: RR=1.49 (1.25, 1.77)	*No reliable evidence of an association* One out of two studies showed no association between drinking frequency on the rate of women developing depression at a later time point. One study reported that those who drank monthly had less chance of depression, while those drank occasionally had more chance of depression. The risk of bias, and inconsistency between results of Meng et al. 2017 means the certainty of evidence is very low.	Critical
Depressive symptoms	N=382 K=1 prospective cohort study (Johnson et al. 2013)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Hazardous drinking (≥84g alcohol/occasion) vs non-hazardous drinking or abstinence: $\beta=0.18$, $p<0.05$	*Limited evidence of an association* A single small study reported a positive association between hazardous drinking and depressive symptoms after 4 years. The evidence was rated down due to imprecision and a moderate threat to internal validity in the study.	Important
Suicidal ideation	N=62,790 K=1 cross-sectional study	Risk of bias: -1 Inconsistency: N/A Indirectness: 0	⊕⊖⊖⊖	HED vs no HED and suicidal ideation athe same time point: OR=1.94 (1.74, 2.16)	*Limited evidence of an association* A single cross sectional study reported that HED was significantly associated with suicidal ideation in unadjusted	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	(Glasheen et al. 2015)	Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0			analyses.	
Suicide attempts	N=62,790 K=1 cross-sectional study (Glasheen et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED vs no HED and suicidal attempt athe same time point: OR=2.77 (2.12, 3.61)	*Limited evidence of an association* A single cross sectional study reported that women (with or without MDE) who participated in HED were over twice as likely to attempt suicide compared with those who did not participate in HED.	Important
				Interaction between MDE and HED and suicide attempt Adjusted Wald χ2=14.58(1), p<0.001).	*Limited evidence of an association* In those without MDE, participating in HED significantly increased the likelihood of attempted suicide, whereas in those with MDE, HED did not increase the risk.	Important
Anxiety	N=18,146 for males and females (N not stated by sex) K=1 prospective cohort study (Flensborg-Madsen et al. 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Alcohol quantity per day vs abstinence 0-24 g/day: HR=<1.0 >24 g/day: HRs 1.92 (1.10, 3.33) and 1.74	*No reliable evidence of an association* There was inconsistent evidence within alcohol consumption levels regarding whether higher amounts of alcohol per day were related significantly to anxiety or not.	Critical
				Drinking above guidelines vs within guidelines: HR=2.00 (1.31, 3.04), p<0.05	*Limited evidence of an association* A single study reported that women who drank above drinking guidelines level (0-168g /week) had significantly more likelihood of anxiety than those who drank below guidelines.	Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0				*No evidence for this outcome*	Important

Question: What is the effect of alcohol on mental health outcomes (across ages)?
Patient or population: Males, general population (across youth and adults)
Exposure: 5 drinks or over per week, or being monthly or weekly drinker, unhealthy alcohol use, >9 drinks/week
Reference group: less than 5 drinks per week, or never drinker

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=16,994 K=3 prospective cohort studies (Onwuameze et al. 2013; Ruggles et al. 2017; Sui et al. 2009)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	≥5 vs <5 drinks per week: OR=1.01 (0.87, 1.18) >9 vs <9 drinks per week: RR=0.94 (0.79, 1.13) Unhealthy alcohol use (≥4 on AUDIT-C): OR=1.09 (95%cl not stated)	*No reliable evidence of an association* Three studies provided consistent evidence that males drinking above particular thresholds (5 or 9 drinks per week, or AUDIT-C score 4) did not have a significantly increased likelihood of having depression compared to those drinking below the thresholds. Due to the risk of bias in the studies, the certainty of the evidence is low.	Critical
	N=6,220 K=2 prospective cohort studies (Meng 2017a; Meng et al. 2017b)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Monthly drinker vs < monthly drinker: HR=0.79 (0.64, 0.98) Monthly drinker vs never drinker: RR=0.45 (0.33, 0.62) Occasional drinker vs never drinker: RR=2.62 (1.93, 3.56)	*Limited evidence of an association* Two studies were consistent that men who drank more than once per month were less likely to have depression at follow-up, than those who abstained or drank less regularly. One of these studies also reported that those who drank occasionally had significantly more chance of depression at follow-up than those who abstained.	Critical
Suicidal ideation	N=73,710 K=1 cross-sectional study (Glasheen et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED vs no HED and suicidal ideation athe same time point: OR=1.63 (1.43, 1.85)	*Limited evidence of an association* A single cross sectional study reported that HED was significantly associated with suicidal ideation in unadjusted analyses.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Suicide attempts	N=73,710 K=1 cross-sectional study (Glasheen et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED vs no HED and suicide attempts athe same time point: OR=2.64 (1.76, 3.95)	*No reliable evidence of an association* A single cross sectional study reported that in males without MDE, there was no significant difference in the suicide attempts between HED and non-HED participants	Important
				Interaction between MDE and HED and suicide attempt adjusted Wald χ^2=0.01(1), p=0.989	*No reliable evidence of an association* There was no interaction between HED and MDE on the likelihood of suicide attempt in males.	Important
Anxiety	N=18,146 for males and females (N not stated by sex) K=1 prospective cohort study (Flensborg-Madsen et al. 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Drinking above guidelines vs within guidelines: HR=0.79 (0.42, 1.50)	*No reliable evidence of an association* A single study reported that men who drank above drinking guidelines level (0-252g /week) had no difference in later anxiety levels than those who drank within guideline levels.	Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0				*No evidence for this outcome*	Important

GRADE evidence profiles for adolescents

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Adolescents (males and females combined)
Exposure: HED frequency, volume of alcohol consumed (quantity x frequency), weekly consumption, heavy/excessive or HED
Reference group: HED frequency, volume of alcohol consumed (quantity x frequency), <weekly consumption, abstinence or non-hazardous drinking

Outcomes	**Participants Studies**	**Quality of evidence**	**GRADE**	**Results**	**Interpretation**	**Importance**
Depression	N=0 K=0				*No evidence for this outcome*	Critical
Depressive symptoms	N=4,841 K=2 prospective cohort studies (Hooshmand, Willoughby & Good 2012; Mason, WA et al. 2008)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Cross-sectional correlations of alcohol *quantity* consumed and depressive symptoms at the same time point: r=0.04 (p>0.05), to *r*=0.16 (p<0.05) ß=0.11, p<0.01	*Limited evidence of an association* Two studies reported on an association between volume of alcohol consumed and levels of depressive symptoms at the same time point. The two factors were significantly correlated at ages 14 to 16, but not at age 17.	Important
	N=4,841 K=2 prospective cohort studies (Hooshmand, Willoughby & Good 2012; Mason, WA et al. 2008)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Correlations of alcohol *quantity* consumed and depressive symptoms at later time point: r=0.07, p<0.05, to 0.14, p<0.05. ß=0.10, not significant.	*Limited evidence of an association* Two studies reported on an association between volume of alcohol consumed and levels of depressive symptoms a year or two later. The larger study reported all correlations were significant, while the smaller study showed an effect in the same direction, but was not statistically significant.	Important
	N=5,768 K=3 prospective cohort studies (Hooshmand, Willoughby & Good 2012; Mason, WA	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0	⊕⊖⊖⊖	Cross-sectional data of correlations of alcohol *frequency* consumed and depressive symptoms at same time point: r=0.11, p<0.05 to r=0.22, p<0.05 ß=0.049, p>0.05 to ß=0.19,	*Limited evidence of an association* Three studies reported significant cross-sectional correlations between alcohol frequency and depressive symptoms.Two studies reported significant correlations at all age (14 to 17 years), while the third study reported significant correlations at 14 years but correlations which were not statistically significant at 11 or 16 years.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	et al. 2008; Scholes-Balog et al. 2015)	Large effect: 0 Confounding: 0		p<0.05		
	N=6,388 K=4 prospective cohort studies (Hooshmand, Willoughby & Good 2012; Mason, WA et al. 2008; Parrish et al. 2016; Scholes-Balog et al. 2015)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Correlations of alcohol *frequency* consumed and depressive symptoms at later time point: r=0.09 to 0.11 (all p<0.05) ß=-0.05 to 0.22, p<0.001	*Limited evidence of an association* Three out of four studies reporting on the association between frequency of alcohol consumption and depressive symptoms found significant positive correlations.	Important
	N=544 K=2 prospective cohort studies (Mackie, Castellanos-Ryan & Conrod 2011; Mason, W & Spoth 2011)	Risk of bias: -2 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Cross-sectional correlations of alcohol *frequency x quantity* and depressive symptoms at the same time point: r=0.14, p<0.05 to 0.20, p<0.001 β=0.24, p<0.05	*Limited evidence of an association* Two small studies reported that cross-sectional correlations between alcohol frequency x quantity and depressive symptoms were significant at ages 14, 15 and 16.	Important
	N=7,507 K=3 prospective cohort studies (Mackie, Castellanos-Ryan & Conrod 2011; Mason, W & Spoth 2011; Patwardhan et al. 2017)	Risk of bias: -2 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Correlations of alcohol *frequency x quantity* and depressive symptoms at later time point: r=0.08 to r=0.12, p>0.05 β=0.27, p<0.05 rho=0.072, p<0.001	*Limited evidence of an association* Two out of three studies reported an association between alcohol quantity x frequency and depressive symptoms. The remaining study had results in the same direction, but was too small for the results to be statistically significant.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=10,828 K=1 prospective cohort study (Needham 2007)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	HED frequency at age 15 and depressive symptoms at age 21: *B*=−0.20, p<0.001	*Limited evidence of an association* A single large study reported that high levels of HED at baseline was associated with higher levels of depressive symptoms at baseline, as well as being associated with a faster rate of decline in depressive symptoms over the next 6 years.	Important
	N=1,312 K=2 prospective cohort studies (Birkley, Zapolski & Smith 2015; McCarty et al. 2012)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Cross-sectional correlations of *Any* alcohol consumption and depressive symptoms at the same time point: phi=0.13 (p<0.05) to phi=0.21, (p<0.001) β=0.15 (p<0.01) to β=0.23 (p<0.01)	*Limited evidence of an association* Both studies reported positive associations between adolescents (aged 11 – 14 years) drinking any alcohol (more than a few sips) and depression at the same point.	Important.
	N=1,312 K=2 prospective cohort studies (Birkley, Zapolski & Smith 2015; McCarty et al. 2012)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Any* alcohol consumption and depressive symptoms at later time point: phi=0.14, p<0.05 β=0.02 (p>0.05) to β=0.17, p<0.001	*Limited evidence of an association* Both studies reported positive associations between adolescents (aged 11 – 14 years) drinking any alcohol (more than a few sips) and depression at later time points. One study reported that correlations were not significant for depression at age 13, but the study was underpowered.	Important.

