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Minozzi S, Ambrosi L, Saulle R, Uhm SS, Terplan M, Sinclair JMA, Agabio R

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Psychosocial and medication interventions to stop or reduce alcohol consumption during pregnancy.
Cochrane Database of Systematic Reviews 2024, Issue 4. Art. No.: CD015042.
DOI: 10.1002/14651858.CD015042.pub2.

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[Intervention Review]

Psychosocial and medication interventions to stop or reduce alcohol consumption during pregnancy

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Editorial group: Cochrane Drugs and Alcohol Group, Cochrane Pregnancy and Childbirth Group.
Publication status and date: New, published in Issue 4, 2024.

Citation: Minozzi S, Ambrosi L, Saulle R, Uhm SS, Terplan M, Sinclair JMA, Agabio R. Psychosocial and medication interventions to stop or reduce alcohol consumption during pregnancy. *Cochrane Database of Systematic Reviews* 2024, Issue 4. Art. No.: CD015042. DOI: 10.1002/14651858.CD015042.pub2.

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ABSTRACT

Background

Despite the known harms, alcohol consumption is common in pregnancy. Rates vary between countries, and are estimated to be 10% globally, with up to 25% in Europe.

Objectives

To assess the efficacy of psychosocial interventions and medications to reduce or stop alcohol consumption during pregnancy.

Search methods

We searched the Cochrane Drugs and Alcohol Group Specialised Register (via CRSLive), Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL, Web of Science, and PsycINFO, from inception to 8 January 2024. We also searched for ongoing and unpublished studies via ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). All searches included non-English language literature. We handsearched references of topic-related systematic reviews and included studies.

Selection criteria

We included randomised controlled trials that compared medications or psychosocial interventions, or both, to placebo, no intervention, usual care, or other medications or psychosocial interventions used to reduce or stop alcohol use during pregnancy. Our primary outcomes of interest were abstinence from alcohol, reduction in alcohol consumption, retention in treatment, and women with any adverse event.

Data collection and analysis

We used standard Cochrane methodological procedures.

Main results

We included eight studies (1369 participants) in which pregnant women received an intervention to stop or reduce alcohol use during pregnancy. In one study, almost half of participants had a current diagnosis of alcohol use disorder (AUD); in another study, 40% of participants had a lifetime diagnosis of AUD. Six studies took place in the USA, one in Spain, and one in the Netherlands.

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All included studies evaluated the efficacy of psychosocial interventions; we did not find any study that evaluated the efficacy of medications for the treatment of AUD during pregnancy. Psychosocial interventions were mainly brief interventions ranging from a single session of 10 to 60 minutes to five sessions of 10 minutes each. Pregnant women received the psychosocial intervention approximately at the end of the first trimester of pregnancy, and the outcome of alcohol use was reassessed 8 to 24 weeks after the psychosocial intervention. Women in the control group received treatment as usual (TAU) or similar treatments such as comprehensive assessment of alcohol use and advice to stop drinking during pregnancy.

Globally, we found that, compared to TAU, psychosocial interventions may increase the rate of continuously abstinent participants (risk ratio (RR) 1.34, 95% confidence interval (CI) 1.14 to 1.57; I^2 =0%; 3 studies; 378 women; low certainty evidence). Psychosocial interventions may have little to no effect on the number of drinks per day, but the evidence is very uncertain (mean difference −0.42, 95% CI −1.13 to 0.28; I^2 = 86%; 2 studies; 157 women; very low certainty evidence). Psychosocial interventions probably have little to no effect on the number of women who completed treatment (RR 0.98, 95% CI 0.94 to 1.02; I^2 = 0%; 7 studies; 1283 women; moderate certainty evidence). None of the included studies assessed adverse events of treatments.

We downgraded the certainty of the evidence due to risk of bias and imprecision of the estimates.

Authors' conclusions

Brief psychosocial interventions may increase the rate of continuous abstinence among pregnant women who report alcohol use during pregnancy. Further studies should be conducted to investigate the efficacy and safety of psychosocial interventions and other treatments (e.g. medications) for women with AUD. These studies should provide detailed information on alcohol use before and during pregnancy using consistent measures such as the number of drinks per drinking day. When heterogeneous populations are recruited, more detailed information on alcohol use during pregnancy should be provided to allow future systematic reviews to be conducted. Other important information that would enhance the usefulness of these studies would be the presence of other comorbid conditions such as anxiety, mood disorders, and the use of other psychoactive substances.

PLAIN LANGUAGE SUMMARY

Treatments to reduce alcohol use during pregnancy

Key messages

We found that among pregnant women who report alcohol use during pregnancy, brief psychosocial interventions (BIs) may increase the number of continuously abstinent women when compared to treatment as usual (TAU). There may be no difference between groups in the number of drinks per day, but the evidence is very uncertain. Receiving a BI compared to TAU probably results in little to no difference in the number of women who completed treatment.

What are the consequences of alcohol use during pregnancy?

Alcohol use during pregnancy can have severe consequences for both the pregnant woman and the embryo and fetus. Higher amounts of alcohol are associated with the greatest risk; however, low-to-moderate prenatal alcohol exposure is also linked to certain deficits at birth. Accordingly, any alcohol use confers some risk during pregnancy, and current guidelines recommend avoiding alcohol use during pregnancy. Nevertheless, in Europe, approximately one out of four pregnant women report alcohol use during pregnancy.

Which treatments are available to stop or reduce alcohol use during pregnancy?

Psychosocial interventions and medications have been shown to be effective for unhealthy alcohol use within the general population. Those with alcohol use disorder (AUD), a mental disorder where the person is unable to control their alcohol use, may additionally benefit from medications. It is unclear if these treatments are effective among pregnant women who report alcohol use during pregnancy.

What did we want to find out?

We wanted to find out whether psychosocial interventions or medications can help pregnant women who report alcohol use in reducing or stopping such behaviour.

What did we do?

We searched for randomised controlled trials (studies in which participants are randomly assigned to one of two or more treatment groups) that compared psychosocial interventions or medications, or both, with no treatment, TAU, placebo (dummy treatment), or other treatments to help pregnant women stop or reduce their alcohol use.

What did we find?

We included eight studies involving a total of 1369 pregnant women who reported alcohol use during pregnancy. In two studies, almost half of the participants were diagnosed with current or previous AUD. Most studies (75%) took place in the USA. Treatments were BIs,

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ranging from 10 to 60 minutes in duration, mainly delivered in a single session or few sessions (up to five). The group receiving BIs was compared with a group receiving TAU. Pregnant women received the psychosocial intervention at approximately 15 weeks of pregnancy, and alcohol use was assessed 8 to 24 weeks after the intervention. We did not find any study that looked at the effects of AUD medications during pregnancy.

We found that BIs may increase the rate of continuously abstinent women. The evidence is very uncertain about the effect of BIs on the number of drinks per day. Finally, we found that BIs probably result in little to no difference in the number of women who completed treatment.

What are the limitations of the evidence?

We did not find any study that assessed the effectiveness and safety of AUD medications during pregnancy. Only two studies recruited pregnant women with current or lifetime AUD; this limitation means we cannot generalise our results to pregnant women who have AUD. Further studies are needed to evaluate the effects of psychosocial interventions or medication in helping pregnant women with AUD to stop or reduce alcohol use.

The effects of psychosocial interventions are largely influenced by the social context; given that most of the included studies took place in the USA, this limits the generalisability of the findings to countries and marginalised ethnic groups not recruited to these studies.

Globally, our results are far from being considered conclusive.

How up-to-date is this evidence?

The evidence is current to 8 January 2024.

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Summary of findings 1. Summary of findings table - Any psychosocial intervention compared to treatment as usual for stopping or reducing alcohol consumption during pregnancy

Any psychosocial intervention compared to treatment as usual for stopping or reducing alcohol consumption during pregnancy

Patient or population: stopping or reducing alcohol consumption during pregnancy
Setting: outpatients
Intervention: Any psychosocial intervention
Comparison: Treatment as usual

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Treatment as usual	Risk with Any psychosocial intervention				
Number of continuously abstinent women - total follow-up: range 2 months to 6 months	513 per 1000	**687 per 1000** (584 to 805)	**RR 1.34** (1.14 to 1.57)	378 (3 RCTs)[1,2,3]	⊕⊕⊖⊖ Low[a]	
Number of drinks per day - total follow-up: range 2 months to 6 months	The mean number of drinks per day - total was **0.79**	MD **0.42 lower** (1.13 lower to 0.28 higher)	-	157 (2 RCTs)[2,3]	⊕⊖⊖⊖ Very low[b,c]	
Number of women who completed treatment - total follow-up: range 1 months to 6 months	721 per 1000	**706 per 1000** (677 to 735)	**RR 0.98** (0.94 to 1.02)	1283 (7 RCTs)[1,2,3,4,5,6,7]	⊕⊕⊕⊖ Moderate[d]	
Adverse events - not measured	-	-	-	-	-	
Withdrawal signs and symptoms - not measured	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

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Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_443140931232270317.

[a] Downgraded two levels due to methodological limitations (high risk of bias in measurement of the outcome and some concerns in bias arising from the randomisation process, bias due to deviations from intended interventions, and bias in selection of the reported result): overall high risk of bias in two studies (Reynolds 1995, van der Wulp 2014) and some concerns in one study (Joya 2016) included within the analysis.
[b] Downgraded two levels due to methodological limitations (high risk of bias due to missing outcome data and in measurement of the outcome; some concerns in bias due to deviations from intended interventions and selection of the reported results): overall high risk of bias in all studies (Reynolds 1995, van der Wulp 2014) included within the analysis.
[c] Downgraded two levels because of low number of participants (n < 400), and confidence interval includes important benefits and important harms.
[d] Downgraded one level due to methodological limitations (some concerns in bias arising from the randomisation process, bias due to deviations from intended interventions, and bias in selection of the reported result): one study. All studies at overall some concerns risk of bias.
[1] Joya, . . 2006.
[2] Reynods, . . 1995.
[3] Wulp, van,der. . 2014.
[4] Handmaker, . . 1999.
[5] O'Connor, . . 2007.
[6] Tzilos, . . 2011.
[7] Rubio, . . 2014.

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BACKGROUND

Description of the condition

Prevalence and patterns of alcohol use during pregnancy

Estimating the prevalence and patterns of alcohol use during pregnancy is complicated by the associated stigma (Roberts 2010), and the large variability in the definitions for alcohol consumption (Stade 2009). This stigma may lead to underestimations of alcohol consumption during pregnancy (Roberts 2010). In addition, recognition of pregnancy may occur late, resulting in alcohol use in early pregnancy and underestimates of total alcohol consumption during pregnancy (Dozet 2021; Strandberg-Larsen 2008). Finally, the use of generic terms such as 'light drinker', without providing their exact definition, further contributes to an inaccurate description of alcohol consumption during pregnancy (Stade 2009).

Definition of unhealthy alcohol use for the general population

Given the significant global variations in definitions and measurements around alcohol use, the US Preventive Services Task Force (USPPTF) has proposed adoption of the term 'unhealthy alcohol use' to define any alcohol consumption exceeding the recommended daily, weekly, or per-occasion limits expressed in number of standard drink, related to an increased risk for health consequences, whether or not it meets the criteria for alcohol use disorder (AUD) (USPPTF 2018). On the other hand, 'low-risk alcohol use' is alcohol consumption lower or equal to these recommended limits (USPPTF 2018). However, the definition of a 'standard drink' varies between countries: one drink contains 10 to 12 g of alcohol in Europe, 8 g in the UK, 19.75 g in Japan, and a standard drink in the USA is 14 g of alcohol (Dawson 2011). According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the USA, risky alcohol use is defined as more than four drinks (56 g) in a day or 14 drinks (196 g) per week for healthy adult men, and more than three drinks (42 g) per day or seven drinks (98 g) per week for adult women (NIAAA 2005). According to the World Health Organization (WHO), the term 'hazardous drinking' refers to heavy episodic drinking, associated with a significant increase in the risk of alcohol-related consequences, defined as consuming 60 g of pure alcohol, at least once per month (WHO 2018). According to the American Psychiatric Association (APA), AUD is a medical disease characterised by the inability to control alcohol consumption (APA 2013). Its diagnosis requires meeting at least two out of 11 criteria in a 12-month period, and its severity (mild, moderate, or severe) is based on the number of criteria met (APA 2013). The latest revision of the International Classification of Diseases (ICD-11; Saunders 2019) provides a definition for alcohol dependence that only partially overlaps the definition of severe AUD provided by the APA (APA 2013). None of these diagnoses includes the level of alcohol use among the diagnostic criteria (Rehm 2019). Finally, the term 'binge drinking' describes alcohol consumption of five or more drinks for men and four or more drinks for women within approximately two hours (NIAAA 2004).

Definition of unhealthy alcohol use during pregnancy

According to the USPPTF, any alcohol use during pregnancy or when planning a pregnancy is considered unhealthy; in both of these cases, alcohol should be completely avoided (USPPTF 2018).

Prevalence of unhealthy alcohol use during pregnancy

A recent meta-analysis estimated that the prevalence of consuming any amount of alcohol during pregnancy, in the general population, is 9.8% globally, with large variability between countries, ranging from over 60% in Ireland to 0% in the United Arab Emirates and Saudi Arabia (Popova 2017). In Europe, about a quarter of people drink alcohol while pregnant (Popova 2017). In the USA, among large samples of pregnant people, similar prevalences of binge drinking (around 4%; Albright 2021) and AUD (3.6%) have been estimated (Vesga-López 2008). The prevalence of binge drinking during pregnancy varies significantly among countries, with rates ranging from 0.2% in the Western Pacific Region to 13.9% in the African Region, as reported by Lange 2017a. Another study observed that the highest rate was among pregnant people who belonged to underserved racial/ethnic groups (almost 20%; Albright 2021). Binge drinking after recognition of pregnancy has been associated with unintended pregnancy, younger age, being unmarried, having other children, and having mental illness (Strandberg-Larsen 2008).

Risk and consequences of different patterns of alcohol use

Alcohol use is a major risk factor for injuries, mortality, and global disease burden (GBD 2016 Alcohol Collaborators 2018). It is associated with increased risk of several diseases like cancer, liver cirrhosis, and neuropsychological impairment, as well as suicides, accidents, domestic violence, economic costs, and loss of productivity (Rehm 2009; Roerecke 2013). The risk of alcohol-related consequences rises with increasing levels of consumption, and the level of consumption with the lowest risk for health loss is zero (GBD 2016 Alcohol Collaborators 2018). Negative consequences may harm both people who consume alcohol and other people (Nutt 2010).

Alcohol use during pregnancy can result in negative consequences for the health of the pregnant person as well as the embryo and fetus (Harvey 2019; Popova 2021; Sundermann 2019), including miscarriage, preterm labour, placental abruption, bleeding, and intra-amniotic infections (Aliyu 2011; Coyne 2008; Ohira 2019; Salihu 2011; Sokol 1980). Alcohol is a teratogen, meaning that it can disrupt the development of the brain and other organs of the embryo and fetus (Sulik 2014). Alcohol use during pregnancy is also a risk factor for spontaneous abortion, stillbirth, premature birth, intrauterine growth restriction, low birthweight, and cognitive impairment (Harvey 2019; Sundermann 2019). The type and severity of birth defects induced by prenatal alcohol exposure are largely dependent on the dose and pattern of exposure, as well as the developmental stage of the embryo or fetus at the time of exposure (Flak 2014; Sulik 2014). In addition to the amount of alcohol consumed and the gestational timing of consumption, multiple other factors (e.g. variability in the xenobiotic metabolism and genetic background of the pregnant person and fetus, environmental influences, as well as age, cigarette use, nutritional status, and stress levels of the pregnant person, and possibly lifestyle factors of the other parent) modify fetal susceptibility to the teratogenic effects of alcohol (Eberhart 2016; Harvey 2019).

The term 'fetal alcohol spectrum disorder' (FASD) is used to refer to all the possible effects associated with prenatal alcohol exposure comprising fetal alcohol syndrome (FAS), partial FAS (PFAS), alcohol-related neurodevelopmental disorder (ARND), alcohol-related birth defects (ARBD), and neurobehavioural disorder

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associated with prenatal alcohol exposure (ND-PAE; Mattson 2019). FAS represents the most severe clinical picture in the child, characterised by developmental delay or mental impairment together with physical defects such as distinct craniofacial anomalies, short palpebral fissures and maxillary hypoplasia, joint and palmar crease anomalies, and cardiac defects (Riley 2011), associated with chromosomal abnormalities (Popova 2017). These alterations may lead, later in life, to scholar and academic failure, increased risk of developing substance abuse or other mental health problems, aggressive and conduct disorders, and inability to live independently or obtain and maintain employment (Popova 2017). A recent study evaluated the relationship between different maternal drinking patterns and the type and severity of birth defects (Bandoli 2019). Prenatal alcohol exposure ranged from minimal or no exposure throughout gestation to high exposure sustained across gestation. The results confirmed that sustained prenatal alcohol exposure was related to the highest risk for adverse infant outcomes. However, even low-to-moderate prenatal alcohol exposure continued across gestation was associated with certain deficits at birth (Bandoli 2019). Accordingly, any alcohol use is considered unhealthy during pregnancy; current guidelines recommend screening during pregnancy for unhealthy alcohol use and advising pregnant people to avoid drinking alcohol (USPPTF 2018).

Estimates of the prevalence of these consequences

Alcohol use during pregnancy dose-dependently increases the risk of negative consequences (Aliyu 2011; Coyne 2008; Currie 2020; Ohira 2019; Salihu 2011; Sokol 1980). Pregnant people who consume higher amounts of alcohol (five or more alcoholic drinks per week) have a more than twofold increased risk of these conditions compared to those who consume one to two drinks per week (Salihu 2011). A large study found that people who consume alcohol during pregnancy are 40% more likely to experience stillbirth as compared with those who do not drink, and for those who consume five or more drinks per week, this risk increases to a 70% elevated risk of stillbirth (Aliyu 2011). In addition, the risk of early stillbirth is 80% higher among pregnant people who drink alcohol compared with those who do not, and the risk of placental abruption is 33% greater (Aliyu 2011). In Japan, a large nationwide survey revealed that, compared to pregnant people who drink alcohol less than three days a week, those who drink alcohol three or more days a week have a three times higher risk of developing placenta accreta, a condition associated with premature birth and excessive vaginal bleeding during delivery (Ohira 2019).

Regarding the prevalence of negative consequences of alcohol use during pregnancy to the embryo and fetus, a recent meta-analysis estimated that worldwide, on average, about 15 of every 10,000 people (14.6/10,000) have FAS (Popova 2017). Considering that globally, about 10% of people consume alcohol during pregnancy, this prevalence means that one in every 67 people who drink during pregnancy will deliver a child with FAS. In Europe, where about a quarter of people drink alcohol during pregnancy, FAS prevalence is 2.6 times higher than the mean prevalence worldwide (37.4/10,000; Popova 2017). Heavy drinking during pregnancy is related to about a three times greater FAS prevalence - about one in every 23 heavy-drinking pregnant people will deliver a child with FAS (Abel 1995). Similar differences in the prevalence of FASD have been found between countries, related to the differences in alcohol use during pregnancy. Worldwide, the prevalence of FASD among children and youth has been estimated to be 7.7 per 1000 people, ranging from 19.8 per 1000 people in Europe to 0.1 per 1000 people in the Eastern Mediterranean Region (Lange 2017b).

Description of the intervention

Current guidelines for the general population

Current guidelines recommend that the general population screen for unhealthy drinking using tools such as the Alcohol Use Disorders Identification Test (AUDIT), its short form (AUDIT-C), or the NIAAA-recommended Single Alcohol Screening Question (SASQ; Kranzler 2018; USPPTF 2018). Screening, Brief Intervention, and Referral for Treatment (SBIRT) is a public health approach to substance use that tailors clinical interventions based on level of risk (Knox 2019). When people screen positive, clinicians should confirm unhealthy alcohol use or AUD, or both, to determine the next steps of care. Shortly, psychosocial treatments of low intensity are recommended for people who screen positive for unhealthy drinking without satisfying the diagnostic criteria for AUD (Knox 2019). These low-intensity treatments are aimed at helping people with unhealthy drinking to reduce alcohol consumption and prevent AUD, and may be delivered by healthcare providers without specific expertise in addiction, such as primary care physicians (Knox 2019). On the other hand, people with a diagnosis of AUD require interventions at higher intensity, delivered by healthcare providers with specific expertise in addiction (Kranzler 2018). These treatments comprise psychosocial interventions, support groups (e.g. Alcoholics Anonymous), and medications (Kranzler 2018). Psychosocial interventions comprise motivational interviewing, cognitive behavioural therapy, and contingency management (see Knox 2019 and MacKillop 2022 for a detailed description of these interventions). Despite the evidence of efficacy, less than 10% of people with AUD receive any kind of treatment (Grant 2015), and less than 2% receive specific medications for AUD (Han 2021). Reasons that contribute to the undertreatment of AUD include the lack of sufficient well-trained healthcare providers with expertise in addiction (Nunes 2020), as well as the stigma around AUD (Volkow 2021). Furthermore, lower rates of women than men receive AUD treatment (Grant 2015; Rehm 2015), with even lower rates during pregnancy (Terplan 2012).

Current guidelines during pregnancy

Currently, specific guidelines are available for screening and interventions to reduce any alcohol consumption during pregnancy, such as those from Canada, Graves 2020, and the UK, Schölin 2019, as well as international guidelines for the treatment of AUD during pregnancy (Thibaut 2019; WHO 2014). Additionally, guidelines are available for AUD treatment for the general population, which include specific information on screening and AUD treatment during pregnancy, such as those from the USA (Reus 2018; USPPTF 2018), Germany (Kiefer 2021), France (Rolland 2016), and Australia (Haber 2021). For example, in the USA, the guidelines during pregnancy recommend screening for unhealthy alcohol use (Thibaut 2019; USPPTF 2018) using the questionnaires AUDIT-C and SASQ (USPPTF 2018). When people screen positive on these brief instruments, clinicians should confirm unhealthy alcohol use or AUD, or both, and determine the next steps of care (Thibaut 2019; USPPTF 2018). Longer screening tests may include AUDIT; Tolerance, Worried, Eye-opener, Amnesia, Kut down (TWEAK); Tolerance, Annoyed, Cut down, Eye-opener (T-ACE); Parents, Partner, Past, Present Pregnancy (4P's Plus); and

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Normal drinker, Eye-opener, Tolerance (NET; Thibaut 2019; USPPTF 2018). Unfortunately, no studies have reported the accuracy of these screening tests across the spectrum of alcohol use during pregnancy (Thibaut 2019; USPPTF 2018).

According to the international guidelines for the treatment of AUD during pregnancy (Thibaut 2019), some biological markers like aspartate aminotransferase, alanine transaminase, gamma-glutamyl transferase, mean corpuscular volume, carbohydrate-deficient transferrin (CDT), ethyl glucuronide (EtG), ethyl sulphate, and fatty acid ethyl esters may also be used to detect alcohol consumption during pregnancy (Thibaut 2019). Nevertheless, these markers are of low sensitivity and specificity when compared to self-report (Howlett 2017).

According to these guidelines (Graves 2020; USPPTF 2018), and similar to the general population, psychosocial interventions are recommended for individuals with unhealthy drinking during pregnancy. Among the general population, people with AUD should receive treatment comprising both psychosocial interventions and, where appropriate, medications (MacKillop 2022). On the other hand, the role of medications for AUD in pregnancy is unclear, mainly because of the exclusion of pregnant people from clinical trials. Some authors describe medications as contraindicated during pregnancy because of potential harms (Reus 2018). For this reason, current guidelines recommend psychosocial interventions during pregnancy for unhealthy drinking, ranging from any alcohol use to severe AUD, to achieve abstinence or at least reduce alcohol consumption (Thibaut 2019; USPPTF 2018). A recent descriptive review concluded that though efficacy and safety data are lacking for medications for AUD in pregnancy, the harms of alcohol are well-established, and a more nuanced risk/benefit analysis is warranted (Kelty 2021).

Differences between guidelines for the general population and those during pregnancy

The main difference between the guidelines for the general population and those during pregnancy is the definition of low-risk alcohol use (USPPTF 2018). During pregnancy or when planning a pregnancy, any alcohol use is considered unhealthy (USPPTF 2018). Consequently, all pregnant people who report drinking any amounts of alcohol should receive low-intensity interventions when they do not meet diagnostic criteria for AUD, while individuals with AUD should receive treatments comprising both psychosocial interventions and, where appropriate, medications.

Psychosocial interventions

Several psychosocial or educational treatments have been used during pregnancy to reduce or stop alcohol consumption (Erng 2020; Fergie 2019; Gebara 2013; Samawi 2021). These interventions vary in their specific components, administration, length, and number of interventions delivered during pregnancy (frequency) (Adebiyl 2019; Bottorff 2014; Chang 2015; Crawford-Williams 2015; DeVido 2015; Erng 2020; Fergie 2019; Floyd 2009; Gebara 2013; Heberlein 2012; Jones 2013; Lui 2008; O'Connor 2018; Samawi 2021; Stade 2009; Symons 2018; Turnbull 2012; Ujhelyi Gomez 2020).

According to the latest Cochrane reviews, psychological and educational interventions available to reduce alcohol use during pregnancy comprise educational sessions, motivational enhancement therapy, self-help groups, psychotherapeutic techniques, and cognitive behavioural interventions (Stade 2009). For a detailed description of each intervention, see the previous Cochrane reviews (Lui 2008; Stade 2009). The more recent guidelines for the treatment of AUD in pregnant people describe the behavioural intervention as "a patient-centered form of counselling that uses brief versions of cognitive behavioral therapies and motivational interviewing or some combination of both" (Thibaut 2019).

Educational interventions comprise brief educational counselling sessions, structured long-term educational programmes with motivational enhancement interventions, individual-focused educational strategies, family-focused programmes, professional group education interventions, and self-help group educational interventions (Stade 2009).

In evaluating the efficacy of medications to reduce alcohol consumption, psychosocial interventions are often included in both the intervention and control arms as an integral part of the trial rather than as a sham treatment (Litten 2013; Weimer 2015). In evaluating the efficacy of psychosocial treatments, the placebo effect may represent a methodological challenge, as there is no consensus on what constitutes a suitable placebo (Weimer 2015), but psychosocial interventions should not be thought of as a placebo.

Medications

Four medications - naltrexone, acamprosate, disulfiram, and nalmefene - have been approved for the treatment of severe AUD to help individuals achieve and maintain abstinence or reduce alcohol consumption (Kranzler 2023; MacKillop 2022; Reus 2018). Indications for use during relapse differ across countries, based on local regulations. When aiming for full abstinence, before starting pharmacological relapse prevention treatment, people who are physically dependent on alcohol may require a medically assisted withdrawal. The first-line agents for medically assisted withdrawal are benzodiazepines, which are effective in both reducing the severity of alcohol withdrawal syndrome and protecting against seizures (Amato 2011).

Despite the well-known sex and gender differences in the response to pharmacological treatments (Mauvais-Jarvis 2021), and in the pharmacokinetics and negative consequences of alcohol (Agabio 2016a), medications approved for the treatment of AUD have been studied almost exclusively in male animals and men (Agabio 2016b; Hilderbrand 2018). As a result, knowledge of the efficacy and safety of these medications for the treatment of women with AUD is limited (Agabio 2016a). Regarding the use of medications for the treatment of AUD during pregnancy, a recent descriptive review concluded that although individuals with AUD may benefit from their use, at present there is little evidence to support the safety of these medications in pregnancy (Kelty 2021), and the guidelines contraindicate the use of medications for the treatment of AUD during pregnancy because of their potential harms (Reus 2018).

How the intervention might work

This review involved individuals who received any kind of treatment, including medications, psychosocial interventions, educational interventions, or a combination of the above, to achieve abstinence from alcohol or reduce alcohol consumption during pregnancy. Medications include acamprosate, naltrexone, disulfiram or any other medication administered to stop or reduce

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alcohol consumption. Psychological interventions might work by reducing dysfunctional beliefs, negative thoughts, unwanted symptoms, and dangerous habits, and facilitating the adoption of healthier and safer behaviours during pregnancy. Educational interventions might work by modifying learned beliefs, norms, and patterns of behaviour that are potentially dangerous for pregnant people and their children. Taken together, interventions may have their effect by increasing awareness that alcohol use may be dangerous for the health of both the pregnant person and the embryo and fetus, and by helping to reduce or stop drinking during pregnancy.

A range of outcomes have been reported to evaluate the efficacy of these interventions, including the number or rate of abstinent participants, number or rate of abstinent days, alcohol consumed per week expressed in grams or standard alcohol units, levels of biological markers like CDT or EtG, or scores on questionnaires such as AUDIT-C, TWEAK, or Cut down, Annoyed, Guilty, Eye-opener (CAGE) (Erng 2020). Other studies evaluated the changes induced in the health of infants using outcomes like the Apgar score, birthweight, birth length, gestational age, number and rate of children affected by FASD, or length of stay in the neonatal intensive care unit (Erng 2020). Other studies investigated changes in knowledge and attitudes regarding the wider negative effects induced by alcohol use during pregnancy (Erng 2020).

Why it is important to do this review

Two Cochrane reviews on the efficacy of psychosocial interventions during pregnancy in reducing alcohol consumption, published more than 10 years ago, found inconsistent results precluding any clear conclusions (Lui 2008; Stade 2009). The first review did not find any randomised controlled trials (RCTs) (Lui 2008); the second review included four studies with 715 pregnant women, but the outcomes were too different to be pooled (Stade 2009). Another Cochrane review investigated the effectiveness of home visits during pregnancy for individuals with alcohol problems (Turnbull 2012). This review included seven studies, and the authors conducted several meta-analyses to evaluate the effectiveness of this intervention on continued alcohol use (risk ratio (RR) 1.18, 95% confidence interval (CI) 0.96 to 1.46; 3 studies; 379 women), infant death (RR 0.70, 95% CI 0.12 to 4.16; 3 studies; 288 infants), and other outcomes related to infant health. The authors concluded that there was insufficient evidence to recommend the routine use of home visits for individuals with alcohol problems during pregnancy (Turnbull 2012).

Three recent non-Cochrane systematic reviews investigated the efficacy of psychosocial interventions in reducing alcohol consumption during pregnancy (O'Connor 2018; Popova 2023; Ujhelyi Gomez 2020). One of these systematic reviews was aimed at investigating the efficacy of behavioural counselling interventions to reduce unhealthy alcohol use in adolescents and adults, including during pregnancy (O'Connor 2018). This systematic review selected 11 studies with pregnant or postpartum people and found that, among pregnant people, abstinence was higher in the intervention groups compared with the control groups (pooled odds ratio 2.26, 95% CI 1.43 to 3.56; I^2 = 0%; 5 studies; 796 women). In other words, counselling interventions were associated with an odds ratio of 2.26 for remaining abstinent from alcohol during pregnancy, with a number needed to treat for an additional beneficial outcome of 6. The authors reported that other alcohol use outcomes were very sparsely reported.

The second systematic review selected 24 RCTs (20 conducted in pregnancy and four during parenting) and investigated the efficacy of psychosocial interventions in helping pregnant people to achieve abstinence, and mothers with dependent children to reduce their alcohol consumption (Ujhelyi Gomez 2020). The authors conducted two meta-analyses: one with six RCTs on abstinence during pregnancy, and one with four RCTs on the reduction of alcohol consumption in mothers. Overall, the systematic review found that, compared with usual care or no intervention, psychosocial interventions were effective in increasing abstinence rates during pregnancy and in reducing alcohol consumption in mothers. Other RCTs that provided data on reduction in alcohol consumption in pregnant people were only described narratively. Both systematic reviews evaluated the efficacy of psychological treatments during pregnancy to achieve abstinence, but included different RCTs in their meta-analyses: only three RCTs out of five and six, respectively, were included in both systematic reviews.

The latest systematic review selected 26 studies and investigated the efficacy of brief interventions (BIs) in stopping or reducing alcohol consumption during pregnancy (Popova 2023). The authors conducted three meta-analyses and found modest effects that BIs increased the odds of abstinence and reduced preterm birth, while not finding any differences between BIs and the control group in alcohol consumption. However, this systematic review also included studies that recruited pregnant women who did not drink alcohol at baseline. Other recent systematic reviews evaluated the literature on this topic without conducting meta-analyses (Chang 2023; Erng 2020; Fergie 2019; Gebara 2013; Samawi 2021).

No Cochrane review has been conducted evaluating the efficacy and safety of medications in helping individuals with AUD in achieving abstinence and/or reducing alcohol consumption during pregnancy. Our new Cochrane review on this topic is therefore aimed at investigating the efficacy of psychosocial interventions and medications in increasing abstinence from alcohol and/or reducing alcohol consumption during pregnancy.

OBJECTIVES

To assess the efficacy of psychosocial interventions and medications to reduce or stop alcohol consumption during pregnancy.

METHODS

Criteria for considering studies for this review

Types of studies

We included parallel, individually randomised RCTs and cluster-RCTs aimed at determining the efficacy of medications or psychosocial interventions, or both, in reducing or stopping alcohol consumption during pregnancy. We also included quasi-randomised studies, that is studies that use methods to allocate participants to groups that are not truly random, such as alternation, day of the week, or date of birth or entry to the study. We included studies irrespective of outcomes reported.

Types of participants

Individuals who consume alcohol during pregnancy. Alcohol use was demonstrated by self-report or laboratory tests. Pregnant

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individuals with any amount of alcohol at baseline were included, as any alcohol use is considered unhealthy during pregnancy. Among them, we intended two different subpopulations for subgroup analyses: individuals with AUD and without AUD; and individuals with AUD were to be further divided into different categories according to the severity of AUD (mild, moderate, and severe, according to the number of criteria met; APA 2013). In this review, the diagnoses provided by the primary RCTs (i.e. AUD or alcohol dependence) are described in the Results and Studies sections (Included, Excluded, Awaiting classification, and Ongoing), whereas in the other sections (Abstract, Plain language summary, Background, Methods, Discussion, and Authors' conclusions), the term 'AUD' is used to indicate both definitions. We excluded pregnant individuals who did not drink alcohol at baseline. When heterogeneous populations were recruited (e.g. women who used alcohol and women who used other substances), we contacted the authors to obtain data of the sample of women who used alcohol. We excluded individuals with a diagnosis of a substance use disorder involving substances other than alcohol. We included individuals using substances other than alcohol without a diagnosis of substance use disorder.

Types of interventions

Experimental intervention

Any medication or psychosocial intervention that is validated or described by the study's authors as aiming to reduce alcohol consumption or achieve abstinence from alcohol. Medications could be acamprosate, naltrexone, disulfiram, nalmefene, or any other medication that is described by the study authors as aiming to reduce alcohol consumption or achieve abstinence. Psychological interventions could include cognitive behavioural therapy, brief psychodynamic psychotherapy, interpersonal psychotherapy, and supportive counselling or supportive therapy. Educational interventions could include brief educational counselling sessions, structured long-term educational programmes with motivational enhancement interventions, individual-focused educational strategies, family-focused programmes, professional group education interventions, and self-help group educational interventions. We also included any combination of medications and psychosocial interventions when compared to the medication or psychosocial intervention alone. Medications or psychosocial interventions could be delivered to pregnant people at home, in any medical setting, or other places.

Comparison intervention

Placebo, no intervention, treatment as usual (TAU), or other psychosocial interventions.

Types of outcome measures

Primary outcomes

- Abstinence from alcohol expressed as the number of continuously abstinent women at the end of treatment or at the latest available follow-up.
- Reduction in alcohol consumption expressed as the difference between alcohol consumption at baseline and at the end of treatment or at the latest follow-up, or both, according to data provided by each study and measured as:
  - number of drinks per day (expressed as the mean number of drinks consumed per day, when abstinent days are included);
  - number of drinks per drinking day (expressed as the mean number of drinks consumed per day, when only drinking days are included);
  - percentage of days abstinent;
  - percentage of heavy drinking days (heavy drinking is defined as four or more drinks in a day for women and five or more drinks in a day for men; Anton 2005);
  - number of pregnant women with no heavy drinking days;
  - number of grams of alcohol consumed per day; and
  - scores on any questionnaire or scale to evaluate alcohol consumption (e.g. AUDIT, AUDIT-C, or timeline follow-back method (TLFB)).
- Retention in treatment, measured by the number of women who completed treatment.
- Adverse events, measured by the number of women with at least one adverse event at the end of treatment.

Secondary outcomes

Withdrawal signs and symptoms expressed as the number of women who report tremors, insomnia, nausea and vomiting, hallucinations or illusions, psychomotor agitations, anxiety, seizures, delirium tremens, or scores on questionnaires or scales validated to evaluate withdrawal severity.

Search methods for identification of studies

Electronic searches

The Cochrane Drugs and Alcohol Group Information Specialist conducted systematic searches in the following databases for RCTs without language, publication year, or publication status restrictions:

- Cochrane Drugs and Alcohol Group's Specialised Register of Trials (searched on 8 January 2024);
- Cochrane Central Register of Controlled Trials (CENTRAL; 8 January 2024, Issue 1) via the Cochrane Library;
- MEDLINE (Ovid) (1946 to 8 January 2024);
- Embase (Ovid) (January 1974 to 8 January 2024);
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCOhost) (1982 to 8 January 2024);
- Web of Knowledge, Web of Science (1990 to 8 January 2024);
- PsycINFO (Ovid) (1806 to 8 January 2024).

The Information Specialist modelled subject strategies for databases on the search strategy designed for MEDLINE. Where appropriate, these were combined with subject strategy adaptations of the Highly Sensitive Search Strategy designed by Cochrane for identifying RCTs, as described in Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011). Search strategies for major databases are provided in Appendix 1.

We searched the following trial registries on 8 January 2024:

- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/);
- ClinicalTrials.gov (clinicaltrials.gov).

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Searching other resources

We searched the reference lists of all relevant papers to identify additional studies, as well as conference proceedings that are likely to contain trials relevant to the review. We contacted investigators to seek information about unpublished or incomplete trials.