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=1,102 K=1 prospective cohort study (Skogen et al. 2016)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Weekly* alcohol consumption by age 13: β=0.40 (0.16, 0.65), p<0.05 < weekly alcohol consumption by age 13: β=0.15 (−0.09, 0.39) Late onset (no drinking until age 18): β=0.14 (−0.12, 0.41)	*Limited evidence of an association* Children who were drinking weekly at age 13, were more likely to have depressive symptoms at ages 15 – 18. Only one time-point showed a significant association between occasional drinking and depressive symptoms. There was no association between regular drinking and having depressive symptoms, if the drinking was started after age 13.	Important
	N=6,113 K=4 prospective cohort studies (Chan, Kelly & Toumbourou 2013; Gustafson 2012; Mason, W & Spoth 2011; Mason, WA et al. 2008)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*HED or drinking to intoxification* and depressive symptoms at the same time point rho=0.13, p<0.05 to 0.20, p<0.001 β=0.11, p>0.05 (n=429) r=0.141, p<0.01 to 0.20, p<0.05	*Limited evidence of an association* Three out of four studies reported significant cross-sectional associations between HED or drinking to intoxification, and depressive symptoms. The remaining study was small so may have been underpowered.	Important
	N=9,726 K=6 prospective cohort studies (Chan, Kelly & Toumbourou 2013; Cisler et al. 2012; Gustafson 2012; Mason, W & Spoth 2011; Mason, WA et al. 2008; Skogen et al. 2016)	Risk of bias: -2 Inconsistency: -2 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*HED or drinking to intoxification* and depressive symptoms at 1-12 years later rho=0.08 (p<0.05) to 0.15, p<0.05 β=-0.065 (p<0.05) to 0.37, (p<0.05) r=0.029 (p>0.05) to 0.069 (p<0.05)	*No reliable evidence of an association* The majority of the studies showed a positive association between HED, and later depressive symptoms (up to 6 years). However, one study found negative associations, suggesting that HED may result in fewer depressive symptoms.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=1,883 K=1 prospective cohort study (Pesola et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Heavy or harmful drinking* (not defined) and depressive symptoms at the same time point rho=0.13, p<0.05	*Limited evidence of an association* A single large study reported a cross-sectional association between heavy or harmful drinking and depressive symptoms at the same time point.	
	N=2,985 K=2 prospective cohort studies (Pesola et al. 2015; Skogen et al. 2016)	Risk of bias: -2 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Heavy or harmful drinking* (not defined) and depressive symptoms at a later time point rho=0.33, p<0.001 β=0.35, p<0.05 to β=0.40, p<0.05	*Limited evidence of an association* Two studies reported significant associations between heavy or harmful drinking and depressive symptoms 2-5 years later.	Important
Suicidal ideation	N=15,363 K=1 cross-sectional study (Gart & Kelly 2015)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED and suicidal ideation at the same time point: *B*=0.02, β=0.02, p=0.027	*Limited evidence of an association* One large cross-sectional study at high risk of bias reported that HED and suicidal ideation were significantly associated. The direction of effect was not determined.	Important
	N=6,540 K=1 cross-sectional study (Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 years vs non-initiators: OR=1.95 (1.32, 2.89) <12 years vs non-initiators: OR=3.39 (2.44, 4.71)	*Limited evidence of an association* One large cross-sectional study with a low risk of bias reported that those who had started drinking alcohol as a pre-teen or teen were more likely to have suicidal ideation than those who did not consume alcohol.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Large effect: 0 Confounding: 0				
	N=1,039 K=1 cross-sectional study (Souza et al. 2010)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Drank alcohol in past month vs abstinence: OR=1.64 (1.04, 2.58), p=0.033	*Limited evidence of an association* A single cross-sectional study reported that those who drank alcohol in the past month were more likely to also have suicidal ideation than those who were abstinent, to also have suicidal ideation. The direction of effect is unknown.	Important
				Drunkenness in past month vs no drunkenness: OR=1.94 (0.86, 4.36)	*No reliable evidence of an association* A single cross-sectional study reported that those who got drunk in the past month were more likely to also have suicidal ideation than those who did not, but after adjusted analysis this was not significant.	Important
Suicide attempt	N=47,316 K=2 cross-sectional studies (Gart & Kelly 2015; Schilling et al. 2009)	Risk of bias: -2 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED and suicide attempt at the same time point: *B*= 0.03, β=0.05, p<0.001 *B*=0.20 (0.06, 0.34), p<0.05 and	*Limited evidence of an association* Two large cross-sectional studies were consistent in reporting that there were significant associations between HED and attempting suicide in adolescents. In further analyses, one of these studies determined that the association between ‘drinking while down’ and suicide attempt was much stronger than for HED, and so the motive for drinking was more important than the occurrence of HED.	Important.
	N=6,540 K=1 cross-sectional study (Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 years vs non-initiators: OR=1.64 (1.16, 2.32) <12 years vs non-initiators: OR=4.55 (3.34, 6.21)	*Limited evidence of an association* One large cross-sectional study with a low risk of bias reported that those who had started drinking alcohol as a pre-teen or teen were more likely to attempt suicde than those who did not consume alcohol. The direction of effect is unknown.	Important.
Anxiety	N=2,070 K=1 prospective cohort study	Risk of bias: -1 Inconsistency: N/A	⊕⊕⊖⊖	*Drinking at least once per week vs less than weekly:* OR=1.3 (0.6, 2.8)	No reliable evidence of an association A single study found no association between frequency of gettingweekly drinking and anxiety at a later time point.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	(Fröjd et al. 2011)	Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0		*Drunk at least once a week vs less than weekly:* *OR=0.8 (0.2, 3.6)*	*No reliable evidence of an association* A single study found no association between frequency of getting drunk and anxiety at a later time point.	Critical
Anxiety symptoms	N=620 K=1 prospective cohort study (Parrish et al. 2016)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Drinking frequency:* ß=0.02, p>0.05	*No reliable evidence of an association* A single study showed that drinking frequency in 14 year olds did not predict anxiety symptoms at 16 years.	Important
	N=780 K=2 prospective cohort studies (Mackie, Castellanos-Ryan & Conrod 2011; Pardee, Colder & Bowker 2014)	Risk of bias: -2 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Drinking quantity x frequency* There was no significant directional effects between Q×F and anxiety (p>0.39). B=0.001, p>0.05	*No reliable evidence of an association* Two studies were consistent in that quantity x frequency of alcohol consumed was not a significant predictor of anxiety symptoms after 6 months to 3 years.	Important
	N=3,614 K=1 prospective cohort study (Cisler et al. 2012)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	For PTSD 1 year later: Multiple imputations: ß=0.02, t=1.01, p>0.05 For PTSD 2 years later: Multiple imputations: ß=0.14, t=2.20, p<0.05	*Limited evidence of an association* HED frequency predicted PTSD diagnosis after 2 years, but not after 1. This study was not adjusted for multiple comparisons, and is therefore at risk of a type II error.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
PTSD	N=3,614 K=1 prospective cohort study (Cisler et al. 2012)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	For PTSD 1 year later: Multiple imputations: ß=0.02, t=1.01, $p>0.05$ For PTSD 2 years later: Multiple imputations: ß=0.14, t=2.20, $p<0.05$	*Limited evidence of an association* HED frequency predicted PTSD diagnosis after 2 years, but not after 1. This study was not adjusted for multiple comparisons, and is therefore at risk of a type II error.	Important
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Female adolescents
Exposure: Alcohol frequency, HED, moderate drinking
Reference group: Never HED, low drinking