Data collection and analysis

Selection of studies

Three review authors (RA, LA, SU) independently screened titles and abstracts for potentially relevant studies. Any disagreements between the review authors were resolved by discussion and deferring to another review author (SM). We obtained the full texts of papers deemed potentially relevant, and three review authors (RA, LA, SU) independently assessed the full-text papers for inclusion in the review. Any disagreements were resolved by discussion or by deferring to another review author (SM, JMAS). One review author (SU) contacted study authors to resolve any uncertainties as needed.

We contacted the corresponding authors of papers that were not available in full-text format and allowed a period of one month for the authors to respond. In case of a lack of response, we considered the studies without full-text access as awaiting classification.

Data extraction and management

Two review authors (LA, SU) independently extracted data. We used standardised data extraction forms and piloted the forms on an initial set of three studies between the review authors. Any disagreements between the review authors were resolved by discussion and deferring to other review authors (SM, RA). We extracted the following data.

- Bibliographic details: authors, year, country
- Methods: study design, number of participants
- Participant characteristics: age and gestational age
- Alcohol consumption at baseline to assign participants to one of the two categories (people who report use of alcohol during pregnancy without having a diagnosis of AUD or people with a diagnosis of AUD at baseline, and among people with an AUD diagnosis, severity of AUD)
- Interventions: type of medication and/or psychosocial intervention, setting, frequency, duration
- Comparator: type of comparison intervention
- Outcomes: alcohol consumption and use of other substances during pregnancy
- Funding of the study and conflict of interest of study author
- Potential influencing factors, e.g. spouse's drinking

When we found multiple publications from the same study, we made sure to include participants only once in the analyses. We used RevMan software to manage data storage and complete the data analysis (RevMan 2024).

Assessment of risk of bias in included studies

Two review authors (SM, RS) independently assessed the risk of bias in the included studies for the primary outcomes using Cochrane's RoB 2 tool (Higgins 2022). For the scope of this review, we assessed the effect of assignment to the intervention (intention-to-treat effect) for our primary outcomes. We assessed risk of bias based on the following domains.

- Bias arising from the randomisation process
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

We assessed cluster-RCTs using the variation of the RoB 2 tool for cluster-RCTs and the special issues to be considered as described in Chapter 23 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Eldridge 2021; Higgins 2022).

We used the Excel tool to implement RoB 2.

We judged each domain as being at low risk of bias, some concerns, or high risk of bias. We reached an overall risk of bias assessment for each included study according to the following criteria.

- Low risk of bias: low risk of bias for all domains
- Some concerns: some concerns in at least one domain, but not at high risk of bias for any domain
- High risk of bias: high risk of bias in at least one domain, or some concerns for multiple domains such that our confidence in the result is substantially lowered

The risk of bias assessment feeds into one domain of the GRADE approach for assessing the certainty of a body of evidence.

Measures of treatment effect

In studies with dichotomous outcomes (e.g. abstinent participants), we summarised trial outcomes as risk ratios (RRs) with 95% confidence intervals (CIs). For continuous data (e.g. score on AUDIT), we calculated the mean difference (MD) from baseline to each follow-up point in the intervention and control groups. If the studies used different measures of alcohol consumption, we attempted to convert them into one cumulative outcome (e.g. number of drinks per day into number of grams per day). When such transformation was not possible, different scales were used to evaluate alcohol consumption, or when data referred to different periods of time, we used the standardised mean difference (SMD).

Unit of analysis issues

When multi-armed studies were included, and one arm was considered more than once in the same comparison (e.g. two different intensities of the psychosocial intervention compared with the same control group), we combined all relevant experimental groups into a single group and compared it with the control to avoid double-counting of participants.

We analysed cluster-RCTs according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022). If results did not control for clustering, we contacted the trialists to request an estimate of the intracluster correlation coefficient (ICC). If we were unable to obtain an ICC from the trialists, we imputed ICC from other cluster-RCTs included in the review. We divided the effective sample size of each arm by the 'design effect' quantity (1 + (M − 1) x ICC), where M is the average cluster size. The details of calculations are available here.

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Dealing with missing data

We contacted the authors of the included studies if key study characteristics, including outcome data, were missing. If standard deviations (SDs) were missing, we used the mean of the available SDs of the other included studies (Fukurama 2006).

Assessment of heterogeneity

We analysed statistical heterogeneity using the I^2 statistic and the Chi^2 test. We regarded heterogeneity as substantial if I^2 was greater than 50%, or the P value was lower than 0.10 for the Chi^2 test for heterogeneity. Following the guidance in the *Cochrane Handbook for Systematic Reviews of Interventions*, we distinguished the following values to denote unimportant, moderate, substantial, and considerable heterogeneity, respectively: 0% to 40%, 30% to 60%, 50% to 90%, and 75% to 100% (Higgins 2011; Higgins 2022). We aimed to explore possible reasons for considerable levels of heterogeneity (i.e. ≥ 75%) by visually inspecting the forest plot to identify studies that might be contributing to the heterogeneity. However, we acknowledge that uncertainty in the I^2 value is substantial when the number of studies is small (Higgins 2022).

Assessment of reporting biases

We aimed to use funnel plots (plots of the effect estimate from each study against the sample size or effect standard error) to assess the potential for bias related to trial size, which could indicate possible publication bias. A plot with greater scatter designates lower levels of bias, indicating the inclusion of studies regardless of results. We planned to inspect funnel plot symmetry if there were at least 10 studies included in the meta-analysis.

Data synthesis

We combined the outcomes from the individual trials through meta-analysis where possible (comparability of intervention and outcomes between trials) using a random-effects model, as we expected a certain degree of heterogeneity between trials. If the clinical or statistical heterogeneity between trials was too high (i.e. I^2 of 75% to 100%), we would consider not pooling the data because of the high clinical diversity to be included in the preplanned comparisons and add further comparisons, providing a rationale for post hoc changes. If we included studies with incompletely reported outcomes or effect measures, we would consider other methods for summarising and displaying results, such as vote counting based on the direction of effect or structured tabulation of the results across studies according to the comparisons considered (Higgins 2022).

Subgroup analysis and investigation of heterogeneity

If we identified substantial heterogeneity, we would use the formal test for subgroup differences in RevMan to perform separate subgroup analyses.

When aimed to conduct subgroup analyses to investigate the role of the following confounders/effect modifiers.

- Type of medication or psychosocial intervention, or both
- Amount of alcohol consumption: any alcohol consumption, diagnosis of AUD (according to standardised criteria such as the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*) or equivalent; APA 2013), severity of AUD
- Dose of medication, intensity or frequency of psychosocial intervention

Sensitivity analysis

We planned to perform sensitivity analyses to assess the impact of excluding studies with high risk of bias.

Summary of findings and assessment of the certainty of the evidence

Two review authors (RS, SM) assessed the certainty of evidence using the GRADE approach (Atkins 2004; Guyatt 2008; Guyatt 2011; Schünemann 2006). GRADE takes into account issues not only related to internal validity, but also to external validity, such as directness of results. The summary of findings tables present the main findings of the review in a transparent and simple tabular format. In particular, they provide key information concerning the certainty of the evidence, the magnitude of effect of the interventions examined, and the sum of the available data on the main outcomes. We presented a summary of findings table for each of the analyses as described in the Data synthesis section. We assessed the certainty of the evidence for the primary and secondary outcomes evaluated at the end of treatment. The GRADE approach uses the following criteria for assigning grades of evidence.

- High: we are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- Very low: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

The certainty of the evidence is downgraded for the following reasons.

- Serious (−1) or very serious (−2) study limitation for risk of bias
- Serious (−1) or very serious (−2) inconsistency between study results
- Some (−1) or major (−2) uncertainty about directness (the correspondence between the population, the intervention, or the outcomes measured in the studies actually found and those under consideration in our review)
- Serious (−1), very serious (−2), or extremely serious (−3) imprecision of the pooled estimate
- Publication bias strongly suspected (−1)

For the domain 'study limitation', we downgraded one level if we found high risk of bias in one domain, or some concerns in most domains in the studies most contributing to the summary estimate; we downgraded two levels if we found high risk of bias in more than one domain in the studies most contributing to the summary estimate (Guyatt 2011). For the domain 'publication bias', we downgraded one level if we found asymmetry in the funnel plot (Guyatt 2011 b). For the domain 'inconsistency', we downgraded one or two levels on the basis of the magnitude of the I^2 and the overlap of the CI of the estimates of the individual studies

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(Guyatt 2011 c). For the domain 'indirectness', we considered downgrading one level if the characteristics of participants, setting, interventions, or countries would limit the generalisability of the results to the population and/or interventions as defined in our PICO (Population, Intervention, Comparison, Outcome; Guyatt 2011 d). For the domain 'imprecision', we downgraded one, two, or three levels on the basis of the wideness of CI of the absolute estimate (Zeng 2022).

RESULTS

Description of studies

Results of the search

We identified 4411 studies from all possible sources following the removal of duplicates. We excluded 4300 studies based on title and abstract, and assessed 111 full-text articles.

Overall, we identified eight trials meeting our inclusion criteria reported in 15 references (see Characteristics of included studies). We excluded 31 trials (35 references; see Characteristics of excluded studies); 22 trials (36 references) are awaiting classification (see Characteristics of studies awaiting classification); and 21 trials (25 references) are ongoing studies (see Characteristics of ongoing studies). A PRISMA flow diagram is shown in Figure 1.

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Figure 1. PRISMA flow diagram.

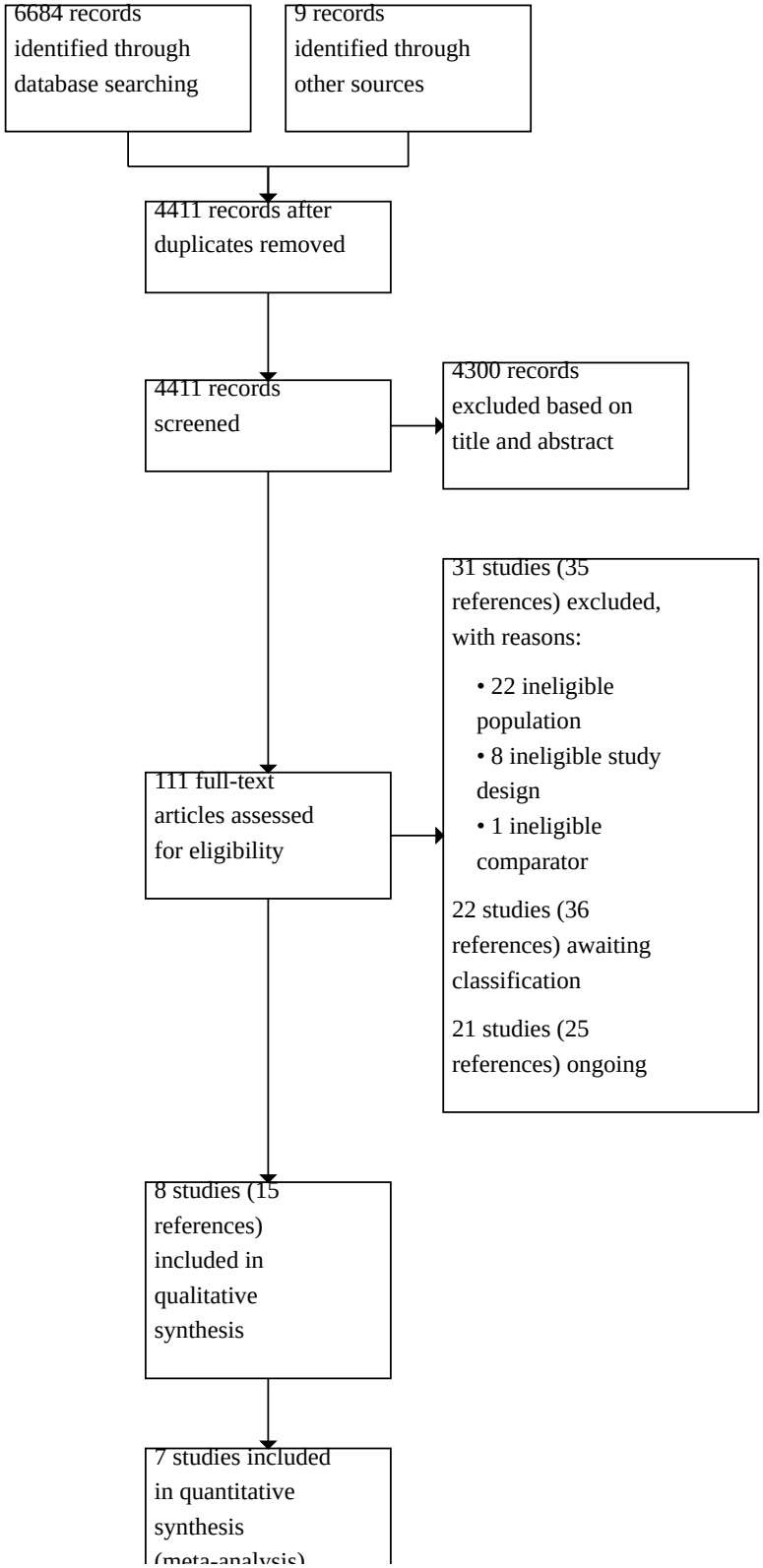

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Figure 1. (Continued)

synthesis
(meta-analysis)

Regarding the 22 studies awaiting classification (see Studies awaiting classification), despite our attempts to obtain data of women who were drinking during pregnancy, we did not find the full text of two trials (9.1% of the 22 studies awaiting classification); the email addresses were incorrect for three trials (13.6%); and most of the corresponding authors that we contacted did not reply (14 trials, 82.4% of the 17 corresponding authors contacted). Among the three corresponding authors that replied, two provided unclear data, and we are awaiting data from the third. The studies awaiting classification recruited heterogeneous samples of participants comprising women who were not pregnant (5 trials; 22.7% of the studies awaiting classification) or women who did not drink alcohol during pregnancy (15 trials, 72.7%) in rates ranging from 20%, Chang 2005, to more than 95% of the participants, Rotheram-Borus 2023.

Regarding the 21 ongoing trials (see Ongoing studies), 12 (57.1%) are clinical registrations; eight (38.1%) are protocols; and one (5.0%) is a conference abstract. Four ongoing trials (20.0%) plan to assess brief intervention (NCT00540319; NCT01971398) or computer-delivered brief intervention (Ondersma 2022; Tzilos 2019); two (10.0%) mobile health to support women (Bendtsen 2020; Brunelli 2022); two (10.0%) providing educational brochures (NCT01971398; NCT05976776); and two (10.0%) motivational interviewing (NCT04275570) or motivational enhancement theory (NCT05766761). The following interventions will be assessed by one ongoing trial each: text message intervention (ACTRN12616000072415), healthy conversation skills support (Baird 2016), activation of fast-track referral for specialised units (Barros 2022), intervention group monitoring (y4k7w RBR 2018), psychotherapeutic programme delivered by app/internet and telephone (Carmona Camacho 2022), mindfulness-oriented experimental group therapy (Lenz 2018), interpersonal psychotherapy (NCT01550913), specialised breathalyser face recognition technology (NCT02759874), community parenting programme (NCT04441307), targeted nurse-led home visiting (NCT04749888), and online acceptance and commitment therapy (ACTRN12623000683639).

Included studies

We included eight RCTs involving a total of 1369 participants (see Characteristics of included studies). The study size ranged from 42 participants, Handmaker 1999, to 349 participants, van der Wulp 2014. Four studies recruited more than 100 participants (Chang 1999; O'Connor 2007; Rubio 2014; van der Wulp 2014).

All studies but one were parallel individually randomised RCTs; van der Wulp 2014 was a cluster-RCT.

All studies but one were two-arm trials; van der Wulp 2014 was a three-arm study that evaluated two different types of psychosocial interventions compared to a control group.

One study was not included in the meta-analyses (Chang 1999). This study evaluated a single outcome, the number of drinks per drinking days, expressed as difference compared to the baseline values without providing the SDs. As this outcome was evaluated only in this study, it was not possible to conduct a meta-analysis (see Effects of interventions).

All participants were pregnant women who reported alcohol use while pregnant. The mean age of participants was 27.4 years. Alcohol use during pregnancy was reported differently by each study: as number of drinks per drinking day (Chang 1999), per day (Rubio 2014), per week (van der Wulp 2014), in the last month (Reynolds 1995), or in the last two months (Handmaker 1999). One study reported the maximum number of drinks per drinking occasion (O'Connor 2007), and another the number of grams of ethanol per week (Tzilos 2011). Finally, one study reported the concentration of ethyl glucuronide in hair (Joya 2016).

One study recruited almost half of participants (46.7%) with a current diagnosis of alcohol dependence (Rubio 2014); another study recruited 40% of participants with a lifetime diagnosis of alcohol dependence (Chang 1999). The latter study reported that 28% of participants had a lifetime diagnosis of dependence on substances other than alcohol (Chang 1999). The other studies did not provide this information. Three studies reported the rate of participants who smoked during pregnancy (Chang 1999; Joya 2016; van der Wulp 2014), which ranged from 8% to 20%.

Six studies took place in the USA (Chang 1999; Handmaker 1999; O'Connor 2007; Reynolds 1995; Rubio 2014; Tzilos 2011); the other two studies were conducted in Spain (Joya 2016) and the Netherlands (van der Wulp 2014).

Only a few studies adopted the same measures of alcohol consumption in the description of their results: Joya 2016, Reynolds 1995, and van der Wulp 2014 the number of continuously abstinent participants; Reynolds 1995 and van der Wulp 2014 the number of drinks per day; and Handmaker 1999, Joya 2016, O'Connor 2007, Reynolds 1995, Rubio 2014, Tzilos 2011, and van der Wulp 2014 the number of continuously abstinent participants. Other studies provided different measures. Chang 1999 reported the reduction of drinks per drinking day, O'Connor 2007 the maximum number of drinks per drinking occasion, and Joya 2016 ethyl glucuronide concentrations in maternal hair.

Sources of funding

Seven studies (87.5%) received funds from public institutes; one study did not provide this information. No study reported funding by private companies, or declared any conflict of interest.

Interventions

All of the included studies evaluated the efficacy of psychosocial interventions in helping pregnant women to achieve and maintain

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abstinence or at least reduce their alcohol use during pregnancy. We did not find any study that evaluated the efficacy of medications among pregnant women who used alcohol while pregnant.

According to the definitions provided by the individual study authors, the psychosocial interventions were brief interventions in two studies (Chang 1999; O'Connor 2007), motivational interviewing in two studies (Handmaker 1999; Joya 2016), a self-help programme in one study (Reynolds 1995), brief motivational enhancement intervention in one study (Rubio 2014), brief computer-delivered intervention in one study (Tzilos 2011), and health counselling and computer tailoring in one study (van der Wulp 2014). In four studies, the duration of the psychosocial interventions was equal to 10 to 15 minutes (O'Connor 2007; Reynolds 1995; Rubio 2014; van der Wulp 2014). In another study, the duration was 15 to 50 minutes (Tzilos 2011). Two studies used longer psychosocial interventions with durations of around 45 minutes, Chang 1999, and one hour, Handmaker 1999. Information on duration was lacking in one study (Joya 2016). In six studies, women received a single session (Chang 1999; Handmaker 1999; Joya 2016; O'Connor 2007; Reynolds 1995; Tzilos 2011); in the other two studies, women received three sessions, van der Wulp 2014, or five sessions, Rubio 2014.

Pregnant women received the psychosocial intervention on average at 15.1 weeks of pregnancy, ranging from 7.9 weeks, van der Wulp 2014, to 25.3 weeks, Tzilos 2011. Alcohol use was assessed after a period ranging from eight weeks (Handmaker 1999; Reynolds 1995; Tzilos 2011) to 24 weeks (van der Wulp 2014) after the psychosocial intervention.

The psychosocial intervention was delivered by research assistants (Chang 1999; Handmaker 1999), trained nutritionists (O'Connor 2007), educators (Reynolds 1995), registered nurses or lay counsellors (Rubio 2014), midwives (van der Wulp 2014), or was self-administered using a tablet (Tzilos 2011). This information was lacking for one study (Joya 2016).

Comparisons

In three studies, women in the control group received treatment as usual (TAU) (Reynolds 1995; Rubio 2014; van der Wulp 2014). In the other five studies, women received comprehensive assessment of alcohol use and advice to stop drinking during pregnancy (Chang 1999; Handmaker 1999; Joya 2016; O'Connor 2007; Tzilos 2011); we considered these treatments as similar to TAU.

Any psychosocial intervention versus TAU

Globally, we considered all the psychosocial interventions together and treatments received by women in the control groups as TAU.

The comparison evaluated was any psychosocial intervention versus TAU (eight studies) (Chang 1999; Handmaker 1999; Joya 2016; O'Connor 2007; Reynolds 1995; Rubio 2014; Tzilos 2011; van der Wulp 2014).

Excluded studies

We excluded 31 studies (35 references) (see Figure 1; Characteristics of excluded studies), for the following reasons:

- ineligible participants (22 studies);
- ineligible comparator (one study);
- ineligible study design (eight studies).

Risk of bias in included studies

For the outcome number of continuously abstinent individuals, we judged two studies at overall high risk of bias and one as some concerns. The domains at high risk of bias were: bias due to missing outcome data in one study, and bias in measurement of the outcomes in two studies. The domains at some concerns were: bias arising from the randomisation process in two studies, and bias due to deviations from intended interventions and bias in selection of the reported results in all studies.

For the outcome reduction in alcohol consumption measured as number of drinks per day, we judged both studies contributing data to this outcome at overall high risk of bias. The domains at high risk of bias were: bias due to missing outcome data in two studies, and bias in measurement of the outcomes in all studies. The domains at some concerns were: bias arising from the randomisation process in one study, and bias due to deviations from intended interventions and bias in selection of the reported results in all studies.

For the outcome retention in treatment measured as number of participants who completed the treatment, we judged all studies as some concerns. The domains at some concerns were: bias arising from the randomisation process in four studies, bias due to deviations from intended interventions in five studies, and bias in selection of the reported results in all studies.

To access further detailed risk of bias assessment data, please use the following link: figshare.com/s/1163fa5d8da243268842

Effects of interventions

See: **Summary of findings 1** Summary of findings table - Any psychosocial intervention compared to treatment as usual for stopping or reducing alcohol consumption during pregnancy

Any psychosocial intervention versus treatment as usual (TAU)

Primary outcomes

See Summary of findings 1.

1. Abstinence from alcohol expressed as the number of continuously abstinent women at the end of treatment or at the latest available follow-up

Psychosocial interventions may increase the rate of continuously abstinent women (risk ratio (RR) 1.34, 95% confidence interval (CI) 1.14 to 1.57; I^2 =0%; 3 studies; 378 women; low certainty evidence). See Analysis 1.1 and Figure 2.

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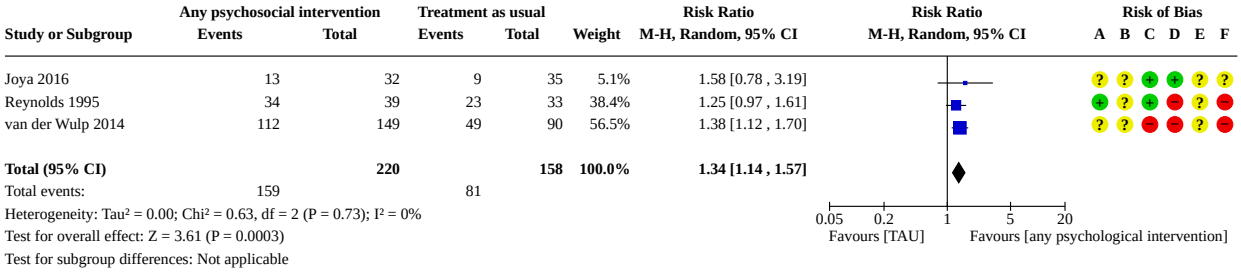
Figure 2. Forest plot of comparison: Any psychosocial intervention versus treatment as usual; outcome: 1 Number of continuously abstinent women.



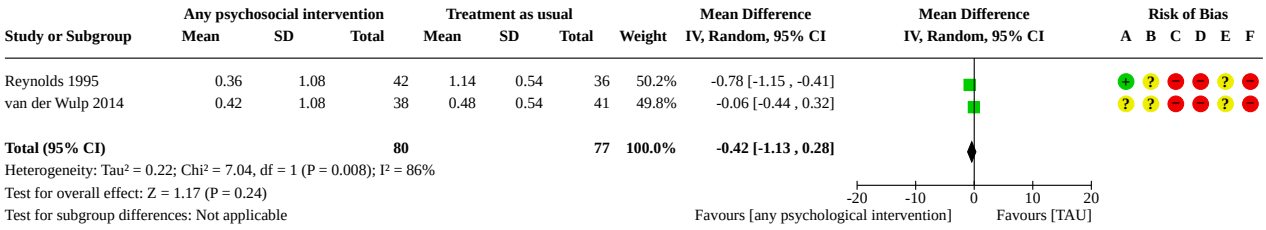
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

We could not perform sensitivity analysis excluding studies at high risk of bias as two out of three studies were at overall high risk of bias.

2. Reduction in alcohol consumption expressed as the difference between alcohol consumption at baseline and at the end of treatment and/or at the latest follow-up, according to data provided by each study and measured as number of drinks per day (expressed as the mean number of drinks consumed per day, when abstinent days are included)

Psychosocial interventions may have little to no effect on the number of drinks per day, but the evidence is very uncertain (mean difference −0.42, 95% CI −1.13 to 0.28; I^2 = 86%; 2 studies; 157 women; very low certainty evidence). The SD was missing for one study (Reynolds 1995); we used the same SD as in the other study (van der Wulp 2014). See Analysis 1.2 and Figure 3.

Figure 3. Forest plot of comparison: Any psychosocial intervention versus treatment as usual; outcome: 2 Number of drinks per day.



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

We were unable to evaluate possible differences between psychosocial interventions and TAU in the number of drinks per drinking day, as only one study reported this outcome, without SD (Chang 1999; baseline: experimental group (52 pregnant women) = 1.5 (SD 1.2) versus control group (56 pregnant women) = 2.1 (SD 1.5); end of treatment: experimental group (52 pregnant women) = 0.3 (SD not provided) versus control group (56 pregnant women) = 0.4 (SD not provided)).

We could not perform sensitivity analysis excluding studies at high risk of bias as both studies were at overall high risk of bias.

3. Retention in treatment, measured as number of women who completed treatment

Psychosocial interventions probably result in little to no difference in the number of women who completed treatment (RR 0.98, 95% CI 0.94 to 1.02; I^2 =0%; 7 studies; 1283 women; moderate certainty evidence). See Analysis 1.3 and Figure 4. The difference between the total number of women included in this analysis and the total number of women included in the review is due to the adjusted number of women in this analysis for the cluster effect.

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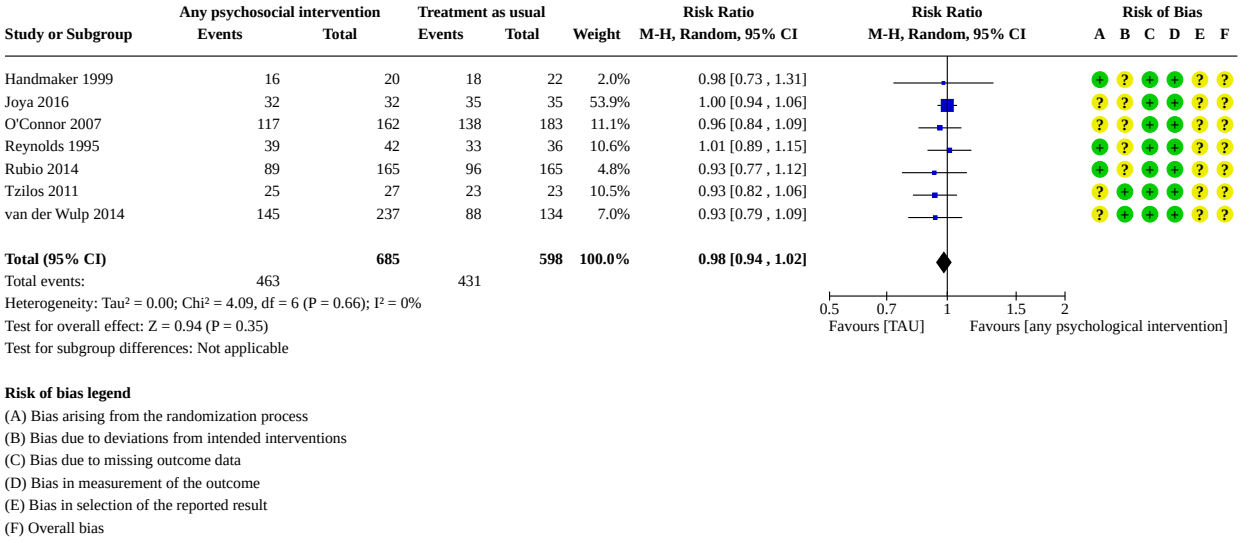
Figure 4. Forest plot of comparison: Any psychosocial intervention versus treatment as usual; outcome: 3 Number of women who completed treatment.



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

We could not perform sensitivity analysis excluding studies at high risk of bias as none of the studies were at overall high risk of bias.

4. Adverse events, measured by the number of women with at least one adverse event at the end of treatment

None of the included studies assessed adverse events.

Subgroup analysis for type of medication or psychosocial intervention

We could not perform subgroup analyses for type of medication as we did not find any study that evaluated the efficacy of medications among pregnant women who used alcohol while pregnant.

We could not perform subgroup analyses for type of psychosocial intervention as all the included studies used brief interventions.

Subgroup analysis for severity of alcohol consumption

We could not perform subgroup analyses for severity of alcohol consumption at baseline as only two studies included women with AUD.

Subgroup analysis for intensity or frequency of psychosocial intervention

We could not perform subgroup analyses for intensity or frequency of psychosocial interventions as the number of studies was too few to render any result of subgroup analyses meaningful (Higgins 2022).

Secondary outcomes

Withdrawal signs and symptoms expressed as the number of people who report tremors, insomnia, nausea and vomiting, hallucinations or illusions, psychomotor agitations, anxiety, seizures, delirium tremens, or scores on questionnaires or scales validated to evaluate withdrawal severity

None of the included studies assessed withdrawal signs and symptoms.

DISCUSSION

This Cochrane review was aimed at evaluating the efficacy of psychosocial interventions or medications, or both, in helping pregnant women to achieve and maintain abstinence or at least reduce their alcohol use during pregnancy. Overall, our search identified eight studies that met our inclusion criteria, of which seven were included in the meta-analyses. The first matter of discussion is the limited number of included studies. This is somewhat surprising considering the high prevalence of consuming any amount of alcohol during pregnancy and its relevant harms (Popova 2017). One of the main reasons for the limited number of included studies is related to the exclusion of those studies in which participants were not entirely composed of pregnant women who reported alcohol use while pregnant. Of note, our search identified several studies in which participants were at risk for alcohol use during pregnancy or used alcohol before pregnancy, but for whom it was unclear if the women actually drank alcohol during pregnancy. Other studies provided information on alcohol use during pregnancy of heterogeneous populations of participants including women who were not pregnant, who were at risk for other problems like smoking or used other psychoactive substances. We contacted the authors of these studies asking them for data of the subsamples of pregnant women who reported alcohol use during pregnancy. However, many authors replied that they were not able to provide us these data. Another reason for the limited number of included studies is related to the lack of studies in which the efficacy and safety of AUD medications have been evaluated among pregnant women, despite certain AUD medications like acamprosate and naltrexone appearing not to have a substantial risk of serious consequences during pregnancy (Kelty 2021).

Summary of main results

Our search identified eight studies (1369 women) in which pregnant women received an intervention to reduce alcohol use during pregnancy. In one study, almost half the participants recruited had a current diagnosis of AUD, and in another, 40% of participants had

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a lifetime diagnosis of AUD. Six studies took place in the USA, and one study each took place in Spain and the Netherlands.

All the included studies evaluated the efficacy of a psychosocial intervention; we did not find any study that evaluated the efficacy and safety of AUD medications during pregnancy. Psychosocial interventions mainly consisted of brief interventions, with a duration ranging from single sessions of 10 to 60 minutes or up to five sessions of 10 minutes each. Pregnant women received the psychosocial interventions approximately at the end of the first trimester of pregnancy, and their alcohol use was reassessed 8 to 24 weeks after the psychosocial intervention. Women in the control group received TAU or similar treatments like a comprehensive assessment of alcohol use and advice to stop drinking during pregnancy. We considered all treatments received by women in the control groups as TAU.

Globally we found that, compared to TAU, psychosocial interventions may increase the rate of continuously abstinent women. Psychosocial interventions may have little to no effect in the number of drinks per day, but the certainty of the evidence was very low. Unfortunately, the small number of included studies and the heterogeneity in the outcomes provided by these studies for alcohol use prevented any clear conclusions regarding differences between psychosocial interventions and TAU in alcohol use expressed as number of drinks per day or per drinking days. Finally, we found that there was probably no difference between psychosocial intervention and TAU groups in the number of women who completed treatment. This could in part be due to the fact the women were evaluated during pregnancy, and participants of both groups were highly motivated to adhere to treatment because of pregnancy rather than treatment itself. Nevertheless, the lack of differences between the two groups also indicates that receiving psychosocial interventions does not interfere with completing treatment.

Overall completeness and applicability of evidence

Only two studies recruited pregnant women with current or lifetime diagnoses of AUD. In addition, we did not find any study in which the efficacy and safety of AUD medications were evaluated among pregnant women with AUD. Accordingly, our findings do not provide evidence for pregnant people with AUD, and further studies should be conducted to provide evidence indicating or contraindicating the use of AUD medications during pregnancy.

Most of the included studies (75%) took place in the USA. As the effects of psychosocial interventions are largely influenced by the social context, this limits the generalisability of the findings to countries and marginalised ethnic groups not recruited to these studies. Considering the high prevalence of alcohol use during pregnancy observed in the African Region and among pregnant people who belong to underserved racial/ethnic groups, further studies should be conducted to specifically investigate the efficacy and safety of psychosocial treatments and medications in low- and middle-income countries and underserved ethnic groups.

The limited number of included studies prevents an evaluation of possible differences according to the number of sessions delivered during pregnancy.

We did not evaluate pregnancy outcomes (e.g. Apgar score and birthweight) in this review, as they not only depend on the amount of alcohol consumed during pregnancy, but also on several other factors like the gestational timing of alcohol consumption, variability in the xenobiotic metabolism and genetic background of the pregnant woman and fetus, environmental influences like age, cigarette use, nutritional status, and stress levels of the pregnant woman, and lifestyle factors of the other parent (see Background).

Globally, our results are far from being considered conclusive.

Quality of the evidence

The majority of the included studies were published more than a decade ago and the quality of reporting was poor, making it difficult to assess risk of bias as information was insufficient. For the outcome number of continuously abstinent women, we judged two studies at overall high risk of bias and one as some concerns.

For the outcome reduction in alcohol consumption measured as number of drinks per day, we judged both studies providing data for this outcome at overall high risk of bias.

For the outcome retention in treatment, measured as number of women who completed treatment, we judged one study at overall high risk of bias and the other study as some concerns.

Overall, we judged the certainty of evidence as moderate for retention in treatment, low for number of continuously abstinent women due to high risk of bias, and very low for reduction in alcohol consumption, measured as number of drinks per day, due to high risk bias and imprecision in the estimate.

Potential biases in the review process

Despite our comprehensive bibliographic search and the evaluation of full-text reports of 111 studies, we were only able to include eight studies with roughly 1400 participants. We found several studies that included both drinking and non-drinking pregnant women; we wrote to the studies' corresponding authors asking for data only for participants who drank at baseline, but unfortunately the majority of the contacted authors did not respond to our email or were unable to provide our data of interest. We were not able to assess the risk of publication bias by the visual inspection of funnel plots, as fewer than 10 studies were included.

Agreements and disagreements with other studies or reviews

Our results agree with those of other systematic reviews that evaluated the efficacy of psychosocial interventions in reducing alcohol consumption during pregnancy. While previous Cochrane reviews published more than 10 years ago found no RCTs or insufficient data to draw clear conclusions (Lui 2008; Stade 2009; Turnbull 2012), more recent non-Cochrane reviews found that psychosocial interventions increase the rate of abstinent people during pregnancy (O'Connor 2018; Popova 2023; Ujhelyi Gomez 2020). However, the populations recruited by these systematic reviews do not completely overlap our population as, other than pregnant women who used alcohol during pregnancy, they also included adolescents and adults (O'Connor 2018), mothers (Ujhelyi Gomez 2020), and pregnant women who did not drink alcohol at baseline (Popova 2023).

This is the first systematic review specifically investigating the efficacy of psychosocial interventions and medications in

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increasing abstinence from alcohol and/or reducing alcohol use exclusively among pregnant women who reported alcohol use during pregnancy.

AUTHORS' CONCLUSIONS

Implications for practice

We found that, among pregnant women who report alcohol use during pregnancy, psychosocial interventions may increase the rate of participants continuously abstinent without modifying the number of participants who complete treatment when compared to treatment as usual. It is unclear if psychosocial interventions reduce the amount of alcohol consumed expressed as number of drinks per day or per drinking day.

Implications for research

The limited number of included studies underlines the need to conduct further clinical studies specifically designed to investigate the efficacy and safety of treatments to achieve and maintain abstinence or at least reduce alcohol use during pregnancy. These studies should provide detailed information on alcohol use before and during pregnancy using consistent alcohol consumption measures such as the number of drinks per drinking day. When heterogeneous populations are recruited, more detailed information on alcohol use during pregnancy should be provided to allow future systematic reviews to be conducted. Other important information that would enhance the usefulness of these studies would be the presence of other comorbid conditions such as anxiety, mood disorders, and the use of other psychoactive substances.

ACKNOWLEDGEMENTS

Editorial and peer-reviewer contributions

Cochrane Drugs and Alcohol supported the authors in the development of this review update.

The following people conducted the editorial process for this article.