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=6,466 K=1 prospective cohort study (Powers, J et al. 2016)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*HED:* Rarely vs never: OR=1.02 (0.82, 1.27) Monthly vs never: OR=0.94 (0.75, 1.17) Weekly vs never: OR=0.93 (0.76, 1.14) >Weekly vs never: OR=1.30 (1.04, 1.63)	*Limited evidence of an association* One large study reported that HED more frequently than once per week when aged 16-21 was significantly associated with having depression between ages 22 and 27. HED weekly or less was not associated with depression.	Critical
	N=2,414 K=1 prospective cohort study (Edwards et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Moderate vs low drinking: OR=1.63 (1.04, 2.55), p<0.05 High vs low drinking: OR=1.93 (1.08, 3.44), p<0.05	*Limited evidence of an association* One study reported that 14 year old girls who drank moderately or highly (occasionally or weekly) were significantly more likely to have depression at age 16 than those who didn't drink.	Critical
Depressive symptoms	N=661 K=2 prospective cohort studies (Fleming et al. 2008; Wymbs et al. 2014)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Alcohol frequency* Correlation coefficients: ß=0.10 to 0.23 (not significant)	*No reliable evidence of an association.* No significant association was found between frequency of alcohol consumption and depressive symptoms, although a consistent trend was identified, and the studies were small.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=291 K=1 prospective cohort study (Danzo, Connell & Stormshak 2017)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Quantity x frequency* and depressive symptoms at the same time point Correlation coefficients: r=0.29 (p<0.05) to 0.38 (p<0.05)	*Limited evidence of an association* A single small study reported that cross-sectional associations between quantity x frequency of alcohol and concurrent depressive symptoms were significant at all ages for female adolescents (12 to 15 years).	Important
	N=291 K=1 prospective cohort study (Danzo, Connell & Stormshak 2017)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Quantity x frequency* and depressive symptoms at a 1-3 years later Correlation coefficients: r=0.07 (p>0.05) to 0.30 (p<0.05)	*Limited evidence of an association* A single small study reported on the association of quantity x frequency and depressive symptoms after 1 to 3 years. The correlations were significant at nearly all time points, suggesting that in females, the number of drinks consumed in a month over ages 12 – 14 predict depressive symptoms 1 to 3 years later.	Important
	N=15,167 K=3 prospective cohort studies (Needham 2007; Pesola et al. 2015; Wilkinson, Halpern & Herring 2016)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*HED* Correlation coefficients: β=−0.03 (−0.09, 0.03) β=0.01 (SE 0.01) *B*=-0.03, p<0.001	*No reliable evidence of an association* One study reported that HED was associated with a faster reduction in depressive symptoms, while the remaining two studies reported no association.	Important
	N=3,096 K=1 prospective cohort study (Schuler, Vasilenko & Lanza 2015)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0	⊕⊕⊕⊖	*HED* Time-varying coefficients β~0.4 (0.0, 0.8) to 3.7 (2.1m 5.3)	*Evidence of an association* A single high quality study reported significant associations between HED and depressive symptoms during adolescence (with predictors and outcomes as continuous functions of time, i.e. both predictors and outcomes measured at the same multiple time points).	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Confounding: 0				
Suicidal ideation	N=35,001 K=2 cross-sectional studies (Kim & Kim 2010; Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 or 13 years vs non-initiators: ORs=1.21 (1.12, 1.30) and 2.12 (1.34, 3.34) <12 or 13 years vs non-initiators: ORs=1.34 (1.33, 1.59) and (3.12 (1.95, 4.90)	*Limited evidence of an association* Two cross-sectional studies reported consistent evidence that girls who start consuming alcohol before age 12 or 13 have a higher risk of having suicidal ideation than those who do not start drinking alcohol. Those who start drinking as a teen also have a higher risk than those who don't start drinking.	Important
Suicide attempts	N=35,001 K=2 cross-sectional studies (Kim & Kim 2010; Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 or 13 years vs non-initiators: ORs=1.23 (1.05, 1.43) and 2.31 (1.51, 3.52) <12 or 13 years vs non-initiators: ORs=1.61 (1.37, 1.89) and 5.76 (3.84, 8.64)	*Limited evidence of an association* Two cross-sectional studies reported consistent evidence that girls who start consuming alcohol before age 12 or 13 or as a teen have a higher risk of attempting suicide than those who don't start drinking as an adolecent.	Important
Anxiety	N=2,414 K=1 prospective cohort study (Edwards et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Moderate vs low drinking: OR=1.25 (0.88, 1.77) High vs low drinking: OR=1.78 (1.13, 2.81), $p<0.05$	*No reliable evidence of an association.* One study reported that teenage girls who drank weekly were more likely to have anxiety after 2 years than those who did not drink. However, after adjustments for housing tenure and conduct problems, this was no longer significant.	Critical
PTSD	N=0 K=0					

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Male adolescents
Exposure: Alcohol frequency, moderate or high consumption, quantity, frequency, quantity x frequency, HED
Reference group: Low alcohol consumption, non-HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=1,878 K=1 prospective cohort study (Edwards et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Moderate vs low alcohol consumption: 2.25 (1.09, 4.66), $p<0.05$ High vs low alcohol consumption: 2.54 (1.06, 6.10), $p<0.05$	*Limited evidence of an association* One study showed that moderate alcohol consumption (occasional use) and high levels of consumption (weekly use) in 14 year old males, significantly predicted having a depressive episode by age 16.	Critical
Depressive symptoms	N=745 K=2 prospective cohort studies (Fleming et al. 2008; Wymbs et al. 2014)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*Alcohol frequency* and depressive symptoms at the same time point Correlation coefficients: ß=0.05 ($p>0.05$) to ß=0.16 ($p<0.05$)	*No reliable evidence of an association* Two small studies reported cross-sectional associations between frequency of alcohol consumption and level of depressive symptoms. One study reported no significant association at any age (13-16 years), while the second study reported no association at age 14, but a significant association at age 15.	Important
	N=745 K=2 prospective cohort studies (Fleming et al. 2008; Wymbs et al. 2014)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0	⊕⊖⊖⊖	*Alcohol frequency* and depressive symptoms at later time points Correlation coefficients: ß=0.02 to 0.13	*No reliable evidence of an association* Two small studies reported no significant association was found between frequency of alcohol consumption and depressive symptoms.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Dose-response: 0 Large effect: 0 Confounding: 0				
	N=302 K=1 prospective cohort study (Danzo, Connell & Stormshak 2017)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Quantity x frequency* and depressive symptoms at the same time point Correlation coefficients: r=0.09 (p>0.05) to 0.28 (p<0.05)	*No reliable evidence of an association* A single small study reported on the association of quantity x frequency and concurrent levels of depressive symptoms in adolescent males. The association was significant at age 14, but not at ages 12, 13 or 15.	Important
	N=302 K=1 prospective cohort study (Danzo, Connell & Stormshak 2017)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Quantity x frequency* and depressive symptoms at 1 to 3 years later Correlation coefficients: r=0.00 (p>0.05) to 0.17 (p<0.05)	*No reliable evidence of an association* A single small study reported on the association of quantity x frequency and depressive symptoms after 1 and 2 years. Only 1/6 correlations was significant, suggesting that overall, the number of drinks consumed in the past month does not predict depressive symptoms.	Important
	N=12,519 K=3 prospective cohort studies (Needham 2007; Pesola et al. 2015; Wilkinson, Halpern & Herring 2016)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*HED* Correlation coefficients: β=−0.03 (−0.10, 0.05) β=−0.01 (SE 0.01) and *B*=−0.06 (0.03), p<0.05	*No reliable evidence of an association* Three studies were consistent that there was no significant association between between HED in male adolescents, and levels of depressive symptoms 2-13 years later.	Important
	N=2974 K=1 prospective cohort study (Schuler, Vasilenko &	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0	⊕⊕⊕⊖	*HED* Age-related coefficients: β=0.0 (-0.3, 0.3) to 2.1 (1.7, 4.4)	*Evidence of an association* A single large good quality study reported significant associations between HED and depressive symptoms at ages 12 and 17 years, but non-significant associations at ages 18.5 and 31 years. The associations were smaller in males than	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	Lanza 2015)	Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0			female adolescents.	
Suicidal ideation	N=35,263 K=2 cross-sectional studies (Kim & Kim 2010; Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 or 13 years vs non-initiators: ORs= OR=1.11 (1.01, 1.22) and 1.88 (1.14, 3.10) <12 or 13 years vs non-initiators: ORs=1.28 (1.16, 1.41), and 3.37 (2.16, 5.27)	*Limited evidence of an association* Two cross-sectional studies reported consistent evidence that boys who start consuming alcohol before age 12 or 13 have a higher risk of having suicidal ideation than those who do not start drinking alcohol. Those who start drinking as a teen also have a higher risk than those who don't start drinking.	Important
Suicide attempts	N=35,263 K=2 cross-sectional studies (Kim & Kim 2010; Peltzer & Pengpid 2015)	Risk of bias: 0 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Age at alcohol consumption initiation: ≥12 or 13 years vs non-initiators: ORs=1.06 (0.89, 1.27), n=13,595 and 1.19 (0.77, 1.85)	*No reliable evidence of an association* Two cross-sectional studies reported consistent evidence that boys who start consuming alcohol as a teen are not at an increased risk of suicide attempt compared to those who have not started drinking.	Important
				Age at alcohol consumption initiation: <12 or 13 years vs non-initiators: ORs=1.27 (1.06, 1.52) and 3.94 (2.46, 6.32)	*Limited evidence of an association* Two cross-sectional studies reported consistent evidence that boys who start consuming alcohol before age 12 or 13 have a higher risk of attempting suicide than those who don't start drinking as an adolecent.	
Anxiety	N=1,878 K=1 prospective cohort study (Edwards et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0	⊕⊕⊖⊖	Moderate vs low drinking: OR=1.13 (0.65, 1.95) High vs low drinking: OR=1.20 (0.55, 2.62)	*The evidence shows no association* No association was found between occasional or weekly drinking and anxiety after 2 years.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Large effect: 0 Confounding: 0				
Anxiety symptoms	N=503 K=1 prospective cohort study (Cerdá et al. 2016)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Alcohol frequency: ß=−0.00002 (95%CI −0.003, 0.003) Alcohol quantity: age 13-14: ß=−0.36 (95%CI −0.62, −0.11), $p<0.05$ age 15-16: ß=−0.26 (95%CI −0.84, 0.32) age 17-19: ß=−0.20 (95%CI −0.38, −0.02), $p<0.05$	*Limited evidence of an association* A single study reported significant associations between the volume of alcohol consumed per drinking occasion and the level of anxiety symptoms reported 13 years later.	Important
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