- Sign-off Editor (provided editorial guidance to authors, final editorial decision): Prof Michael Farrell, MB, BCh, BAO, MRCP, MRCPsych, Director Professor of Addiction Psychiatry National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia
- Managing Editor (selected peer reviewers, collated peer-reviewer comments): Zuzana Mitrova, Cochrane Drugs and Alcohol
- Copy Editor (copy editing and production): Lisa Winer, Cochrane Central Production Service
- Peer reviewers (provided comments and recommended an editorial decision): Ashraf Nabhan, Faculty of Medicine, Ain Shams University (clinical/content review), Nandi Siegfried, Mental Health, Alcohol, Substance and Tobacco Research Unit, South African Medical Research Council (clinical/content review), Emma Axon, Cochrane Methods Support Unit (methods review)

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chang 1999

Study characteristics

Methods	**Design:** Parallel RCT
	Setting: Obstetrics practices of the Brigham and Women's Hospital in Boston, MA, USA

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Chang 1999 *(Continued)*

	Country: USA
Participants	**Inclusion criteria:** Pregnant women who drank in the previous 6 months and had T-ACE positive **Exclusion criteria:** (1) gestational age greater than 28 weeks, (2) no alcohol consumption in the immediate 6 months before study participation, (3) miscarriage in the time between survey completion and telephone interview, (4) intention to receive prenatal care elsewhere, (5) non-English-speaking, (6) intended abortion or false pregnancy, (7) current substance abuse treatment **Mean age:** 30.76 ± 5.4 years (range 18 ± 43) **Civil state:** 74% married or permanent relationship (10%), 14% single, 2% separated/divorced **Ethnicity:** 78% Caucasian (understood to be white), 14% African American (including Haitian), 6% Hispanic, and 2% Asian **Education:** 22% completed graduate or professional school, 34% completed 4 years of college, 29% had some college education, 11% graduated from high school, and only 4% had less than a 4-year high school education **Work:** NR **Pregnancy:** 53% nulliparous, 16 ± 4.6 weeks' gestation at assessment **Alcohol use before pregnancy:** 40% satisfied DSM-III-R criteria for lifetime alcohol abuse or dependence diagnoses; 39% had more than 2 drinks per drinking day before pregnancy; all participants consumed alcohol in the 6 months before study assessment **Other substance use:** 8% of study participants smoked cigarettes, 28% satisfied DSM-III-R criteria for lifetime drug abuse or dependence diagnoses **Alcohol use during pregnancy:** In the current review, only data of women who were drinking while pregnant were evaluated (108 out of 250). Alcohol use was equal to 1.5 (1.2) and 2.1 (1.5) drinks per drinking days for women in the experimental and control groups, respectively. None satisfied DSM-III-R criteria for current alcohol abuse or dependence.
Interventions	**Intervention:** BI + comprehensive assessment of alcohol use, n = 52 **Number of sessions:** 1 session **Description of the intervention:** BI was structured to: (1) review the woman's general health and course of pregnancy, (2) review the woman's lifestyle changes made since pregnancy, including work schedule, exercise, diet, cigarette smoking, and alcohol consumption, (3) request that the woman articulate her drinking goals while pregnant and their reason, (4) have the woman identify circumstances when she might be tempted to drink, (5) identify alternatives to drinking when she is tempted to drink, and (6) summarise by emphasising 4 key points (drinking goal, motivation, risk situations for drinking, and alternatives to alcohol) and noting them in the take-home manual, How to prevent alcohol-related problems, given to the woman **Control:** Comprehensive assessment of alcohol use (assessment only), n = 56 **Period of pregnancy when intervention occurred:** 16 ± 4.6 weeks **Follow-up:** Postpartum (first postpartum obstetric visit of each participant) **People who delivered the interventions:** Research assistant **Time required:** 45 minutes
Outcomes	Reductions in antepartum alcohol consumption measured as reduction in drinks per drinking day
Notes	**Identification** Trial registration number: None

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Chang 1999 *(Continued)*

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	Institution: Brigham and Women's Hospital, Boston, USA
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	Funding: Supported by ROI AA 9670 from the NIAAA
	Conflict of interest: NR

Handmaker 1999

Study characteristics	
Methods	**Design:** Parallel RCT **Setting:** Medical centre obstetric clinic **Country:** USA
Participants	**Inclusion criteria:** Pregnant women who reported consuming at least 1 drink in the past month **Exclusion criteria:** NR **Mean age:** 24 ± 5.76 years **Civil state:** 62% unmarried **Ethnicity:** 53% Hispanic, 38% white, 9% black **Education:** 12 ± 2.71 years **Work:** Half unemployed **Pregnancy:** NR **Alcohol use before pregnancy:** Varied according to the method used to collect information: • using self-administered screening questionnaires: 9 ± 20.48 drinks in the past month; • personal interviews: 33 ± 74.48 drinks in the prior 2 months (peak BAC = 85 ± 115 mg%); • when asked by their healthcare providers: 74% denied drinking during pregnancies. **Other substance use:** NR **Alcohol use during pregnancy:** All women in the sample consumed at least 1 drink in the past month. Alcohol use reported during non-judgemental person interviews was equal to a mean of 33 (74.5) drinks during the previous 2 months.
Interventions	**Intervention:** MI (n = 20) **Number of sessions:** 1 session **Description of the intervention:** The session typically began by asking the woman what she already knew about the effects of drinking during pregnancy. She was given feedback on the severity of her drinking, and shown a chart of fetal development by gestational week to personalise the potential impact on the fetus. The interview was conducted in the empathic client-centred but directive style described by Miller and Rollnick (1991). **Control:** Written information about the risks related to drinking during pregnancy following a comprehensive alcohol use assessment (n = 22) **Period of pregnancy when intervention occurred:** NR

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Handmaker 1999 *(Continued)*

	Follow-up: 2 months later in pregnancy **People who delivered the interventions:** Research assistant **Time required:** 1 hour following a comprehensive alcohol use assessment
Outcomes	Number of continuously abstinent participants
Notes	**Identification** Trial registration number: None Contact author: NR Institution: Department of Psychology, University of New Mexico, Albuquerque, USA Email address: NR Funding: Supported in part by a grant from the New Mexico Developmental Disabilities Planning Council and by grants T32-AA07460 and K05-AA00133 from the NIAAA Conflict of interest: NR

Joya 2016

Study characteristics	
Methods	**Design:** Parallel RCT **Setting:** Hospital del Mar **Country:** Spain (Barcelona)
Participants	**Inclusion criteria:** Pregnant women consenting to participate in the study and with a maternal hair length of minimum 9 cm at delivery **Exclusion criteria:** NR **Mean age:** • Experimental group: 32.3 ± 5.0 years • Control group: 29.9 ± 5.7 years **Civil state:** NR **Ethnicity:** • Experimental group: 36.8% Spanish • Control group: 47% Spanish **Education:** • Experimental group: 3.6% primary school, 42.5% high school, 21.2% university • Control group: 6.9% primary school, 48.2% high school, 19.7% university **Work:** • Experimental group: 59.0% unskilled job, 18.5% skilled job • Control group: 64.4% unskilled job, 16.8% skilled job **Pregnancy:**

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Joya 2016 *(Continued)*

- Experimental group: 58.6% had previous pregnancies
- Control group: 58.6% had previous pregnancies

Alcohol use before pregnancy:

- Experimental group:
  - Hair testing EtG 7 to 30 pg/mg (repetitive moderate consumers): n = 28/83
  - Hair testing EtG > 30 pg/mg (chronic excessive consumers): n = 4/83
- Control group:
  - Hair testing EtG 7 to 30 pg/mg (repetitive moderate consumers): n = 25/85
  - Hair testing EtG > 30 pg/mg (chronic excessive consumers): n = 10/85

Other substance use:

- Experimental group: 2.5% used other psychoactive substances, 9.6% smoked cigarettes
- Control group: 5.7% used other psychoactive substances, 13.8% smoked cigarettes

Alcohol use during pregnancy: First trimester of gestation (before intervention):

- Ethanol consumption self-reported: 53/168
- Hair EtG > 7 pg/mg: 67/168

Interventions	**Intervention:** MI, n = 83 **Number of sessions:** Single session **Description of the intervention:** MI provided personalised feedback of risk, motivated the woman to change target behaviours, decreased her temptation to engage in risk behaviour and increased her confidence to avoid it, developed change plans, and encouraged her to attend the contraceptive counselling visit. Furthermore, the normal advice for eating, drinking, health screenings, family planning, prevention of sexually transmitted infections, and exercise recommended for women of childbearing age were transmitted to all women. **Control:** ECC, n = 85. Women received the normal advice for eating, drinking, health screenings, family planning, prevention of sexually transmitted infections, and exercise recommended for women of childbearing age. **Period of pregnancy when intervention occurred:** At the end of the first trimester **Follow-up:** At delivery **People who delivered the interventions:** NR **Time required:** NR
Outcomes	EtG concentrations in maternal hair and self-reported ethanol consumption during pregnancy
Notes	In the current review, only pregnant women who were drinking before the intervention were included in the analysis: - MI: n = 32 out of 83 (50 were abstinent) - ECC: n = 35 out of 85 (50 were abstinent) **Identification** Trial registration number: CEIC-IMAS, project number 1333/2012 Contact author: Dr Simona Pichini Institution: Department of Therapeutic Research and Medicines Evaluation, Istituto Superiore di Sanitá, Viale Regina Elena 299, 00161 Rome, Italy

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Joya 2016 *(Continued)*

E-mail address: simona.pichini@iss.it

Funding: This study was supported by grants from Fondo de Investigaciones Sanitarias (FIS) FEDER: Fondo Europeo de Desarrollo Regional (PI13/01135) and Red de Salud Materno-Infantil y del Desarrollo (SAMID) (RD12/0026/0003) from the Instituto Carlos III (Spain), and partially supported by Generalitat de Catalunya (Spain) AGAUR (2014SGR584), RecerCaixa (OG085818) and Fundación Mutua Madrile˜na (AP150572014) grants.

Conflict of interest: None

O'Connor 2007

Study characteristics	
Methods	**Design:** Parallel clinical trial **Setting:** Community setting (PHFE-WIC centres, Southern California) **Country:** USA

Participants	**Inclusion criteria:** Women positive in a postconceptional drinking screening
	
	Exclusion criteria: NR
	
	Mean age:
	
	• Experimental group: 28.52 ± 5.84 years
	• Control group: 27.90 ± 6.09 years
	
	Civil state:
	
	Marital status, married or has partner:
	
	• Experimental group: 71.9%
	• Control group: 71.0%
	
	Ethnicity:
	
	• Experimental group:
	  ◦ White, non-Hispanic: 7.7%
	  ◦ Black, non-Hispanic: 21.4 %
	  ◦ English-speaking Hispanic: 24.8%
	  ◦ Spanish-speaking Hispanic: 41.9%
	  ◦ Other: 4.3%
	• Control group:
	  ◦ White, non-Hispanic: 6.5%
	  ◦ Black, non-Hispanic: 13.8%
	  ◦ English-speaking Hispanic: 27.5%
	  ◦ Spanish-speaking Hispanic: 46.4%
	  ◦ Other: 5.8%
	
	Education:
	
	• Experimental group: 11.19 ± 3.44 years
	• Control group: 11.00 ± 3.42 years
	
	Work: Income, USD 15,000 or less
	
	• Experimental group: 63.9%

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O'Connor 2007 *(Continued)*

- Control group: 69.6%

Pregnancy: NR

Alcohol use before pregnancy: NR

Other substance use:

- Experimental group:
  - *Marijuana: 0.07 ± 0.32
  - *Cocaine: 0.01 ± 0.13
  - Caffeine drinks: 1.61 ± 2.02
  - Cigarettes per day: 0.53 ± 2.29
- Control group:
  - *Marijuana: 0.37 ± 0.22
  - *Cocaine: 0.00 ± 0.00
  - Caffeine drinks: 1.86 ± 2.70
  - Cigarettes per day: 0.47 ± 1.60

*Marijuana and cocaine use were each coded on a scale from 0 to 2: 0 represented no cocaine or marijuana use, 1 represented use 1 to 2 times a week, and 2 represented use 3 or more times a week.

Alcohol use during pregnancy: Only women who were drinking while pregnant were randomised to assessment.

Alcohol consumption (in MAX*):

- Experimental group (n = 162): 2.10 ± 3.35
- Control group (N = 183): 1.73 ± 1.73

**TWEAK

- Experimental group: 1.77 ± 1.36
- Control group: 1.84 ± 1.54

*Maximum drinks per drinking occasion (MAX). One drink was considered to be 0.60 ounces of absolute alcohol, therefore one 12-ounce can of beer that contained 5% absolute alcohol was considered 1 drink, whereas one 16-ounce can of 8% malt liquor was considered 2 drinks.

**The TWEAK 5-question scale, a measure of alcohol tolerance and physical consequences of alcohol consumption.

Interventions	**Intervention:** BI, n = 162 **Number of sessions:** Single session **Description of the intervention:** The workbook consisted of traditional brief intervention techniques, including education and feedback, cognitive behavioural procedures, goal setting, and contracting: (1) feedback aimed at increasing awareness of the negative consequences of drinking, (2) advice focused on identifying risky situations and actions aimed at reducing consumption, and (3) assistance with formulating drinking reduction goals. **Control:** Assessment only, n = 183 Comprehensive assessment of alcohol use and were advised to stop drinking during pregnancy. **Period of pregnancy when intervention occurred:** Weeks gestation at enrolment • Experimental group: 17.78 ± 7.76 • Control group: 18.15 ± 7.99

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O'Connor 2007 *(Continued)*

	Follow-up: Third trimester **People who delivered the interventions:** Trained nutritionists **Time required:** 10 to 15 min
Outcomes	Abstinence from alcohol
Notes	**Identification** Trial registration number: None Contact author: Dr Mary J O'Connor Institution: Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California, 760 Westwood Plaza, Room 68–265A, Los Angeles, CA 90024 Email address: moconnor@mednet.ucla.edu Funding: NR Conflict of interest: NR

Reynolds 1995

Study characteristics	
Methods	**Design:** Parallel clinical trial **Setting:** 2 public health clinics and home **Country:** USA

Participants	**Inclusion criteria:** (1) consume any of these alcohol beverages: beer, wine, liquor, mixed drinks, (2) ≤ 25 weeks pregnant
	
	Exclusion criteria: (1) non-drinkers, (2) women > 25 weeks pregnant
	
	Mean age:
	
	• Experimental group: 22.7 years
	• Control group: 22.2 years
	
	Civil state: NR
	
	Ethnicity:
	
	• Experimental group:
	  ◦ African-American: 69%
	  ◦ European-American: 31%
	• Control group:
	  ◦ African-American: 64%
	  ◦ European-American: 36%
	
	Education: NR
	
	Work: Income: % < USD 5000 annually
	
	• Experimental group: 56%
	• Control group: 61%

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Reynolds 1995 *(Continued)*

	Pregnancy: NR **Alcohol use before pregnancy:** NR **Other substance use:** NR **Alcohol use during pregnancy:** All women were drinking alcohol while pregnant. Alcohol use was equal to 44 and 28 drinks per month for women in the experimental and control groups, respectively.
Interventions	**Intervention:** Educational intervention coupled with SH, n = 42 **Number of sessions:** Single session of the educational intervention + 9-step SH sessions completed at home in 9 days **Description of the intervention:** During the educational session, an educator described the effects of alcohol on the fetus and explained the use of the manual. SH intervention was based on the Social Cognitive Theory. Components of the theory utilised included goal setting, self-monitoring, perceived self-efficacy, negative outcome expectancies of drinking, positive outcome expectancies of cessation, and skills for cessation. Each step in the manual targeted a behaviour or cognition that would enhance the likelihood of cessation. Exercises were included to stimulate thought about key ideas, to build alcohol cessation skills, and to provide practice related to these skills. **Control:** UC, n = 36 Information on effects of alcohol and pregnancy routinely provided by the clinic including brief discussions with clinic staff and a videotape on prenatal care. **Period of pregnancy when intervention occurred:** Weeks pregnant • Experimental group: 13 weeks • Control group: 12 weeks **Follow-up:** 2 months after recruitment **People who delivered the interventions:** An educator **Time required:** 10 min + 9 days
Outcomes	Overall *quit rate in the SH condition versus the UC condition *A woman was coded as quitting only if she had stopped drinking all 4 of the measured alcoholic beverages (beer, wine, liquor, mixed drinks).
Notes	**Identification** Trial registration number: None Contact author: NR Institution: Jefferson County Health Department, University of Alabama at Birmingham Email address: NR Funding: NIAAA, Grant 5R03AA08531 Conflict of interest: NR

Rubio 2014

Study characteristics

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Rubio 2014 *(Continued)*

Methods	**Design:** Parallel clinical trial **Setting:** Large, urban, obstetrics clinic **Country:** USA (Pittsburgh, PA)

Participants	**Inclusion criteria:** (1) 18 years or older, (2) pregnant, planned to continue their pregnancy, and were not over 20 weeks of gestation, (3) spoke English, (4) had consumed at least 3 drinks a week between conception and recognition of pregnancy, (5) consumed at least 1 drink a week after recognition of pregnancy, or had at least 1 episode of binge drinking, defined as drinking ≥ 4 drinks on 1 occasion, after conception
	
	Exclusion criteria: NR
	
	Mean age:
	
	• Experimental group: 23.5 ± 4.0 years
	• Control group: 24.1 ± 5.4 years
	
	Civil state: Marital status
	
	• Experimental group:
	  ○ Never married: 92 (63.0%)
	  ○ Presently married: 10 (6.8%)
	  ○ Marriage-like relationship: 29 (19.9%)
	  ○ Divorced or separated: 6 (4.1%)
	  ○ Other: 9 (6.2%)
	• Control group:
	  ○ Never married: 97 (64.7%)
	  ○ Presently married: 17 (11.3%)
	  ○ Marriage-like relationship: 27 (18.0%)
	  ○ Divorced or separated: 6 (4.0%)
	  ○ Other: 3 (2.0%)
	
	Ethnicity:
	
	• Experimental group:
	  ○ Black: 75 (45.5%)
	  ○ White: 85 (51.5%)
	  ○ Other: 5 (3.0%)
	• Control group:
	  ○ Black: 67 (40.6%)
	  ○ White: 92 (55.8%)
	  ○ Other: 6 (3.6%)
	
	Education:
	
	• Experimental group:
	  ○ Less than a high school diploma: 27 (18.8%)
	  ○ High school diploma or GED: 72 (50.0%)
	  ○ Some post–high school education: 33 (22.9%)
	  ○ Degree past high school diploma: 12 (8.3%)
	• Control group:
	  ○ Less than a high school diploma: 38 (25.5%)
	  ○ High school diploma or GED: 51 (34.2%)
	  ○ Some post–high school education: 42 (28.2%)
	  ○ Degree past high school diploma: 18 (12.1%)
	
	Work:

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Rubio 2014 *(Continued)*

- Experimental group:
  - Unemployed: 12 (8.2%)
  - Full-time homemaker: 45 (30.8%)
  - Part-time student: 7 (4.8%)
  - Full-time student: 18 (12.3%)
  - Part-time worker (not student): 27 (18.5%)
  - Full-time worker: 37 (25.3%)
- Control group:
  - Unemployed: 18 (12.2%)
  - Full-time homemaker: 48 (32.4%)
  - Part-time student: 3 (2.0%)
  - Full-time student: 19 (12.8%)
  - Part-time worker (not student): 17 (11.5%)
  - Full-time worker: 43 (29.1%)

Pregnancy: Number of previous pregnancies:

- Experimental group:
  - 0: 32 (21.9%)
  - 1: 33 (22.6%)
  - 2: 32 (21.9%)
  - ≥ 3: 49 (33.6%)
- Control group:
  - 0: 37 (24.8%)
  - 1: 41 (27.5%)
  - 2: 29 (19.5%)
  - ≥ 3: 42 (28.2%)

Alcohol use before pregnancy: Number of drinks per day (mean ± SD (median; range)):

- Experimental group: 3.6 ± 5.4 (2.0; 0 to 48.7)
- Control group: 3.4 ± 4.7 (2.0; 0 to 31.8)

Binge drinking (≥ 4 drinks on 1 occasion):

- Experimental group: 153 (92.7%)
- Control group: 149 (90.3%)

Other substance use: NR

Alcohol use during pregnancy: 330 women drink alcohol during pregnancy.

Number of drinks per day (mean ± SD (median; range)):

- Experimental group: 0.2 ± 0.8 (0; 0 to 7)
- Control group: 0.5 ± 3.4 (0; 0 to 31.8)

Binge drinking (≥ 4 drinks on 1 occasion):

- Experimental group: 16 (9.7%)
- Control group: 17 (10.3%)

Interventions	**Intervention:** MI, n = 165 **Number of sessions:** 5 sessions (4 sessions during pregnancy; 1 session after delivery) **Description of the intervention:** Women in the intervention group were asked to attend 5 sessions that used motivational interviewing strategies. The FRAMES structure was used for the brief intervention content.

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Rubio 2014 *(Continued)*

	The 5 intervention sessions focused on alcohol use, provided specific feedback based on use and alcohol risks to the fetus, and included a plan for changes in behaviour. The sessions took place at enrolment, 4 and 8 weeks later, at 32 weeks of gestation, and at 6 weeks postpartum during participants' regular scheduled clinic visits with their obstetrical providers. For the 6-week postpartum visit only, the intervention was conducted by telephone if the participant missed the clinic visit. This intervention session focused on safe drinking behaviours. The motivational sessions are face-to-face. **Control:** UC, n = 165 UC received the standard warnings on alcohol use that are administered by the prenatal clinic staff but did not receive any other intervention. **Period of pregnancy when intervention occurred:** Gestational age • Experimental group: 9.9 ± 4.3 weeks • Control group: 9.7 ± 3.8 weeks **Follow-up:** Follow-up telephone interviews at 4 and 8 weeks after enrolment, 32 weeks of gestation, and 6 weeks, 6 months, and 12 months postpartum **People who delivered the interventions:** Registered nurse or lay counsellor who had been trained by 2 study investigators **Time required:** The prenatal sessions lasted 10 to 15 minutes, and the postpartum session lasted 10 to 30 minutes.
Outcomes	• Proportion of women with any alcohol use • Number of drinks per day
Notes	**Identification** Trial registration number: None Contact author: Dr DM Rubio Institution: Center for Research on Health Care, Division of General Internal Medicine, Department of Medicine, University of Pittsburgh School of Medicine, 200 Meyran Avenue, Suite 200, Pittsburgh, PA 15213, USA Email address: rubiodm@upmc.edu Funding: This research was supported by grant AA012485 from the NIAAA, and UL1TR000005 from the National Center for Advancing Translational Sciences, National Institutes of Health.

Tzilos 2011

Study characteristics	
Methods	**Design:** Parallel clinical trial **Setting:** Inner-city prenatal care clinic **Country:** USA
Participants	**Inclusion criteria:** (1) being pregnant, between ages 18 and 45 (with at least 1 month expected gestation remaining), (2) able to understand spoken English, (3) either (i) meeting T-ACE criteria for problem alcohol use, (ii) exceeding the NIAAA ‘‘normal’’ sensible drinking limits before pregnancy (> 7 standard drinks a week or > 2 drinks at a time), or (iii) reporting drinking at least 1 time per month during pregnancy

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Tzilos 2011 *(Continued)*

Exclusion criteria: (1) inability to provide informed consent (e.g. due to psychosis, intoxication, or other clear cognitive impairment), (2) inability to communicate in English, (3) not having access to a phone (for follow-up)

Mean age:

- Experimental group: 25.0 ± 4.93 years
- Control group: 26.4 ± 5.52 years

Civil state:

Single

- Experimental group: 7 (26%)
- Control group: 6 (26%)

Ethnicity:

- Experimental group:
  - African-American: 21 (78%)
  - Caucasian (understood to be white): 5 (19%)
  - Hispanic: 1 (3%)
- Control group:
  - African-American: 20 (87%)
  - Caucasian (understood to be white): 3 (13%)
  - Hispanic: 0 (0%)

Education:

- Experimental group:
  - 0 to 8 grades: 2 (7%)
  - 9 to 11 grades: 12 (44%)
  - High school graduate or GED: 9 (33%)
  - Some college: 4 (15%)
- Control group:
  - 0 to 8 grades: 3 (13%)
  - 9 to 11 grades: 12 (52%)
  - High school graduate or GED: 6 (26%)
  - Some college: 2 (9%)

Work: NR

Pregnancy: NR

Alcohol use before pregnancy: Exceeding the NIAAA ''normal'' sensible drinking limits before pregnancy (more than 7 standard drinks a week or more than 2 drinks at a time) was an inclusion criterion.

Other substance use: NR

Alcohol use during pregnancy: Reporting drinking at least once per month during pregnancy was an inclusion criterion.

Alcohol, quantity:

- Experimental group: 89.5 ± 91.3 g/week
- Control group: 83.4 ± 147 g/week

Interventions	**Intervention:** MI, n = 27 **Number of sessions:** Single session

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Tzilos 2011 *(Continued)*

	Description of the intervention: This brief intervention was self-administered and solely computer-delivered, with assistance available from the investigator as needed, and took approximately 15 to 20 minutes to complete. The computer-based brief MI was specifically tailored to pregnant women in a number of ways. For example, the intervention itself included a brief educational component that delivered current information about FASD. For women who reported they had already quit, the narrator presented a section that focused on relapse prevention (''My plan to remain abstinent'') while asking the participant to provide the reasons/benefits to them of having made this change. The remaining participants were asked about their current interest in quitting (Are you willing/ready to quit?), leading to a bifurcated treatment response such that those participants reporting a goal of immediate abstinence moved more quickly to a section consistent with phase 2 of MI (primarily goal setting), whereas those who did not wish to quit received elements consistent with phase 1 of MI. **Control:** Information only + "placebo" computer-delivered intervention, n = 23 Series of questions about television show preferences and participant viewed a brief series of videos of popular entertainers/shows, with subsequent requests for ratings of subjective preference. The duration and level of interactivity for this control condition were equivalent to that of the intervention condition, thus controlling for time effects and facilitating blinding of the investigator to the experimental condition. On completion of study, all women in the control condition received a brochure specifically designed to facilitate reductions in drinking during pregnancy. **Period of pregnancy when intervention occurred:** • Experimental group: 25.0 ± 8.45 weeks • Control group: 25.5 ± 7.63 weeks **Follow-up:** 1 month after psychosocial intervention (mean follow-up duration: 33 days, SD 7.9, range 25 to 72) **People who delivered the interventions:** Self-administered and solely computer-delivered (tablet) **Time required:** 15 to 50 minutes
Outcomes	Alcohol consumption 30 days after single-session intervention
Notes	Overall, 72% of all participants reported any drinking at baseline assessment, and 10% reported any drinking at follow-up. **Identification** Trial registration number: None Contact author: Golfo K Tzilos Institution: Brown University Center for Alcohol & Addiction Studies Email address: golfo_tzilos@brown.edu Funding: This research was supported under NIAAA training grant AA16256 (to GKT; mentor, SJO). Conflict of interest: None

van der Wulp 2014

Study characteristics

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van der Wulp 2014 *(Continued)*

Methods	**Design:** Cluster-randomised trial **Setting:** Where and whenever patients have access to the internet **Country:** Netherlands

Participants	**Inclusion criteria:** (1) ability to understand Dutch, (2) aged 18 years or older, (3) pregnant for a maximum of 12 weeks (because respondents received follow-up questionnaires until 6 months after baseline), (4) having drunk alcohol since knowing to be pregnant
	
	Exclusion criteria: NR
	
	Mean age:
	
	• Health counselling: 31.75 ± 4.37 years
	• Computer tailoring: 32.31 ± 4.22 years
	• Control group: 33.53 ± 3.85 years
	
	Civil state: Steady partner
	
	• Health counselling: 73 (64.0%)
	• Computer tailoring: 66 (59.5%)
	• Control group: 59 (47.6%)
	
	Ethnicity: NR
	
	Education:
	
	• Health counselling:
	  ◦ Low: 5 (4.5%)
	  ◦ Medium: 47 (42.0%)
	  ◦ High: 60 (53.6%)
	• Computer tailoring:
	  ◦ Low: 1 (0.9%)
	  ◦ Medium: 41 (36.9%)
	  ◦ High: 69 (62.2%)
	• Control group:
	  ◦ Low: 3 (2.4%)
	  ◦ Medium: 20 (16.3%)
	  ◦ High: 100 (81.3%)
	
	Work: NR
	
	Pregnancy: Nulliparous:
	
	• Health counselling: 44.7%
	• Computer tailoring: 33.3%
	• Control group: 50.0%
	
	Alcohol use before pregnancy: Standard alcohol drinks per week:
	
	• Health counselling: 5.61 ± 8.9
	• Computer tailoring: 4.53 ± 4.6
	• Control group: 7.18 ± 7.6
	
	Other substance use: Smokes in pregnancy, n (%):
	
	• Health counselling: 30 (27.0%)
	• Computer tailoring: 25 (23.4%)
	• Control group: 14 (11.3%)

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van der Wulp 2014 *(Continued)*

Alcohol use during pregnancy: Having drunk alcohol since knowing to be pregnant was an inclusion criterion.

Standard alcohol drinks per week (mean and SD):

- Health counselling: 1.44 ± 3.33
- Computer tailoring: 1.21 ± 3.14
- Control group: 0.76 ± 2.02

Binge drinkers n (%):

- Health counselling: 3 (2.7%)
- Computer tailoring: 0 (0.0%)
- Control group: 1 (0.8%)

Risky drinkers (T-ACE positive) n (%):

- Health counselling: 73 (64.6%)
- Computer tailoring: 55 (50.9%)
- Control group: 70 (56.5%)

Interventions	**Intervention:**
	• Health counselling, n = 114
	• Computer tailoring, n = 111
	Number of sessions: 3 sessions
	Description of the intervention:
	(1) The health counselling protocol consisted of 7 steps that were addressed in 3 feedback sessions.
	• Feedback session 1, approximately 2 weeks after baseline assessment, consisted of 5 steps taking approximately 10 minutes of the initial consultation (Feedback 1-health counselling).
	  ◦ In step 1, the midwife assessed the amount and frequency of alcohol use of the pregnant woman before and during pregnancy, of her partner during pregnancy, and the pregnant woman's motivation to stop drinking alcohol.
	  ◦ In step 2, women strongly motivated to stop alcohol consumption during pregnancy were prompted to state the advantages of abstinence. Moderately or not motivated women were asked to report on their perceived disadvantages of drinking during pregnancy. The midwife then advised them to stop drinking alcohol.
	  ◦ In step 3, the barriers for successful abstinence and the mobilisation of social support were discussed.
	  ◦ In step 4, a self-help guide, adapted from an intervention on smoking in pregnancy, and relevant websites were mentioned. The midwife stimulated the pregnant woman to develop action plans for abstinence and coping with problems they might encounter when trying not to drink alcohol. If appropriate, access to alcohol addiction services was discussed.
	  ◦ In step 5, women were asked to set a date for stopping their alcohol use (goal setting).
	• Feedback session 2, approximately 8 weeks after baseline, consisted of step 6, which was addressed in approximately 1 minute (Feedback 2-health counselling). In this step, midwives again assessed the alcohol use of the pregnant women and asked her if she needed additional support for not drinking alcohol.
	• Feedback session 3, after T1 assessment questionnaire and approximately 14 weeks after baseline, consisted of step 7, which was also addressed in approximately 1 minute (Feedback 3-health counselling). In this step, midwives discussed alcohol use and its implications for breastfeeding.
	(2) Respondents in the computer-tailoring group received usual care from their midwife and computer-tailored feedback via the internet, which was iterative and item-based.

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van der Wulp 2014 *(Continued)*

- Feedback 1, given immediately after baseline, consisted of 4 to 5 pages (Feedback 1-computer tailoring). This feedback was tailored to several respondent characteristics assessed in the baseline questionnaire: alcohol use, knowledge, risk perception, attitude, social influence, self-efficacy, intention, and action and coping plans. Specifically, the first feedback letter contained the recommendation of complete alcohol abstinence during pregnancy and information on possible consequences of prenatal alcohol use and the associated risk factors. In addition, feedback was provided on the respondent's risk perception of prenatal alcohol use; her attitude (perceived advantages and disadvantages toward prenatal alcohol use and alcohol abstinence; perceived social influence (not) to drink during pregnancy; self-efficacy to refrain from prenatal alcohol use in specific situations, including suggestions on how to cope with these situations; the extent to which respondents were planning to undertake specific actions (action plans) to abstain from prenatal alcohol use; and how to cope with certain difficult situations (coping plans), including the formulation of personal plans in the shape of if-then statements).
- Feedback 2, 6 weeks after baseline, letter with personalised information on the respondents' choice of characteristics assessed with the baseline questionnaire (e.g. risk perception or attitude; Feedback 2-computer tailoring). Depending on the number of characteristics chosen by the respondent, this feedback consisted of 1 or 2 pages.
- Feedback 3, given immediately after T1 assessment questionnaire, letter of 3 to 4 pages of ipsative feedback tailored to changes in the respondent characteristics assessed at T1 in comparison to the baseline questionnaire (Feedback 3-computer tailoring).

The 2 groups were combined into a single group as they used the same psychological intervention delivered in different ways and adjusted for cluster effect (experimental group: n = 237; control group: n = 134).

Control: UC, n = 124

Midwives in the usual care group were instructed to give routine alcohol care. In-line with national guidelines, midwives recommend complete alcohol abstinence to clients who are using alcohol in the initial consultation.

Period of pregnancy when intervention occurred: Gestational weeks

- Health counselling: 7.96 ± 1.81 weeks
- Computer tailoring: 7.73 ± 2.06 weeks
- Control group: 7.92 ± 1.99 weeks

Follow-up:

- T1: 3 months after the baseline questionnaire
- T2: 6 months after the baseline questionnaire: end of treatment

People who delivered the interventions:

- Health counselling: midwife
- Computer tailoring: midwife and computer

Time required:

- Health counselling: 12 min (10'+1'+1')
- Computer tailoring: NR

Outcomes	• Drinking behaviour • Average weekly alcohol consumption
Notes	**Identification** Trial registration number: Dutch Trial Register NTR 2058 Contact author: Dr Nickie Y van der Wulp Institution: Dutch Institute for Alcohol Policy STAP PO Box 9769 Utrecht, 3506 GT Netherlands

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van der Wulp 2014 *(Continued)*

Email address: nvanderwulp@stap.nl

Funding: This study was funded by a grant from the Netherlands Organisation for Health Research and Development (ZonMw).

Conflict of interest: HdV is the scientific director of Vision2Health, a collaborating company between the University of Maastricht and OSE with the aim of offering proven effective methods in the field of health education. NvdW, CH, KE, MC, and WvD declare that they have no conflicts of interest.

BAC: blood alcohol concentration; BI: brief psychosocial intervention; DSM: Diagnostic and Statistical Manual of Mental Disorders; ECC: educational control condition; EtG: ethyl glucuronide; FASD: fetal alcohol spectrum disorder; FRAMES: Feedback, Responsibility, Advice, Menu, Empathy, Self-efficacy; MI: motivational intervention; NIAAA: National Institute on Alcohol Abuse and Alcoholism; NR: not reported; PHFE-WIC: Public Health Foundation Enterprises Management Solutions Special Supplemental Nutrition Program for Women, Infants, and Children; RCT: randomised clinical trial; SD: standard deviation; SH: self-help intervention; T-ACE: Tolerance, annoyed, cut down, eye-opener; TWEAK: Tolerance, worried, eye-opener, amnesia, kut down; UC: usual care

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Barrison 1982	Ineligible study design (not an RCT)
Belizan 1995	Ineligible population
Brittain 2023	Ineligible population
Byrnes 2013	Ineligible population
Calabro 1996	Ineligible comparison (2 different modalities to deliver the same intervention)
Catherine 2021	Ineligible population (only 5.7% drank at baseline)
Clayson 1995	Ineligible study design (not an RCT)
Crawford-Williams 2016	Ineligible population (84% of women did not drink at baseline)
Evans 2012	Ineligible population (only 3.5% of women reported consuming alcohol at baseline after finding out about their pregnancy)
Evans 2014	Ineligible population (only 2% of women reported consuming alcohol at baseline after finding out about their pregnancy)
Freedman 2018	Ineligible population
In 't Veld 2012	Ineligible population
Kaufman 2023	Ineligible population
NCT00244062	Ineligible population
NCT00373750	Ineligible population
NCT01252706	Ineligible study design
NCT01961050	Ineligible population (not pregnant women)

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Study	Reason for exclusion
NCT02128880	Ineligible population (secondary publication of a study excluded at title and abstract stage; Ingersoll 2018)
NCT03397277	Ineligible population
NCT03633149	Ineligible population (not pregnant women)
NCT03833245	Ineligible population (women with opioid use disorder)
NCT03887910	Ineligible population (not pregnant women)
NCT03900312	Ineligible study design (not an RCT)
NCT04089800	Ineligible population (women did not drink alcohol)
NCT04194489	Ineligible study design
NCT04313348	Ineligible study design
NCT05028517	Ineligible population
NL7493	Ineligible study design (not an RCT)
Osterman 2017	Ineligible population (women with substance use disorder)
Tzilos 2017	Ineligible population (not all pregnant women drank alcohol during pregnancy)
Walkup 2009	Ineligible study design

RCT: randomised controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Armstrong 2009

Methods	Randomised controlled trial
Participants	Pregnant women at risk for alcohol use
Interventions	2 brief alcohol use interventions in prenatal clinics: Early Start (ES), a substance abuse screening and treatment program integrated with prenatal care focused on abstention (n = 298), and Early Start Plus (ESP), adding a computerised drink-size assessment tool and intervention focused on drinking less (n = 266). Controls were untreated alcohol users (n = 344).
Outcomes	Maternal and infant outcomes
Notes	It is unclear if women were drinking at baseline.