GRADE evidence profiles for young adults

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Young adults (males and females combined)
Exposure: Any alcohol consumption, medium-risk drinking, high-risk drinking, HED/heavy drinking, alcohol quantity, frequent HED
Reference group: No alcohol consumption, low-risk drinking, occasional HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depressive symptoms	N=429 K=1 prospective cohort study (Mason, WA et al. 2008)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Cross-sectional correlation between consumption *quantity* and depressed mood at age 18: β=0.10 Cross-sectional correlation between consumption *frequency* and depressed mood at age 18: β=0.07	*No reliable evidence of an association* The single small study in young adults assessing link between alcohol consumption quantity or frequency and concurrent diagnosis diagnosis of depression reported no significant association between either quantity or frequency of alcohol consumption a.	Critical
Depressive symptoms	N=429 K=1 prospective cohort study (Mason, WA et al. 2008)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Alcohol consumption *quantity:* β=0.06 Alcohol consumption frequency: β=0.03	*No reliable evidence of an association* A single study reported that there was no significant association between quantity of alcohol at age 18 and depressed mood at age 22 as a continuous variable. Likewise, there was no association between frequency of alcohol consumption at age 18 and depressed mood at age 22 as a continuous variable.	Important
	N=522 K=1 prospective cohort study (Armeli, Sullivan & Tennen 2015)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Alcohol *quantity x frequency*: *b*=0.001	*No reliable evidence of an association* One small study found no association between total alcohol consumed (quantity x frequency) and depressive symptoms.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=4,809 K=3 prospective cohort studies (Gustafson 2012; Mason, WA et al. 2008; Piasecki, Trela & Mermelstein 2017)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Frequency of HED* and depressive symptoms at the same time point Correlations: r=-0.004 to 0.01 β=-0.009 to 0.05	*No reliable evidence of an association* Three studies were consistent that there was no significant cross-sectional association between HED and depressive symptoms in young adults.	Important
	N=4,809 K=3 prospective cohort studies (Gustafson 2012; Mason, WA et al. 2008; Piasecki, Trela & Mermelstein 2017)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Frequency of HED* Correlations: r= -0.045 ($p<0.05$) to r=0.01 ($p>0.05$) β=-0.026 to 0.05	*No reliable evidence of an association* One out of three studies reported a statistically significant negative association between HED and a reduced number of depressive symptoms.	Important
	N=7,386 K=1 prospective cohort study (Sloan, Grossman & Platt 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Frequent HED vs occasional HED Difference in propensity scores: 3.7 (95%CI 0.41, 7.1)	*Limited evidence of an association* A single study reported that frequent HED drinkers had higher depressive symptoms than occasional HED drinkers.	Important
Suicide attempts	N=0 K=0					
Anxiety	N=0 K=0					Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
PTSD	N=904 K=1 prospective cohort study (Read et al. 2016)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: -2 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	ORs for transitioning to PTSD or more severe PTSD with alcohol vs no alcohol: 0.76 – 1.35 ORs for transitioning to no PTSD or less severe PTSD with alcohol vs no alcohol: 0.82 – 1.34	*No reliable evidence of an association* There was a similar likelihood of that any alcohol consumption was associated with PTSD or worsening of PTSD as there was of alcohol consumption being associated with no longer having PTSD or improving PTSD	Important
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Young adults (females)
Exposure: Any alcohol consumption, medium-risk drinking, high-risk drinking, HED/heavy drinking, alcohol quantity, frequent HED
Reference group: No alcohol consumption, low-risk drinking, occasional HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=1,196 K=1 prospective cohort study (Zhang et al. 2018)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*Alcohol quantity* and depression 17 months later: Medium risk (20-40 g/day) vs low risk (<20 g/day): OR=1.50 (0.56, 4.05) High risk (>40 g/day) vs low risk (<20 g/day): OR=1.73 (0.37, 8.18)	*No reliable evidence of an association* A single large study reported that the average quantity which young adult women drank per day did not predict the likelihood of developing depression 17 months later. However, the large confidence intervals suggest that this study may have been underpowered for this outcome.	Critical
Depressive symptoms	N=249 K=1 prospective cohort study (Wymbs et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0	⊕⊖⊖⊖	*Drinking frequency* and depressive symptoms at the same time: β=0.18	*No reliable evidence of an association* A single small study reported no significant association between drinking frequency and cross-sectional levels of depressive symptoms in young adult women. However, this study may have been underpowered.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Dose-response: 0 Large effect: 0 Confounding: 0				
	N=200 K=1 prospective cohort study (Mushquash et al. 2013)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	*HED* and depressive symptoms at 1-2 weeks later: β=0.02 to 0.05	*No reliable evidence of an association* A single small study found no significant association between HED and depressives symptoms a short time later.	Important
Suicide attempts	N=0 K=0					
Anxiety	N=0 K=0					Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol on mental health outcomes in youth?
Patient or population: Young adults (males)
Exposure: Any alcohol consumption, medium-risk drinking, high-risk drinking, HED/heavy drinking, alcohol quantity, frequent HED
Reference group: No alcohol consumption, low-risk drinking, occasional HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depressive symptoms	N=272 K=1 prospective cohort study (Wymbs et al. 2014)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0	⊕⊕⊖⊖	Alcohol *frequency* at the same time point β=−0.17, p>0.05	*No reliable evidence of an association* A single small study reported no association between frequency of alcohol consumption in young adult males, and depressive symptoms at the same time point.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0				
	N=4,617 K=1 prospective cohort study (Grazioli et al. 2018)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Alcohol *quantity x frequency (total drinks per week)* and depressive symptoms at the same time*:* rho=0.06 and 0.08 (both $p<0.001$)	*Limited evidence of an association* A single large study in males, reported that alcohol quantity x frequency (total drinks consumed per week) was significantly positively correlated with depressive symptoms at the same time point (unadjusted). The direction of effect is unknown.	Important
	N=4,617 K=1 prospective cohort study (Grazioli et al. 2018)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Alcohol *quantity x frequency (total drinks per week)* and depressive symptoms 15 months later: rho=0.03, $p<0.05$ $\beta=-0.100$ [−0.145, −0.053]	*Limited evidence of an association* A single large study in males, reported that amount of alcohol consumed per week was associated with fewer depressive symptoms after adjusting for covariates such as drinking to cope (i.e. positive effect is for drinking for pleasure, rather than drinking in total).	Important
	N=4,617 K=1 prospective cohort study (Grazioli et al. 2018)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*HED* and depressive symptoms at the same time*:* rho=0.04 to 0.07 (both $p<0.05$)	*Limited evidence of an association* A single large study in males, reported that HED was associated with the concurrent level of depressive symptoms (unadjusted).	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=4,617 K=1 prospective cohort study (Grazioli et al. 2018)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	*HED* and depressive symptoms 15 months later: rho=0.03, p>0.05 β=−0.144 (-0.224, -0.065)	*No reliable evidence of an association.* A single large study in males, reported that frequency of HED was not correlated with depressive symptoms 15 months later in unadjusted analyses. Significant associations were found after adjusted for drinking to cope.	Important
Suicide attempts	N=4,617 K=1 prospective cohort study (Grazioli et al. 2018)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Direct effect: alcohol on suicide Total drinks /week: β=−0.019 (−0.289, 0.260) HED: β=0.119 (−0.408, 0.665)	*No reliable evidence of an association* Alcohol use (total drinks per week or HED) was not directly associated with suicide attempts. Indirect effects were found through the effect of alcohol on baseline depressive symptoms.	Important
Anxiety	N=0 K=0					Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

Evidence statements:

No reliable evidence of an association between alcohol consumption and mental health outcomes was identified in young adults (GRADE ⊕⊖⊖⊖ to ⊕⊕⊕⊖).

Limited evidence suggests that frequent HED in young adults may be associated with a higher risk of depressive symptoms than occasional HED (k=1; GRADE ⊕⊕⊖⊖).

GRADE evidence profiles for adults

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Adults general population
Exposure: Weekly alcohol consumption, alcohol in toxicology, low consumption, hazardous or harmful consumption, HED
Reference group: Not stated (assumed abstinence or consumption less than weekly), abstainers

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=7,478 K=1 prospective cohort study (Bell & Britton 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 1 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Abstainers vs drinking within guidelines (≤21g for men; ≤14g for women per week): HR=1.02 (0.89, 1.16) Exceeding guidelines vs within guidelines: HR=0.86 (0.53, 1.39)	*No reliable evidence of an association* A single study reported no difference in rate of depression over a 28 year period in those who drank within guidelines and either abstainers or those who exceed drinking guidelines.	Critical
	N=7,478 K=1 prospective cohort study (Bell & Britton 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 1 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	HED vs non-HED drinkers: HR=1.0 (0.91, 1.15) Abstinent vs non-HED drinkers: HR=1.23 (0.98, 1.53)	*No reliable evidence of an association* A single study reported no difference in rate of depression over a 28 year period between those who drank without HED, vs either abstinence or HED	Critical
	N=7,478 K=1 prospective cohort study (Bell & Britton 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 1 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Hazardous drinkers (>40g/session) vs non-hazardous drinkers: HR=0.81 (0.49, 0.86)	*Limited evidence of an association* A single study reported a statistically significant difference in the rate of depression over 28 years, such that those who participated in hazardous drinking at baseline had a lower rate of depression than non-hazardous drinkers.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=7,478 K=1 prospective cohort study (Bell & Britton 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 1 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Abstainers and daily drinkers vs weekly drinkers HR=1.24 (0.99,1.56) and 1.17 (1.05,1.32), p=0.01 Monthly and occasional drinkers vs weekly drinkers HR=1.07 (0.92,1.25) and 0.97 (0.83,1.15)	*Limited evidence of an association* One study reported that daily drinkers had a higher risk of depression over a 28 year period than weekly drinkers. there was a trend for abstainers having a higher risk of depression than weekly drinkers There was no difference in the odds of depression between weekly, monthly and occasional drinkers.	Critical
	N=13,619 K=1 prospective cohort study (Gea et al. 2012)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Low consumption vs abstainers: HRs=0.65 (0.49, 0.86) to 0.94 (0.75, 1.19)	*Limited evidence of an association.* A single large study reported that those who drank low levels of alcohol (<30g/day) had lower depression rates than those who were abstinent.	Critical
	N=13,619 K=1 prospective cohort study (Gea et al. 2012)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Hazardous or harmful consumption vs abstainers: HR=0.73 (0.50, 1.06)	*No reliable evidence of an association* One study provided evidence that moderate to high levels of alcohol (>15g/day) was not significant associated with the odds of depression.	Critical
Depressive symptoms	N=15,926 K=1 prospective cohort study (Paljärvi et al. 2009)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 1 but not rated	⊕⊕⊖⊖	Low consumption vs abstainers: ORs=1.02 (0.89, 1.04) to 1.16 (1,04, 1.30) Hazardous or harmful consumption vs abstainers: ORs=1.43 (1.28, 1.60)	*Limited evidence of an association* One study reported that anything over 10 g of alcohol per day for women, or over 15 g for men, was associated with an increased risk of depressive symptoms.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		up due to risk of bias in the study Large effect: 0 Confounding: 0				
Incident bipolar disorder	N=34,653 K=1 prospective cohort study (Cougle et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Weekly alcohol vs abstinence or <weekly alcohol: OR=0.79 (0.73, 0.86), p<0.001	*Limited evidence of an association* One study (with no adjustments for multiple comparisons) found that weekly alcohol use was associated with a reduced risk of being diagnosed with an incident bipolar disorder.	Important
Suicide	N=346 K=1 case control study (Conner et al. 2017)	Risk of bias: -1 Inconsistency: N/A Indirectness: -1 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	OR of dying by suicide rather than motor vehicle accident if blood toxicology showed alcohol alone or in combination with other drug: Alcohol alone vs neither: OR=1.22 (0.74, 2.00) Alcohol plus drug vs neither: OR=4.33 (1.70, 11.03), p<0.05 Drug alone vs neither: OR=1.03 (0.37, 2.88)	*No evidence of an association* There was no significant difference in the proportion of people dying by suicide or motor vehicle, based on whether they had alcohol in their blood stream or not. People who had alcohol and drugs in their blood stream, were more likely to die by suicide than motor vehicle accident than if they had neither in their blood.	Important
Suicidality (ideation or attempt)	N=3,813 K=1 cross-sectional study (Herberman Mash et al. 2016)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Quantity of alcohol per day: <48 g for men and 24.3 g for women per day, vs drinking more than these amounts: OR=1.04 (0.67, 1.65)	*No reliable evidence of an association* A single cross-sectional study reported that amount of alcohol consumed per day (light to moderate vs heavy) was not associated with suicidality rate, after adjustments for confounding factors such as motives for drinking.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Anxiety	N=34,653 K=1 prospective cohort study (Cougle et al. 2015)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Weekly consumption vs less than weekly consumption: OR=0.88 (0.82, 0.95), p<0.01	*Evidence of an association* A large study from U.S. found that adults who consume alcohol at least weekly, have less chance of developing depression after 3 years, than those who drink less than weekly or abstain.	Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Adult females
Exposure: Drinks per day, AUDIT score percentile, frequency of drinking
Reference group: Abstinence

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=7082 K=1 prospective cohort study (Gea et al. 2012)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Low consumption vs abstainer: HR=0.62 (0.42, 0.88) to 0.97 (0.75, 1.27) ORs=0.4 (0.1, 1.1) to 0.6 (0.4, 1.2) High consumption vs abstainer: HR=1.06 (0.43, 2.63) OR=3.3 (0.7, 14.8)	*No reliable evidence of an association* There was a (predominantly non-significant) trend supporting low levels of consumption (either in drinks/day or on AUDIT score percentile) compared with total abstinence. There was no significant difference in the odds of having depression at follow-up in abstainers or high consumers of alcohol.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=3,353 K=1 prospective cohort study (Augestad, Slettemoen & Flanders 2008)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Low frequency (no recent or 1-4 times in 2 weeks) drinking vs abstainer: OR=1.17 (0.61, 2.24) to 1.18 (0.61, 2.27) High frequency (≥10 times/2 weeks) vs abstainer: OR=0.72 (0.15, 3.47)	*No reliable evidence of an association* Neither low frequency drinking nor high frequency drinking was associated with depression 4-years later.	Critical
Depressive symptoms	N=306 K=1 prospective cohort study (Otten, van der Zwaluw & Engels 2018)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Mean no. of drinks consumed: $\beta=0.05$, $p=0.36$	*No reliable evidence of an association* A single study found no association between number of drinks consumed and level of depressive symptoms 4 years later.	Important
Suicide	N=0 K=0					Important
Anxiety	N=approx. 9455 K=2 prospective cohort studies (Flensborg-Madsen et al. 2011; Johnson et al. 2013)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	>14 drinks/week vs <14 drinks/week: HR=2.00 (1.31, 3.04) >14 drinks/week vs abstainer: HR=1.92 (1.10, 3.33) No significant relationship between hazardous drinking (wave 1) and anxiety (wave 2).	*No reliable evidence of an association* One out of two studies reported a significant association between alcohol consumption and a higher risk of developing anxiety. The other small study reported no association.	Critical
PTSD	N=0 K=0					

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Adult males
Exposure: Drinks per day, AUDIT score percentile, frequency of drinking
Reference group: Abstinence

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=6,537 K=1 prospective cohort study (Gea et al. 2012)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Low consumption vs abstainer: HR=0.64 (0.39, 1.07) to 0.82 (0.50, 1.36) High consumption vs abstainer: HR=0.76 (0.40, 1.47)	*No reliable evidence of an association* No significant associations were found between alcohol consumption levels and the risk of depression at follow-up.	Critical
	N=3,308 K=1 prospective cohort study (Augestad, Slettemoen & Flanders 2008)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Low frequency (no recent or 1-4 times in 2 weeks) drinking vs abstainer: OR=0.62 (0.32, 1.21) to 0.75 (0.38, 1.49) High frequency (≥10 times/2 weeks) vs abstainer: OR=0.47 (0.16, 1.38)	*No reliable evidence of an association* Neither low frequency drinking nor high frequency drinking was associated with depression 4-years later.	Critical
Depressive symptoms	N=288 K=1 prospective cohort study	Risk of bias: -2 Inconsistency: N/A Indirectness: 0	⊕⊖⊖⊖	Mean no. of drinks consumed: β=0.01, p=0.87	A single study found no association between number of drinks consumed and level of depressive symptoms 4 years later.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	(Otten, van der Zwaluw & Engels 2018)	Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0				
Suicide	N=0 K=0					Important
Anxiety	N=approx. 9,073 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	>21 drinks/week vs <21 drinks/week: HR=0.79 (0.42, 1.50)	*No reliable evidence of an association* A single study reported no significant difference in rate of anxiety based on alcohol quantity consumed per day (above or below 252 g/week).	Critical
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