Balachova 2014

Methods	Randomised trial

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Balachova 2014 *(Continued)*

Participants	Childbearing women (101 pregnant women; 357 non-pregnant women)
Interventions	• FASD education brochure with positive images and information stated positively, positive group (PG) • FASD education brochure with negatively presented information, negative group (NG) • General health material, control group (CG)
Outcomes	Women's alcohol consumption, knowledge about FASD, and attitudes were conducted at baseline and 1-month follow-up.
Notes	Not all participants were pregnant women.

Balachova 2015

Methods	2-arm cluster-randomised controlled trial
Participants	Non-pregnant women, aged 18 to 44 years, at risk for an alcohol-exposed pregnancy (AEP). During the course of the study, 72 participants became pregnant.
Interventions	A brief physician intervention in reducing the risk for AEP vs usual conditions
Outcomes	Women's alcohol consumption
Notes	Not all pregnant women drank at baseline.

Chang 2005

Methods	Randomised clinical trial
Participants	Pregnant women with a positive T-ACE (total score of 2 or more) and their partner
Interventions	Brief intervention given by the study nurse or principal investigator
Outcomes	Alcohol consumption
Notes	Not all women were drinking at baseline.

Delgado 1996

Methods	
Participants	
Interventions	
Outcomes	
Notes	PDF not available

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Eustace 2000

Methods	Thesis
Participants	
Interventions	
Outcomes	
Notes	PDF not available

Gimenez 2022

Methods	Randomised controlled trial
Participants	Pregnant women who reported alcohol consumption during the last 12 months
Interventions	Brief advice and brief intervention
Outcomes	Quantity and frequency of alcohol consumption, frequency of binge drinking, and alcohol-related problems
Notes	Not all women reported drinking at baseline.

le Roux 2013

Methods	Cluster randomised controlled trial
Participants	Pregnant women
Interventions	Home visits by community health workers (CHWs) on maternal and infant well-being
Outcomes	Several outcomes, including alcohol use during pregnancy
Notes	Only 25% of the pregnant women drank at baseline.

Marais 2011

Methods	Pragmatic cluster randomised trial
Participants	Pregnant women (including women who reported not drinking)
Interventions	Brief interventions (n = 98) vs usual care (n = 96)
Outcomes	Difference between the average AUDIT score for control and intervention clinics
Notes	The study included women who reported not drinking at baseline.

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Martino 2018

Methods	Randomised controlled trial
Participants	Women from reproductive centres who smoked cigarettes or misused alcohol, illicit drugs, or prescription medication
Interventions	Screening, brief intervention, and referral to treatment delivered electronically or by clinician or to enhanced usual care
Outcomes	Days/months of primary substance use and post-intervention treatment use
Notes	Not all women were pregnant and consumed alcohol.

Moura 2019

Methods	Randomised controlled trial
Participants	Pregnant women
Interventions	An intervention and 2 monitoring phone calls, for 2 weeks
Outcomes	Alcohol and tobacco use during pregnancy
Notes	Not all women consumed alcohol at baseline.

Ondersma 2015

Methods	Parallel clinical trial
Participants	Pregnant women with positive on the T-ACE alcohol risk screener reporting either drinking weekly or more in the past month or having 4 or more drinks at least monthly in the 12 months before becoming pregnant
Interventions	Brief intervention (n = 24) built on the principles of motivational interviewing vs time-matched (20 minutes; n = 24) and moderately interactive intervention focused on infant nutrition, with no mention of alcohol use during pregnancy
Outcomes	90-day period prevalence abstinence
Notes	All women were positive to T-ACE at enrolment, but not all women reported drinking during pregnancy.

Osterman 2012

Methods	Randomised controlled trial
Participants	Pregnant women who reported previous-year alcohol use
Interventions	Motivational interviewing

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Osterman 2012 *(Continued)*

Outcomes	Several outcomes, including the number of drink days per week change scores, and number of drinks per day change scores
Notes	It is unclear if all women drank during pregnancy.

Osterman 2014

Methods	Randomised clinical trial
Participants	Pregnant women who drank any amount of alcohol in the previous year
Interventions	A single-session of motivational interviewing
Outcomes	Drinking behaviours, basic psychological need satisfaction, and autonomous motivation to decrease prenatal alcohol use
Notes	It is unclear if women drank during pregnancy.

Rotheram-Borus 2011

Methods	Randomised clinical trial
Participants	Pregnant Mothers at Risk (MAR) for HIV, alcohol, and/or nutrition problems
Interventions	Home visiting by community health workers
Outcomes	Several outcomes, including alcohol use during pregnancy
Notes	Only 27% of women drank alcohol at baseline.

Rotheram-Borus 2023

Methods	Cluster-randomised controlled trial
Participants	Pregnant women
Interventions	Home visits by community health workers on maternal and infant well-being
Outcomes	Several outcomes, including alcohol use during pregnancy
Notes	Less than 5% of pregnant women reported drinking alcohol after pregnancy discovery.

Rotheram-Fuller 2017

Methods	Randomised clinical trial
Participants	Pregnant women

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Rotheram-Fuller 2017 *(Continued)*

Interventions	Home visiting
Outcomes	Several outcomes, including alcohol use
Notes	Not all women drank while pregnant.

Sheehan 2014

Methods	Randomised clinical trial
Participants	Pregnant women
Interventions	Brief intervention
Outcomes	AUDIT score and alcohol use at 32 weeks' gestation
Notes	More than 50% of women did not drink at baseline (since becoming pregnant).

Starn 1992

Methods	Randomised controlled trial
Participants	Pregnant women who smoked cigarettes, consumed alcohol or marijuana, cocaine, or multiple drugs
Interventions	Counselling/supportive interventions established rapport and encouraged women to develop and maintain a healthy lifestyle.
Outcomes	Substance use and perinatal complications
Notes	Only 26% of enrolled women consumed alcohol during pregnancy.

Wagijo 2023

Methods	Stepped-wedge cluster randomised trial
Participants	Participants were recruited from 13 midwife practices and 2 hospitals in the area of Leiden/The Hague in the Netherlands. Women were eligible for inclusion in the study if they were < 24 weeks of gestation and able to understand the study and to communicate (with help) in Dutch or English.
Interventions	CenteringPregnancy (CP)
Outcomes	Smoking behaviour and alcohol use were measured by self-reported frequencies, at 12, 28, and 36 weeks of pregnancy and 6 weeks' postpartum.
Notes	Not all women were drinking at baseline (alcohol use during pregnancy was reported by 0.5% women).

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Winhusen 2008

Methods	Randomised controlled trial
Participants	Pregnant substance users
Interventions	3 individual sessions of Motivational Enhancement Therapy for pregnant substance users (MET-PS) or the first 3 individual sessions normally provided by the programme
Outcomes	Treatment utilisation according to clinic records, qualitative urine toxicology measures, and self-report of substance use
Notes	Not all women reported using alcohol during pregnancy.

Yonkers 2012

Methods	Randomised, parallel, controlled trial
Participants	Pregnant women using alcohol or illicit drugs other than opiates
Interventions	Individual behavioural therapy that combined motivational enhancement therapy with cognitive behavioural therapy
Outcomes	Self-reported percentage of days in which drugs or alcohol were used
Notes	It is unclear if women were drinking at baseline.

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12616000072415

Study name	Evaluation of the effectiveness of an infant and family health and wellbeing text message intervention (Connecting 2u) in supporting expectant and new parents
Methods	Randomised controlled trial
Participants	Mothers are 12 weeks pregnant and over
Interventions	Delivery of C2u text messages to participants in addition to standard practice. The content of the C2u text messages is based on antenatal and postnatal care, focusing on health behaviours (maternal nutrition and weight; physical activity; alcohol, tobacco, drugs, medication consumption; immunisation reminders; appointment reminders), mental health and well-being, communication, bonding and attachment, infant feeding, preparing for parenthood/ becoming a parent, and circle of security.
Outcomes	Change in parental attachment as a result of project implementation
Starting date	4 January 2016
Contact information	Ms Cindy Dawson; Children's Health Queensland 199 Grey St, South Brisbane QLD 4101 Australia
Notes	Clinical trial registration

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ACTRN12623000683639

Study name	An anchor in the storm: the effectiveness of a flexible perspective-taking intervention in supporting the transition to motherhood
Methods	Randomised controlled trial
Participants	Participants will be women aged 18 years and over, who are currently at least 20 weeks pregnant, and living in Australia or New Zealand.
Interventions	Mothers in the intervention group will be given access to online resources specifically designed for use in this study: (i) a brief web-based informational video (approx. 7 min) that begins with a psychoeducation component on flexible perspective taking (self-as-context, a component of Acceptance and Commitment Therapy (ACT)) and relevance to mothers of infants (from birth to 23 months), drawing on ACT metaphors for enhancing a transcendent sense of self; (ii) an audio-guided experiential exercise on flexible perspective taking tailored to pregnant and new mothers (approx. 9 min), which women will be encouraged to listen to and use to guide their own meditation practice; and (iii) a simple tip sheet (designed specifically for this study) summarising key points that will be made available to participants to download and print. Resource use will be monitored using website analytics. Participants will have access to the resources for the full duration of the study and extending to 12 months from the time of enrolment.
Outcomes	Alcohol consumption as assessed using the Alcohol Use and Disorders Identification Test (AUDIT-C) (6 weeks and 4 months post-expected date of delivery)
Starting date	Not yet recruiting
Contact information	koawhittingham@uq.edu.au
Notes	anzctr.org.au/ACTRN12623000683639.aspx

Baird 2016

Study name	Southampton PRegnancy Intervention for the Next Generation (SPRING)
Methods	Randomised clinical trial
Participants	Pregnant women between 8 and 12 weeks gestation attending the maternity hospital in Southampton
Interventions	• Healthy Conversation Skills support plus vitamin D supplementation (1000 IU cholecalciferol) (n = 150) • Healthy Conversation Skills support plus placebo (n = 150) • Usual care plus vitamin D supplementation (n = 150) • Usual care plus placebo (n = 150)
Outcomes	Parity, sunlight exposure, diet assessment allowing assessment of diet quality, cigarette and alcohol consumption, well-being, self-efficacy and food involvement
Starting date	13 September 2013
Contact information	Janis Baird, jb@mrc.soton.ac.uk
Notes	Study protocol

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Barros 2022

Study name	STOP LBW
Methods	Parallel superiority pragmatic clinical trial randomised by clusters
Participants	Pregnant women over 18 years of age attending primary healthcare units (PHCU) located in Portugal
Interventions	Activation of fast-track referral for specialised units and care programmes for smoking, alcohol consumption, depression, and physical violence
Outcomes	**Primary outcome:** • Incidence of birthweight **Secondary outcomes:** • Incidence of preterm births (live births with less than 37 weeks of gestation) • Reduction of the prevalence of each of the 4 psychosocial and behavioural risk factors (smoking, alcohol consumption, depression, and physical violence) when comparing the first prenatal visit and the period of 1 month after birth • Proportion of pregnant women with adherence to care programmes targeted at psychosocial and behavioural risk factors and description of the determinants of adherence
Starting date	Planned to start the clinical trial immediately after the pilot study, but it had to be stopped because of COVID-19 pandemic. The study will resume in 2021.
Contact information	Dr Rosa Domingues; rosa.domingues@ini.fiocruz.br
Notes	Protocol; NCT04866277

Bendtsen 2020

Study name	MoBILE
Methods	Randomised controlled trials
Participants	Each project within the MoBILE programme will focus on a specific group: pregnant women, preschool children, high school and university students, and adults in primary and clinical care.
Interventions	Medical or public health practice that is supported by mobile devices on multiple lifestyle risk behaviours (e.g. alcohol, nutrition, physical activity, and smoking)
Outcomes	Effects of the interventions on multiple lifestyle risk behaviours (e.g. alcohol, nutrition, physical activity, and smoking)
Starting date	The research programme commenced in 2019, and the first results will be available in 2020. Projects involving pregnant women, preschool children, and high school and university students will be completed in the first 3 years, with the remaining projects being planned for the programme's final 3 years.
Contact information	Marcus Bendtsen; marcus.bendtsen@liu.se
Notes	Protocol

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Brunelli 2022

Study name	CARE 1000
Methods	Randomised controlled trial
Participants	Pregnant women during the first 1000 days (from conception to 24 months of age)
Interventions	Mobile health (mHealth) to support women during the first 1000 days (from conception to 24 months of age) and improve health prevention behaviours such as immunisations during pregnancy, weight gain during pregnancy, abstinence from smoking and alcohol consumption, and adherence to the routine childhood immunisation schedule
Outcomes	Immunisations during pregnancy, weight gain during pregnancy, abstinence from smoking and alcohol consumption, and adherence to the routine childhood immunisation schedule
Starting date	Recruitment will end before 31 March 2023.
Contact information	Laura Brunelli; laura.brunelli@phd.units.it
Notes	Protocol; NCT05500339

Carmona Camacho 2022

Study name	WOMAP (Woman Mental Health and Addictions on Pregnancy)
Methods	Randomised clinical trial
Participants	Pregnant women under 26 weeks of pregnancy
Interventions	2 groups of a 10-session pregnancy-adapted psychotherapeutic programme, 1 delivered by app/internet (n = 41) and 1 by telephone (n = 41), vs usual care control group (n = 38)
Outcomes	Mental health symptoms; substance use
Starting date	Not available
Contact information	Not available
Notes	Conference abstract

Lenz 2018

Study name	MINDFUL/PMI Study
Methods	Randomised controlled trial
Participants	Pregnant women
Interventions	The mindfulness-oriented experimental group vs the pregnancy education control group

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Lenz 2018 *(Continued)*

Outcomes	The comparison of the 2D:4D ratio in the children (as a marker for intrauterine testosterone exposure) between the 2 randomisation arms
Starting date	The entire duration of the study comprises the preparation phase with a start in the first quarter of 2016, the active study phase with inclusion of pregnant women expected as of the fourth quarter of 2018 until the second quarter of 2020, the active study phase with the examination of the children from the first quarter of 2020 until the fourth quarter of 2021 and the data analysis, evaluation and post-processing in the fourth quarter of 2021 and the first quarter of 2022.
Contact information	PD Dr. med. Bernd Lenz; bernd.lenz@uk-erlangen.de
Notes	This study is subproject 3 of the “IMAC-Mind” consortium supported by the Federal Ministry of Education and Research (BMBF) (“IMAC-Mind: Improving Mental Health and Reducing Addiction in Childhood and Adolescence through Mindfulness: Mechanisms, Prevention and Treatment, TP3: Reducing stress, alcohol and tobacco use in pregnant women to improve the children’s later mental health”.

NCT00540319

Study name	Prevention for Prenatal Health: the Health in Pregnancy (HIP) Study
Methods	Randomised controlled trial
Participants	Pregnant women who report tobacco, alcohol, or illicit drug use and/or domestic violence during pregnancy
Interventions	Women in the intervention group will receive the Health in Pregnancy (HIP) intervention, consisting of brief, multimedia counselling presented by a "Video Doctor" and an educational worksheet.
Outcomes	• Elimination of cigarette smoking, alcohol drinking, and illicit drug use • Reduction in frequency and/or severity of domestic violence
Starting date	June 2006
Contact information	Barbara Gerbert, PhD
Notes	

NCT01550913

Study name	Sober Network IPT for Perinatal Women With Comorbid Substance Use and Depression
Methods	Randomised controlled trial
Participants	Pregnant women (or has delivered in the past year) reporting the use of an illegal drug and/or consumption of 4 or more drinks on 1 occasion within the last 6 months
Interventions	Sober Network Interpersonal Psychotherapy (IPT)
Outcomes	Change from baseline in heavy drinking/drug using days at 3 months; change from baseline in depressive symptoms at 18 to 20 weeks; change from baseline in depressive symptoms at 3 months

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NCT01550913 *(Continued)*

Starting date	July 2011
Contact information	Caron Zlotnick, PhD
Notes	

NCT01971398

Study name	Development of Education Materials for Prevention of FAS in Russia
Methods	Randomised controlled trial
Participants	Pregnant and non-pregnant childbearing-age women
Interventions	Behavioural: positive FASD education brochure Behavioural: negative FASD education brochure Behavioural: active comparator (a general women's health brochure)
Outcomes	• Changes in knowledge about FAS from baseline (1-month follow-up) • Changes in attitudes from baseline (1-month follow-up) • Changes in alcohol consumption from baseline (1-month follow-up)
Starting date	April 2007
Contact information	Tatiana Balachova, PhD
Notes	

NCT02759874

Study name	Prevention of Fetal Alcohol Spectrum Disorder (FASD) by the Use of Technology
Methods	Randomised controlled trial
Participants	Pregnant, alcoholic, actively in treatment for alcoholism addiction
Interventions	Device: specialised breathalyser face recognition technology
Outcomes	Change in FASD and birth rate levels
Starting date	November 2015
Contact information	Andy Greenshaw, PhD
Notes	

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NCT04275570

Study name	Effectiveness of Repeated MOTivational InterVention to Reduce Ethanol Intake During prEgnancy (EMOTIVE)
Methods	Randomised controlled trial
Participants	Pregnant women
Interventions	Repeated motivational interview
Outcomes	Prevalence of ethanol intake (up to 7 days from delivery) Biomarkers: ethyl glucuronide in mother's hair and phosphatidylethanol in cord blood
Starting date	2020
Contact information	María Dolores Gómez Roig, MD, PhD; lgomezroig@sjdhospitalbarcelona.org
Notes	

NCT04441307

Study name	Promoting Co-Parenting and Reducing Hazardous Drinking in New Families
Methods	Randomised controlled trial
Participants	Pregnant couples with health behaviour such as moderate to heavy drinking
Interventions	Couples will experience a parenting programme for expecting first-time parents. In 1 arm, parents will receive an adapted Family Foundations programme. In the other arm, parents will receive an empirically supported community parenting programme.
Outcomes	• Couple relationship/co-parenting • Parent adjustment • Parent alcohol use • Quantity-frequency of alcohol use (Quantity Frequency Index) and frequency of binge drinking (4 or 5 or more on a single occasion) based on the NIAAA standard drink will be assessed. Higher scores indicate greater quantity and frequency of alcohol use and binge drinking, with moderate drinking being defined as up to 1 standard drink per day for women and up to 2 standard drinks per day for men.
Starting date	25 January 2021
Contact information	Rina D Eiden, PhD
Notes	

NCT04749888

Study name	Impact of the Korea Early Childhood Home-visiting Intervention (KECHI)
Methods	Randomised controlled community trial

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NCT04749888 *(Continued)*

Participants	Pregnant women with 2 or more risk factors at the time of screening
Interventions	Targeted nurse-led home visiting
Outcomes	Several outcomes, including maternal alcohol consumption
Starting date	27 October 2021
Contact information	Young-Ho Khang, MD, PhD; yhkhang@snu.ac.kr
Notes	

NCT05766761

Study name	Reducing Alcohol Exposed Pregnancies
Methods	Randomised controlled trial
Participants	Pregnant women (gestational age is 8 weeks or less with recent alcohol use as assessed by a positive EtG or self-report of alcohol use in the previous 21 days)
Interventions	Intervention condition, usual prenatal care plus the alcohol intervention, which consists of (1) a self-paced computer-delivered component to enhance knowledge, norms, and motivation for alcohol reduction and (2) a nurse-delivered component to reinforce the computer-delivered content and address women's questions. Both components are theory-driven, based on Motivational Enhancement Theory (MET), and use motivational strategies to promote alcohol reduction.
Outcomes	Negative PEth test during pregnancy Reduce the proportion of adverse birth outcomes among infants
Starting date	January 2024
Contact information	Rebecca Lunstroth; cphs@uth.tmc.edu
Notes	