GRADE evidence profiles for older adults

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Older adult subgroup
Exposure: Weekly alcohol consumption / abstinent / occasional HED (<1 per month) / frequent HED (≥1 per month)
Reference group: Not stated (assumed abstinence or consumption less than weekly) / non-HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=8017 K=2 prospective cohort studies (Gea et al. 2013a; Weyerer et al. 2013)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Drinking ≤15g /day vs abstaining: HRs=0.72 (0.53, 0.98), p<0.05 to 0.97 (0.75, 1.25)	*No reliable evidence of an association* One out of two studies reported that elderly people who drank 5-15g of alcohol per day were less likely to have depression than those who abstained.	Critical
				Drinking >15 g/day vs abstaining: HRs=0.79 (0.53, 1.16) to 1.18 (0.79, 1.76)	*No reliable evidence of an association* Two studies were consistent that there was no significant difference in the rate of depression between those elderly people who were abstinent versus those who drank ≥20 g/day.	Critical
	N=25,619 K=2 prospective cohort studies (An & Xiang 2015; Luppa et al. 2012)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Heavy or at-risk drinking (≥14g/day for women and ≥30g/day for men) vs abstinence or non-heavy drinking: HRs=1.05 (0.98, 1.13) and 2.33 (1.09, 4.96)	*No reliable evidence of an association* Two studies compared heavy or at-risk drinking in an elderly population, against those who did not drink heavily. There was contradictory information, with one study reporting no difference in the rate of depression at follow-up, whereas the second study reported over a doubling of risk of subsequent depression in the high-alcohol consumption group. The reason for the hetereogeneity is unclear.	Critical
Depressive symptoms	N=7,939 K=1 prospective cohort study (Brennan et al. 2016)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Never drinkers: OR for increasing depressive symptoms=1.30, p>0.05. OR for decreasing depressive symptoms=1.13 Light drinkers: OR for increasing depressive symptoms=0.76, p>0.05 OR for increasing depressive	*No reliable evidence of an association* Different drinking levels had little influence on the whether participants had an increase or a decrease in their levels of depressive symptoms. Those with a drinking history (who were abstinent; data not shown here) had significantly higher chances of increasing depressive symptoms, as well as decreasing depressive symptoms vs having consistently low depressive symptoms.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
				symptoms=0.66, p>0.05 Moderate drinkers: OR for increasing depressive symptoms=0.59, p<0.01 OR for decreasing depressive symptoms=0.62, p>0.05 Heavy drinkers: OR for increasing depressive symptoms=0.95, p>0.05 OR for decreasing depressive symptoms=1.50, p>0.05		
	N=15,628 K=1 prospective cohort study (Cheng et al. 2016)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Drinking at least monthly vs being abstinent: OR=0.6 (0.5, 0.7) Drinking daily vs <daily: OR=1.2 (0.8, 1.7)	*Limited evidence of an association* A single study reported that those who drank at least monthly had reduced odds of having depression at follow-up, compared to those who never drank. No significant difference was found between those who drank daily or less than daily.	Important.
	N=3,273 K=1 prospective cohort study (Tsai, Chi & Wang 2013)	Risk of bias: 0 Inconsistency:N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Moderate weekly drinker (<2 drinks/time) vs drinking less than weekly: OR=0.89 (0.63, 1.26) Heavy weekly drinker (≥2 drinks/time) vs drinking less than weekly: OR=0.70 (0.30, 1.64)	*The evidence shows no association* A single good quality study reported no significant difference in likelihood of developing depressive symptoms, between those drink at least weekly, and at least 2 drinks per occasion, versus those who drink less than that.	Important
	N=10,463 K=2 prospective cohort studies (Lang et al. 2007; Paulson et al. 2018)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0	⊕⊕⊖⊖	1-2 drinks/day vs 0-1 drinks/day: z=−0.08 (−0.15, −0.02), p<0.05 ≤2 drink/day vs abstinent:	*Limited evidence of an association* Two studies reported that those who drank up to 2 drinks per day had lower rates of depressive symptoms at follow-up than those who didn’t drink, or drank up to 1 drink per day.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Dose-response: 0 Large effect: 0 Confounding: 0		β(SE)=0.151 (0.061), p=0.013		
Anxiety	N=0 K=0					
PTSD	N=0 K=0					
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Older female subgroup
Exposure: Light, moderate, heavy drinking, short term risk drinking, long term risk drinking, HED, monthly drinking
Reference group: Abstinence, light drinking, non-HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=65,598 K=5 prospective cohort studies 1490165122092198(Chang et al. 2016; Gea et al. 2013b; Hiles et al. 2015; Tait et al. 2012; Tanaka et al. 2011)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Light-moderate drinkers vs being abstinent: HRs=0.83 (0.58, 1.18) to 0.99 (0.74, 1.18) ORs=0.67 (0.37,1.19) to 0.70 (0.33, 1.49) Abstinent vs light drinkers: OR=1.23 (1.14, 1.32) and z=0.31 (0.08, 0.54), p<0.01	*No reliable evidence of an association* Four studies were consistent that a light to moderate amount of alcohol per day (<40 g/day) was not significantly associated with either a risk reduction or increase in the risk of depression compared to abstinence. A single very large Australian study reported that those who were abstinent had significantly higher levels of depression at follow-up than those who consumed 0-20 g/day.	Critical
	N=27,314 K=3 prospective cohort studies 1490;2209(Chang et al. 2016; Hiles et al. 2015; Tanaka et al. 2011)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0	⊕⊕⊖⊖	Heavy, or hazardous drinker (20 g/day) vs abstainer: HRs=1.13 (1.01, 1.26) ORs=0.36 (0.04, 3.43) to 0.39 (0.05, 3.08)	*No reliable evidence of an association* Few elderly people consumed hazardous amounts of alcohol, so two out of three studies were underpowered and had no significant association between heavy drinking (>20 or 40 g/day) and depression. The remaining study was very large and reported that heavy drinkers (>40 g/day) had an elevated	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Dose-response: 0 Large effect: 0 Confounding: 0			risk of developing depression compared to abstainers.	
	N=12,132 K=1 prospective cohort study (An & Xiang 2015)740	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Heavy vs non-heavy drinking or abstinence: HR=1.09 (0.98, 1.20)	*No reliable evidence of an association* When high consumption was compared against low consumption, there were no significant differences in the chance of having depression at follow-up.	Important
	N=31,202 K=1 prospective cohort study (Tait et al. 2012)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Short term risk drinking (≥4 drinks/day) vs 0-2 drinks/day: OR=1.54 (1.22, 1.95), $p<0.001$ Long-term risk drinking vs 0-2 drinks/day: OR=1.22 (1.08, 1.38), $p<0.05$	*Limited evidence of association* A single study reported that short-term risk drinkers (4 drinks/day) had a higher likelihood of depression than low risk drinkers (0-2 drinks/day). Long-term risk drinkers (2-4 drinks/day) also had a higher likelihood of depression.	Critical
	N=7,891 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011) #262	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	HED frequency vs non-HED drinkers: OR=0.79 (0.56, 2.86) for HED ≥1 per month and OR=0.89 (0.52, 1.51) for <1 per month	*The evidence shows no association* A single study reported no significant difference in the likelihood of depression in people who participate in HED (< or ≥monthly) vs those who drink without HED.	Critical
Depressive symptoms	N=7,240 K=1 prospective cohort study (Byers et al. 2012)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0	⊕⊕⊕⊖	Frequent vs non-frequent drinking or abstinence: OR=0.99 (0.69, 1.43)	*The evidence shows no association* When frequent drinking (≥14g alcohol /day) was compared against infrequent drinking, there were no significant differences in the chance of having depressive symptoms at	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	#2202	Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0			follow-up.	
	N=8,175 K=1 prospective cohort study (Cheng et al. 2016) #753	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Drinking more than once a month vs never drinking: OR=0.8 (0.5, 1.3) Drinking more than once a month vs former drinkers: OR=1.3 (0.5, 3.8)	*No reliable evidence of an association* A single study at risk of bias reported no significant association between drinking at least monthly, and risk of depressive symptoms, compared to those who do not drink.	Important
	N=3,877 K=1 prospective cohort study (Lang et al. 2007) #638	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	≥1 drink/day (≥14 g alcohol) vs ≤1 drink/day: z=−0.02 (−0.13, 0.09) to z=0.00 (−0.21, 0.22)	*No reliable evidence of an association* There was no difference in the likelihood of developing depressive symptoms between those who drank more than or less than 14 g alcohol per day.	Important
Bipolar disorder	N=7,981 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Abstinent vs non-HED: ORs=1.22 (0.78, 1.91) and 1.16 (0.58, 2.32)	*No evidence of an association* A single large study reported that there was no difference in likelihood of incident bipolar disorder in women who were abstinent vs women who drank without participating in HED.	Important
				HED vs non-HED: ORs between 0.78 (0.25, 2.44) and 2.05 (0.83, 5.03)	*No evidence of an association* There was no difference in likelihood of incident bipolar disorder in women who participated in HED vs women who drank without HED.	Important
Suicide	N=0 K=0					Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Anxiety	N=7,981 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Abstinent vs non-HED: ORs=0.85 (0.49, 1.38) and 1.20 (0.88, 1.64)	*The evidence shows no association* There was no difference in risk of developing anxiety in those who are abstinent and those who drink without HED.	
				HED vs non-HED: ORs=0.50 (0.18, 1.39) to 2.25 (0.87, 5.80)	*No reliable evidence of an association* There was no difference in likelihood of developing an anxiety disorder in those who participated in HED vs those who drank without HED.	
PTSD	N=7,987 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Abstinent vs non-HED: ORs=1.21 (0.80, 1.85) and 0.89 (0.49, 1.62)	*No reliable evidence of an association* There was no difference in risk of developing PTSD in those who are abstinent and those who drink without HED.	Important
				HED vs non-HED: ORs=0.63 (0.13, 2.99) to 2.67 (1.05, 6.84)	*Limited evidence of an association* One study (with no adjustments for multiple comparisons) reported that those who females who participated in HED less than once per month had a higher risk of developing PTSD than non-HED.	Important
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol consumption on mental health outcomes?
Patient or population: Older male subgroup
Exposure: Light, moderate, heavy drinking, short term risk drinking, long term risk drinking, HED, monthly drinking
Reference group: Abstinence, light drinking, non-HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=22,873 K=5 prospective cohort studies (Gea et al. 2013a; Hiles et al. 2015;	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0	⊕⊖⊖⊖	Light-moderate drinkers vs being abstinent: HR=0.51 (0.26, 1.00) ORs=0.54 (0.26, 1.13) to 1.35 (0.45, 4.08)	*No reliable evidence of an association* Four out of five studies were consistent that there was no association between quantity of alcohol per day and likelihood of developing depression. The remaining study reported that older males who were completely abstinent had worse depression outcomes than those who were light drinkers.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	Tanaka et al. 2011) (Lang et al. 2007; Tait et al. 2012)	Dose-response: 0 Large effect: 0 Confounding: 0		Abstinent vs light drinkers: OR=1.47 (1.22, 1.78) and z=0.12 (-0.13, 0.37) Heavy, hazardous drinker vs abstainer: HR=0.75 (0.39, 1.43) ORs=0.83 (0.20, 3.43) and 0.99 (0.46, 2.11)		
	N=13,453 K=2 prospective cohort studies (An & Xiang 2015; Bots et al. 2008)	Risk of bias: 0 Inconsistency: 0 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Heavy vs non-heavy drinking or abstinence: OR=0.64 (0.23, 1.80) HR=1.05 (0.95, 1.17)	*The evidence shows no association* When high consumption or frequent drinking was compared against low consumption or abstinence, there were no significant differences in the chance of having depression at follow-up.	Critical
	N=7,902 K=1 prospective cohort study (Tait et al. 2012)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Short term risk drinking (≥4 drinks/day) vs 0-2 drinks/day: OR=1.30 (1.06, 1.59), $p<0.05$ Long-term risk drinking vs 0-2 drinks/day: OR=0.99 (0.82, 1.19)	*Limited evidence of association* A single study reported that short-term risk drinkers (4 drinks/day) had a higher likelihood of depression than low risk drinkers (0-2 drinks/day). There was no significant difference in the odds of depression in those who drank between 2 and 4 drinks/day vs those who drank less than 2 per day.	Critical
	N=5,461 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	HED vs non-HED: ORs=0.94 (0.44, 2.03) and 1.27 (0.56, 2.86)	*No reliable evidence of an association* A single study reported no significant difference in the likelihood of depression in people who participated in HED (< or ≥monthly) vs those who did not.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
	N=2,683 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	Monthly drinker vs abstainer: OR=0.7 (0.5, 0.9), p<0.05	*Limited evidence of an association* Older males who drank at least monthly were significantly less likely to have depression at follow-up than those who never drank.	Critical
Bipolar disorder	N=5,461 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Abstinent vs non-HED: ORs=1.22 (0.78, 1.91) and 1.16 (0.58, 2.32)	*No evidence of an association* A single large study reported that there was no difference in likelihood of incident bipolar disorder in men who were abstinent vs men who drank without participating in HED.	Important
				HED vs non-HED: ORs between 0.78 (0.25, 2.44) and 2.05 (0.83, 5.03)	*No evidence of an association* There was no difference in likelihood of incident bipolar disorder in men who participated in HED vs men who drank without HED.	Important
Suicide	N=0 K=0					Important
Anxiety	N=1,987 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Abstinence vs non-HED drinking: OR=0.85 (0.49, 1.48) HED vs non-HED drinking: <1 per month: OR=2.25 (0.87, 5.80) >1 per month: OR=0.88 (0.32, 2.42)	*The evidence shows no association* A single study reported no difference in likelihood of incident anxiety based on being abstinent, a HED or non-HED drinker.	Critical
PTSD	N=5,461 K=1 prospective cohort study (Chou, Liang & Mackenzie 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0	⊕⊕⊖⊖	Abstinent vs non-HED: ORs=1.21 (0.80, 1.85) and 0.89 (0.49, 1.62)	*No reliable evidence of an association* There was no difference in risk of developing PTSD in those who are abstinent and those who drink without HED.	Important
				HED vs non-HED: ORs=0.63 (0.13, 2.99) to 2.67	*No reliable evidence of an association* There were no significant diffeences for males.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Dose-response: 0 Large effect: 0 Confounding: 0		(1.05, 6.84)		
Alcohol related psychoses	N=0 K=0					Important

GRADE evidence profiles for people with existing mental and physical illnesses

Question: What is the effect of alcohol on mental health outcomes of someone with unipolar depression?
Patient or population: Youth with existing mental illness (adolescents with depressive disorders)
Exposure: Excessive use of alcohol (weekly drunkenness, or consuming typically more than 7 (females) or 10 (males) units/session).
Reference group: No/occasional use of alcohol.

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Remission of depression (BDI<10)	N=197 K=1 prospective cohort study (Meririnne et al. 2010)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊖⊖	HED vs no/occasional HR=0.49 (0.27, 0.89), p=0.020	*Limited evidence of an association* Particpants of HED had less likelihood of their depression remitting than those who drank less than monthly and with no HED.	Critical
				Regular users vs no/occasional HR=1.02 (0.71, 1.47), p=0.90	*No reliable evidence of an association* Regular drinkers did not show any differences in rate of remission compared to no/occasional drinkers.	Critical
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol consumption in those with existing mental illnesses on mental health outcomes?
Patient or population: Adults with bipolar disorder
Exposure: Frequency of alcohol use, number of drinks consumed daily, or any alcohol consumption
Reference group: (not applicable for continuous outcomes), or no alcohol consumption

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depressive episode	N=418 K=3 prospective cohort studies (Baethge et al. 2008; Jaffee et al. 2009; van Zaane et al. 2014)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Days of alcohol use: OR=1.036 (1.010, 1.062) Time to transition to depression: HRs=1.03 (0.97, 1.11) and 0.97 (0.82, 1.24) Regression coefficient for no. of drinks: 0.058; 95%CI 0.015, 0.100; z-score 2.67, p=0.007	*No reliable evidence of an association* There was conflicting evidence on the relationship between alcohol consumption and depressive episodes in people with bipolar disorder. Two out of three studies showed that alcohol use was associated with later depressive episodes, whereas one study showed that alcohol did not influence the time to transition to a depressive episode for either males or females.	Important
Manic episode	N=303 K=2 prospective cohort studies (Baethge et al. 2008; van Zaane et al. 2014)	Risk of bias: -1 Inconsistency: -1 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Time to transition to mania: HRs=0.81 (0.71, 0.92) males; 1.01 (0.85, 1.18) females Regression coefficient for no. of drinks: -0.014 to 0.011; z-scores -0.74 to 0.64, p=0.046-0.59	*No reliable evidence of an association* One small study reported that males who increased their weekly consumption by one drink per week had a longer time transitioning to a manic state. However, the same was not found for females. A second study found no relationship between alcohol and transition to manic or hypermania.	Important
Anxiety	N=0 K=0					Critical
Alcohol related psychoses	N=0 K=0					

Question: What is the effect of alcohol consumption in those with other physical illnesses on mental health outcomes?
Patient or population: Adults with and without HIV
Exposure: Hazardous drinking, HED or heavy drinking
Reference group: Non-hazardous drinking

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=2,446 K=1 prospective cohort study (Sullivan et al. 2011)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Hazardous drinking: OR=2.53 (1.34, 4.81), p<0.001 HED: OR=2.14 (1.49, 3.07), p<0.001 Interaction between alcohol-related categories and HIV status: OR=0.99 (0.83, 1.18), p=0.88	*There is evidence of an association* Veterans with and without HIV had a significantly higher risk of MDD after 6 years if they were hazardous drinkers or participated in HED compared with non-hazardous drinkers. HIV status did not influence the relationship between alcohol and depression.	Critical
Depressive symptoms	N=391 K=1 prospective cohort study (Sullivan et al. 2008)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Mean difference on CES-D (range 0-60): 1.04 (-0.24, 2.32), p=0.11	*The evidence shows no association* While unadjusted mean CES-D scores were significantly higher for heavy drinkers compared to those who were not current heavy drinkers, the differences decreased after adjustments to be too small to be either clinically or statistically significant.	Important
Suicidal ideation	N=471 K=1 cross-sectional study (Lawrence et al. 2010)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Low risk vs no risk on AUDIT-C: OR=1.43 (0.86, 2.38) High risk vs no risk on AUDIT-C: OR=1.14 (0.61, 2.14)	*No reliable evidence of an association* A single small study reported no significant difference in risk of suicidal ideation between different AUDIT-C risk categories, after adjustments for confounders were made.	Important
Anxiety	N=0 K=0					Critical
Alcohol related psychoses	N=0 K=0					Important

GRADE evidence profiles for people with existing alcohol dependence

Question: What is the effect of alcohol on the mental health of people with alcohol dependence?
Patient or population: People with existing alcohol dependence
Exposure: Alcohol consumption or pattern of consumption
Reference group: Another level or pattern of consumption
Author(s): No studies

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=0 K=0			No studies identified		Critical
Anxiety	N=0 K=0			No studies identified		Critical
Alcohol related psychoses	N=0 K=0					Important

GRADE evidence profiles for people with strong family history of alcohol dependence

Question: What is the effect of alcohol on the mental health of people with a strong family history of alcohol dependence?
Patient or population: People with a strong family history of alcohol dependence
Exposure: Alcohol consumption or pattern of consumption
Reference group: Another level or pattern of consumption
Author(s): No studies

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=0 K=0			No studies identified		Critical
Anxiety	N=0 K=0			No studies identified		Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Alcohol related psychoses	N=0 K=0					Important

GRADE evidence profiles for people on medicines or other drugs

Question: What is the effect of alcohol combined with other drugs on mental health?
Patient or population: Youth on other drugs (starting in adolescence), or
Exposure: Chronic, moderate-to-heavy cigarette, alcohol and marijuana use / Use of all three substances, or other drugs
Reference group: Occasional alcohol alone, neither drugs or alcohol
Author(s): (Brook, Judith S. et al. 2014; Brook, J. S. et al. 2016; Conner et al. 2017)

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Major depressive episode (within 23 years)	N=806 K=1 prospective cohort study (Brook, J. S. et al. 2016)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 1 but not rated up due to risk of bias Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Chronic, moderate-to-heavy cigarette, alcohol and marijuana use vs occasional alcohol use only OR=2.67 (95%CI 1.14, 6.26)	*Limited evidence of an association* A trajectory of chronic, moderate-to-heavy cigarette, alcohol and marijuana use from adolescence to adulthood is associated with a higher risk of major depressive episode over the subsequent 23 years.	Critical
Generalised anxiety disorder (13-23 years)	N=1622 K=2 prospective cohorts studies (Brook, Judith S. et al. 2014; Brook, J. S. et al. 2016)	Risk of bias: -2 Inconsistency: 0 Indirectness: -1 Imprecision: 0 Publication bias: 0 Dose-response: 1 but not rated up due to risk of bias Large effect: 0	⊕⊖⊖⊖	Chronic, moderate-to-heavy cigarette, alcohol and marijuana use vs occasional alcohol use only OR=6.39 (2.62, 15.56) and OR=2.22 (1.33, 3.70)	*Limited evidence of an association* Combined use of cigarettes, alcohol and marijuana is associated with a higher risk of a generalised anxiety disorder over 13 to 23 years.	Critical

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Confounding: 0				
Alcohol related psychoses	N=0 K=0					Important
Suicide	N=346 K=1 case control study (Conner et al. 2017)	Risk of bias: -1 Inconsistency: N/A Indirectness: -1 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	OR of dying by suicide rather than motor vehicle accident if blood toxicology showed alcohol alone or in combination with other drug: Alcohol alone vs neither: OR=1.22 (0.74, 2.00) Alcohol plus drug vs neither: OR=4.33 (1.70, 11.03), $p<0.05$ Drug alone vs neither: OR=1.03 (0.37, 2.88)	*Limited evidence of an association* Adults (aged 18-54) who had alcohol and drugs in their blood stream, were more likely to die by suicide than motor vehicle accident than if they had neither in their blood. The odds of the death being by suicide rather than motor vehicle accident was stronger when both alcohol and drugs were used (OR=4.33) than when drugs alone were use (OR=1.03) or alcohol alone was used (OR=1.22).	Important

Question: What is the effect of alcohol in those dependent on alcohol or other drugs on mental health?
Patient or population: Adults with dependence on either alcohol or other drugs
Exposure: Hazardous drinking (no. of occasions drinking ≥4 drinks/day for women, or ≥5 drinks/day for men, per month)
Reference group: No hazardous drinking

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=0 K=0	N/A				Critical
Depressive symptoms	N=307 K=1 prospective cohort study (Bahorik et al. 2016)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0	⊕⊕⊖⊖	Number of hazardous drinking day per month ß(SE)=0.10 (0.03), t=2.84, p=0.004	*Limited evidence of an association* For every additional hazardous drinking occasion per month, there was a 10% increase in depressive symptoms at follow-up.	Important

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
		Large effect: 0				
Anxiety	N=0 K=0	N/A				Critical
Anxiety symptoms	N=307 K=1 prospective cohort study (Bahorik et al. 2016)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0	⊕⊕⊖⊖	Number of hazardous drinking day per month ß(SE)=0.09 (0.03), t=2.79, p=0.005	*Limited evidence of an association* For every additional hazardous drinking occasion per month, there was a 9% increase in anxiety symptoms at follow-up.	Important
Alcohol related psychoses	N=0 K=0					Important
Evidence statement: *There was evidence that in adults with dependence (either alcohol or drugs), drinking at hazardous levels increases the risk of depressive symptoms and anxiety symptoms (GRADE ⊕⊕⊕⊖).*						

Question: What is the effect of alcohol on mental health outcomes in people exposed to trauma?
Patient or population: Adults exposed to traumatic injuries
Exposure: High or low pre-trauma consumption or problem drinking (AUDIT-C) or post-trauma number of drinks consumed
Reference group: Moderate pre-trauma moderate consumption, non-problem drinking

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
PTSD symptoms	N=3,807 K=2 prospective cohort studies (Hruska et al. 2017; Powers, MB et al. 2014)	Risk of bias: -2 Inconsistency: -1 Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Immediate post-trauma blood alcohol screen: OR=0.65	*No reliable evidence of an association* Blood alcohol concentration did not significantly predict PTSD symptoms 3 months later.	Important
				Post-trauma alcohol consumption: β=0.01 (95%CI -0.01, 0.02)	*No reliable evidence of an association* Post-trauma alcohol consumption was not associated with next day PTSD symptoms.	Important
Anxiety symptoms	N=0 K=0					
Depression	N=1,035 K=1 prospective cohort study (Hoffman et al. 2011)	Risk of bias: 0 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊕⊕⊖	Post-trauma alcohol: No unsafe use of alcohol: OR=1.0 (Reference) Reducing unsafe use: OR=2.95 (95%CI 1.28, 6.79) Beginning unsafe use: OR=1.47 (95%CI 0.62, 3.50) Continued unsafe use: OR=0.28 (95%CI 0.04, 2.18)	*Evidence of an association* Those who reduced their unsafe alcohol use after a spinal cord injury were more likely to have depression at follow-up.	Critical
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol on mental health outcomes in people exposed to trauma?
Patient or population: Adults exposed to terrorism
Exposure: HED, drinks/day, and drinks/month
Reference group: No HED

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
PTSD	N=1,681 K=1 prospective cohort study (Boscarino et al. 2011)	Risk of bias: -1 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	HED: ß(SE)=0.09 (0.04), p=0.018 Drinks/drinking day: ß(SE)=0.29 (0.13), p=0.023 Drinks/month: ß(SE)=0.13 (0.07), p=0.066	*No reliable evidence of an association* Alcohol use in the year prior to and after the World Centre Attacks was associated with PTSD 2 years after the attacks.	Important
Depression	N=0 K=0					Critical
Anxiety	N=0 K=0					Critical
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol on mental health outcomes in people exposed to trauma?
Patient or population: Adult Defence Force personnel or Veterans
Exposure: Different alcohol trajectories or level of alcohol use, or hazardous drinking
Reference group: Average drinkers or non-hazardous drinkers

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
PTSD	N=512 K=1 prospective cohort study (Schultz, Glickman & Eisen 2014)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Alcohol use at T1: estimate(SE): -0.04 (0.13), NS	*No reliable evidence of an association* No statistically significant effects of alcohol trajectory or use at baseline on future likelihood of PTSD.	Important
PTSD symptoms	N=505 K=1 prospective cohort study (Goodwin et al. 2017)	Risk of bias: -2 Inconsistency: N/A Indirectness: 0 Imprecision: 0 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Pre-trauma alcohol: Mean Difference in PCL-C score=0.10 (95%CI -0.04, 0.24), p=0.18 Post-trauma alcohol: Mean Difference in PCL-C score=0.04 (95%CI -0.17, 0.24), p=0.73	*No reliable evidence of an association* Pre- or post-trauma alcohol use did not predict PTSD symptoms at follow-up.	Important
Anxiety	N=0 K=0					Critical
Alcohol related psychoses	N=0 K=0					Important

Question: What is the effect of alcohol on mental health outcomes in people exposed to trauma?
Patient or population: Adult college students exposed to trauma or women exposed to sexual assault
Exposure: Alcohol quantity, peak drinking (greatest amount consumed in one occasion)
Reference group: alcohol quantity, peak drinking (continuous variable)

Outcomes	Participants Studies	Quality of evidence	GRADE	Results	Interpretation	Importance
Depression	N=0 K=0					Critical
Anxiety	N=0 K=0					Critical
PTSD symptoms	N=798 K=2 prospective cohort studies (Kaysen et al. 2011; Read et al. 2016)	Risk of bias: -1 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Publication bias: 0 Dose-response: 0 Large effect: 0 Confounding: 0	⊕⊖⊖⊖	Pre-assault peak drinking x time: *B*=1.65 (-1.63, 4.93) Post-trauma: In cross-lagged panel model including alcohol use, PTSD symptoms, coping and alcohol consequences, alcohol use did not have any significant direct or indirect associations with PTSD symptoms.	*No reliable evidence of an association* One study reported that peak alcohol consumption prior to the trauma had no effect on PTSD symptoms over the follow-up period. Another study reported that post-trauma alcohol consumption was highly correlated with PTSD symptoms, but in an adjusted model, these associations were no longer significant.	Important
Suicide	N=0 K=0					Important
Alcohol related psychoses	N=0 K=0					Important

Appendix F Excluded studies

Wrong alcohol consumption measure (used AUDIT score)

Batterham, PJ, Christensen, H & Mackinnon, AJ 2009, 'Modifiable risk factors predicting major depressive disorder at four year follow-up: A decision tree approach', BMC Psychiatry, vol. 9.

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Wrong study design

'Briefly noted. SAMHSA survey links depression and first use of drugs or alcohol', 2007, *Alcoholism & Drug Abuse Weekly*, vol. 19, no. 19, pp. 7-7.

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Abayomi, O, Onifade, PO, Adelufosi, AO & Akinhanmi, AO 2013, 'Psychosocial correlates of hazardous alcohol use among undergraduates in southwestern Nigeria', *General Hospital Psychiatry*, vol. 35, no. 3, pp. 320-324.

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Abulseoud, OA, Hellmann, G, Calabrese, JR, Verduin, ML, Chirichigno, JW, McKowen, J, Gitlin, MJ, Altshuler, LL & Frye, MA 2008, 'Sex and bipolar subtype association with self-reported hazardous alcohol consumption in bipolar depression', *Journal of Dual Diagnosis*, vol. 4, no. 3, pp. 291-302.

Abulseoud, OA, Karpyak, VM, Schneekloth, T, Hall-Flavin, DK, Loukianova, LL, Geske, JR, Biernacka, JM, Mrazek, DA & Frye, MA 2013, 'A retrospective study of gender differences in depressive symptoms and risk of relapse in patients with alcohol dependence', *American Journal on Addictions*, vol. 22, no. 5, pp. 437-442.

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Wrong outcomes

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