NCT05976776

Study name	Effectiveness of a Childbirth and Parenthood Preparation Education on Maternal Health Needs, Pregnancy-Related Anxiety and Fetal Health Anxiety in Primigravidas
Methods	A randomised controlled trial with pretest-post-test control group
Participants	Primigravidas. Pregnant women who do not have communication and mental difficulties (18 to 40 years old)
Interventions	The "Childbirth and Parenthood Preparation Education" programme will be applied to the experimental group for a period of 1 month (each week, once a week for a total of 4 sessions).
Outcomes	Alcohol consumption among others
Starting date	Not yet recruiting

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NCT05976776 *(Continued)*

Contact information	Emine İbici Akça; emine.akca@amasya.edu.tr
Notes	

Ondersma 2022

Study name	Online randomised factorial trial of electronic screening and brief intervention for alcohol use in pregnancy
Methods	Randomised controlled trial
Participants	Pregnant women who score positive on the Tolerance, Annoyed, Cut Down, Eye-opener (T-ACE)
Interventions	3 levels of brief intervention: none, single 120-minute session, and single session plus two 5-minute boosters
Outcomes	90-day period prevalence abstinence (no self-report of alcohol use in the 90 days prior to the 34-week assessment, and a fingernail sample negative for EtG at approximately 37 weeks' gestation)
Starting date	March 2022
Contact information	Dr Steven J Ondersma; onders12@ msu.edu
Notes	

Tzilos 2019

Study name	Reducing sexual health risks and substance use in the prenatal setting: a study protocol for a randomized controlled trial
Methods	2-group, randomised controlled trial
Participants	Pregnant women with at least 1 unprotected sex occasion in the past 30 days, reporting comorbid recent history of substance use and current alcohol/illicit drug use risk
Interventions	The Health Check-Up for Expectant Moms (HCEM), a computer-delivered brief intervention
Outcomes	Several outcomes, including alcohol use
Starting date	Not reported
Contact information	Dr G Tzilos Wernette; gtzilos@med.umich.edu
Notes	NCT03826342

Wilson 2012

Study name	Brief intervention to reduce risky drinking in pregnancy
Methods	Randomised clinical trial

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Wilson 2012 *(Continued)*

Participants	Pregnant women who screen positive for risky alcohol use
Interventions	5 minutes of structured advice from a community midwife plus a 20-minute brief intervention delivered by a trained alcohol counsellor
Outcomes	Alcohol use
Starting date	1 September 2011
Contact information	Judith Rankin; judith.rankin@ncl.ac.uk
Notes	ISRCTN43218782

y4k7w RBR 2018

Study name	Effect of the follow-up of brief interventions for the use of alcoholic beverages and cigarettes in pregnant women: a randomized clinical trial
Methods	A randomised clinical trial
Participants	Pregnant women identified as current alcohol and/or tobacco users during gestation
Interventions	Intervention group monitoring (GIM) through the use of a programme called Research Randomizer Quick Tutorial
Outcomes	Use of alcohol and tobacco
Starting date	6 December 2017
Contact information	Adaene Alves Machado de Moura; adaene_moura@hotmail.com
Notes	

FAS: fetal alcohol syndrome; FASD: fetal alcohol spectrum disorder

RISK OF BIAS

Legend: ✓ Low risk of bias ✗ High risk of bias ~ Some concerns

Risk of bias for analysis 1.2 Number of drinks per day

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Reynolds 1995	✓	~	✗	✗	~	✗
van der Wulp 2014	~	~	✗	✗	~	✗

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Risk of bias for analysis 1.3 Number of women who completed treatment

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Handmaker 1999	✓	~	✓	✓	~	~
Joya 2016	~	~	✓	✓	~	~
O'Connor 2007	~	~	✓	✓	~	~
Reynolds 1995	✓	~	✓	✓	~	~
Rubio 2014	✓	~	✓	✓	~	~
Tzilos 2011	~	✓	✓	✓	~	~
van der Wulp 2014	~	✓	✓	✓	~	~

DATA AND ANALYSES

Comparison 1. Any psychosocial intervention versus treatment as usual (TAU)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Number of continuously abstinent women	3	378	Risk Ratio (M-H, Random, 95% CI)	1.34 [1.14, 1.57]
1.2 Number of drinks per day	2	157	Mean Difference (IV, Random, 95% CI)	-0.42 [-1.13, 0.28]
1.3 Number of women who completed treatment	7	1283	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.94, 1.02]

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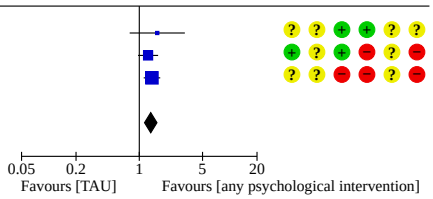
Analysis 1.1. Comparison 1: Any psychosocial intervention versus treatment as usual (TAU), Outcome 1: Number of continuously abstinent women

Study or Subgroup	Any psychosocial intervention Events	Total	Treatment as usual Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Joya 2016	13	32	9	35	5.1%	1.58 [0.78 , 3.19]
Reynolds 1995	34	39	23	33	38.4%	1.25 [0.97 , 1.61]
van der Wulp 2014	112	149	49	90	56.5%	1.38 [1.12 , 1.70]
Total (95% CI)		**220**		**158**	**100.0%**	**1.34 [1.14 , 1.57]**
Total events:	159		81			

Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 2 (P = 0.73); I² = 0%
Test for overall effect: Z = 3.61 (P = 0.0003)
Test for subgroup differences: Not applicable

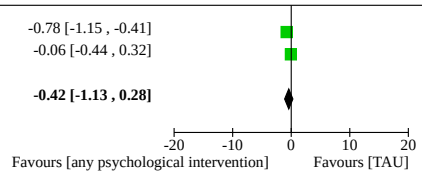


Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Analysis 1.2. Comparison 1: Any psychosocial intervention versus treatment as usual (TAU), Outcome 2: Number of drinks per day

Study or Subgroup	Any psychosocial intervention Mean	SD	Total	Treatment as usual Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Reynolds 1995	0.36	1.08	42	1.14	0.54	36	50.2%	-0.78 [-1.15 , -0.41]
van der Wulp 2014	0.42	1.08	38	0.48	0.54	41	49.8%	-0.06 [-0.44 , 0.32]
Total (95% CI)			**80**			**77**	**100.0%**	**-0.42 [-1.13 , 0.28]**

Heterogeneity: Tau² = 0.22; Chi² = 7.04, df = 1 (P = 0.008); I² = 86%
Test for overall effect: Z = 1.17 (P = 0.24)
Test for subgroup differences: Not applicable



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

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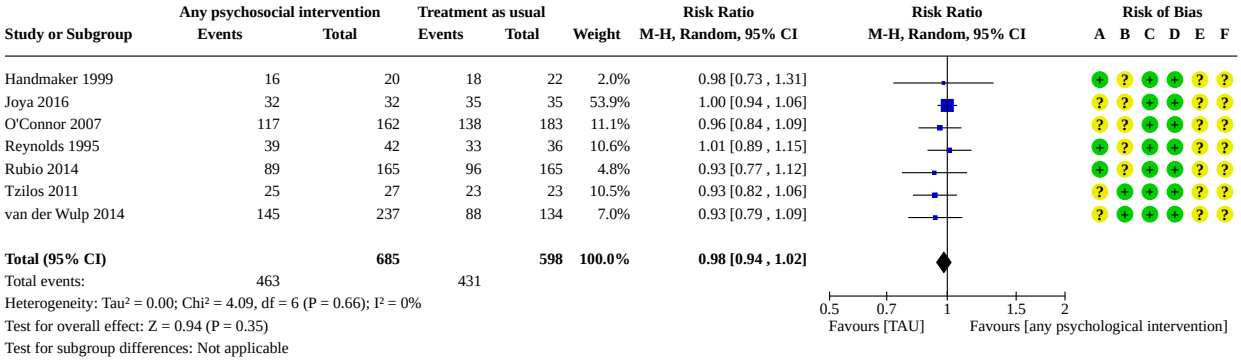
Analysis 1.3. Comparison 1: Any psychosocial intervention versus treatment as usual (TAU), Outcome 3: Number of women who completed treatment



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

APPENDICES

Appendix 1. Search strategy

Cochrane Drugs and Alcohol Group Specialised Register (via CRSLive)

searched on January 8, 2024

#1 (((alcohol* AND (drink* or intoxicat* or use* or abus* or misus* or risk* or consum* or withdraw* or detox* or treat* or therap* or excess* or reduc* or cessation or intervention*))):TI):AB AND INREGISTER

#2 ((alcohol*):XDI):XIN AND INREGISTER

#3 #1 OR #2

#4 pregnan* AND INREGISTER

#5 #3 AND #4

Cochrane Central Register of Controlled Trials

Issue 1 of 12, January 2024

#1 MeSH descriptor: [Alcohol-Related Disorders] explode all trees

#2 MeSH descriptor: [Alcohol-Induced Disorders, Nervous System] explode all trees

#3 (alcohol* NEAR/3 (drink* or intoxicat* or use* or abus* or misus* or risk* or consum* or withdraw* or detox* or treat* or therap* or excess* or reduc* or cessation or intervention*)):ti,ab

#4 (drink* NEAR/3 (excess or heavy or heavily or harm or harmful or hazard* or binge or harmful or problem*)):ti,ab

#5 alcoholic*:ti,ab

#6 #1 or #2 or #3 or #4 or #5

#7 MeSH descriptor: [Pregnancy] explode all trees

#8 MeSH descriptor: [Pregnancy Complications] this term only

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#9 (puerper* or postnatal* or post-natal* or (post NEXT natal*) or postpartum or "post-partum" or "post partum"):ti,ab

#10 pregnan*:ti,ab

#11 #7 or #8 or #9 or #10

#12 #6 AND #11 in Trials

Ovid MEDLINE(R) ALL <1946 to January 8, 2024>

1 exp Alcohol-Related Disorders/

2 Alcohol Drinking/

3 (alcohol adj3 (drink$ or intoxicat$ or use$ or abus$ or misus$ or risk$ or consum$ or withdraw$ or detox$ or treat$ or therap$ or excess $ or reduc$ or cessation or intervention$)).tw.

4 (drink$ adj3 (excess or heavy or heavily or harm or harmful or hazard$ or binge or harmful or problem$)).tw.

5 "alcohol use".tw.

6 alcoholic*.tw.

7 drunk*.tw.

8 or/1-7

9 exp Pregnancy/

10 exp Pregnancy Complications/

11 (puerper* or postnatal* or post-natal* or post natal* or postpartum or post-partum or post partum).tw.

12 pregnan*.tw.

13 or/9-12

14 8 and 13

15 randomized controlled trial.pt.

16 controlled clinical trial.pt.

17 random*.ab.

18 placebo.ab.

19 clinical trials as topic.sh.

20 random allocation.sh.

21 trial.ti.

22 15 or 16 or 17 or 18 or 19 or 20 or 21

23 exp animals/ not humans.sh.

24 22 not 23

25 14 and 24

Embase <1974 to January 8, 2024>

1 exp alcoholism/

2 *drinking behavior/

3 (alcohol adj3 (drink$ or intoxicat$ or use$ or abus$ or misus$ or risk$ or consum$ or withdraw$ or detox$ or treat$ or therap$ or excess $ or reduc$ or cessation or intervention$)).tw.

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4 (drink$ adj3 (excess or heavy or heavily or harm or harmful or hazard$ or binge or harmful or problem$)).tw.

5 alcoholic*.ti.

6 1 or 2 or 3 or 4 or 5

7 exp pregnancy/

8 exp pregnancy complication/

9 (puerper* or postnatal* or post-natal* or post natal* or postpartum or post-partum or post partum).tw.

10 pregnan*.tw.

11 7 or 8 or 9 or 10

12 6 and 11

13 Clinical-Trial/ or Randomized-Controlled-Trial/ or Randomization/ or Single-Blind-Procedure/ or Double-Blind-Procedure/ or Crossover-Procedure/ or Prospective-Study/ or Placebo/

14 (((clinical or control or controlled) adj (study or trial)) or ((single or double or triple) adj (blind$3 or mask$3)) or (random$ adj (assign $ or allocat$ or group or grouped or patients or study or trial or distribut$)) or (crossover adj (design or study or trial)) or placebo or placebos).ti,ab.

15 13 or 14

16 12 and 15

APA PsycInfo <1806 to January Week 1 2024>

1 exp "Alcohol Use Disorder"/

2 alcohol treatment/

3 alcohol drinking patterns/

4 (alcohol adj3 (drink$ or intoxicat$ or use$ or abus$ or misus$ or risk$ or consum$ or withdraw$ or detox$ or treat$ or therap$ or excess $ or reduc$ or cessation or intervention)).ti,ab.

5 (drink$ adj3 (excess or heavy or heavily or hazard$ or binge or harmful or problem$)).ti,ab.

6 1 or 2 or 3 or 4 or 5

7 exp Pregnancy/

8 (puerper* or postnatal* or post-natal* or post natal* or postpartum or post-partum or post partum).tw.

9 pregnan*

10 7 or 8 or 9

11 6 and 10

12 exp Clinical Trials/

13 (random* or (clinical adj3 trial*) or (reserch adj3 design*) or (evaluat adj3 stud*) or (prospective* adj3 stud*)).tw.

14 ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)).tw.

15 12 or 13 or 14

16 11 and 15

CINAHL Ebsco HOST

searched on January 8, 2024

S12 S10 AND S11

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S11 (MH randomized controlled trials OR MH double-blind studies OR MH single-blind studies OR MH random assignment OR MH pretest-posttest design OR MH cluster sample OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR MH (placebos) OR PT (randomized controlled trial) OR AB (control W5 group) OR MH (crossover design) OR MH (comparative studies) OR AB (cluster W3 RCT)) NOT ((MH animals+ OR MH animal studies OR TI animal model*) NOT MH human)

S10 S5 AND S9

S9 S6 OR S7 OR S8

S8 (TI pregnan* OR AB pregnan*)

S7 ((TI puerper* OR AB puerper*) OR (TI postnatal* OR AB postnatal*) OR (TI post-natal* OR AB post-natal*) OR (TI "post natal*" OR AB "post natal*") OR (TI postpartum OR AB postpartum) OR (TI post-partum OR AB post-partum) OR (TI "post partum" OR AB "post partum"))

S6 (MH "Pregnancy+")

S5 S1 OR S2 OR S3 OR S4

S4 ((TI drink* OR AB drink*) N3 ((TI excess OR AB excess) OR (TI heavy OR AB heavy) OR (TI heavily OR AB heavily) OR (TI harm OR AB harm) OR (TI harmful OR AB harmful) OR (TI hazard* OR AB hazard*) OR (TI binge OR AB binge) OR (TI harmful OR AB harmful) OR (TI problem* OR AB problem*)))

S3 ((TI alcohol OR AB alcohol) N3 ((TI drink* OR AB drink*) OR (TI intoxicat* OR AB intoxicat*) OR (TI use* OR AB use*) OR (TI abus* OR AB abus*) OR (TI misus* OR AB misus*) OR (TI risk* OR AB risk*) OR (TI consum* OR AB consum*) OR (TI withdraw* OR AB withdraw*) OR (TI detox* OR AB detox*) OR (TI treat* OR AB treat*) OR (TI therap* OR AB therap*) OR (TI excess* OR AB excess*) OR (TI reduc* OR AB reduc*) OR (TI cessation OR AB cessation) OR (TI intervention* OR AB intervention*))) 37,724

S2 MH "Alcoholism"

S1 MH "Alcohol-Related Disorders+"

Web of Science Core Collection

searched on January 8, 2024

1. TS=((alcohol NEAR/3 (drink* OR intoxicat* OR use* OR abus* OR misus* OR risk* OR consum* OR withdraw* OR detox* OR treat* OR therap* OR excess* OR reduc* OR cessation OR intervention*)))
2. TS=((Pregnan* or puerper* or postnatal* or post-natal* or post natal* or postpartum or post-partum or post partum))
3. TS=(randomised OR randomized OR randomisation OR randomisation OR placebo* OR (random* AND (allocat* OR assign*)) OR (blind* AND (single OR double OR treble OR triple)))
4. #1 AND #2 AND #3

HISTORY

Protocol first published: Issue 4, 2022

CONTRIBUTIONS OF AUTHORS

Draft the protocol: RA, JS, MT, SM

Study selection: RA, LA, SU, SM, JMAS

Data extraction: LA, SU, RA, SM

Enter data into RevMan: LA, RA, SM

Carry out the analysis: RA, RS, LA, SM

Interpret the analysis: RA, RS, JMAS, MT, LA, SU, SM

Draft the final review: RA, RS, JMAS, SU, LA, MT, SM

Disagreement resolution: JMAS, RA, SM, MT

Update the review: RA, RS, JMAS, SM, SU, MT, LA

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DECLARATIONS OF INTEREST

Silvia Minozzi is the Joint-Coordinating Editor of Cochrane Drugs and Alcohol Group. She was not involved in the editorial process of the current review.

Ludovico Ambrosi declares no financial or other conflicts of interest.

Rosella Saulle declares no financial or other conflicts of interest.

Seilin S Uhm declares no financial or other conflicts of interest.

Mishka Terplan declares no financial or other conflicts of interest.

Julia MA Sinclair declares no financial or other conflicts of interest.

Roberta Agabio is an Editor of Cochrane Drugs and Alcohol Group. She was not involved in the editorial process of the current review.

SOURCES OF SUPPORT

Internal sources

- No specific funds, Italy

  Department of Biomedical Sciences, Section of Neuroscience and Clinical Pharmacology, University of Cagliari, Cagliari
- No specific funds, UK

  University of Southampton, Southampton, UK
- No specific funds, Italy

  Department of Epidemiology, Lazio Regional Health Service, Rome
- No specific funds, USA

  Friends Research Institute, Baltimore, USA

External sources

- No specific funds, Other

  No specific funds

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We could not perform subgroup analyses for severity of alcohol use disorder (AUD) at baseline, as only two studies included women with AUD.

We could not perform sensitivity analyses excluding studies at overall high risk of bias because of the limited number of included studies.

We added the following sentence in Types of participants to better describe the selection process of the studies: "When heterogeneous populations were recruited (e.g. women who used alcohol and women who used other substances), we contacted the authors to obtain data of the sample of women who used alcohol". We also added the following sentence: "In this review, the diagnoses provided by the primary RCTs (i.e. AUD or alcohol dependence) are described in the Results and Studies sections (Included, Excluded, Awaiting classification, and Ongoing), whereas in the other sections (Abstract, Plain language summary, Background, Methods, Discussion, and Authors' conclusions), the term 'AUD' is used to indicate both definitions" to better explain the meaning of the term 'AUD'.

In the Assessment of risk of bias in included studies, we specified that we used a variant of the RoB 2 tool for cluster-randomised studies, adding the following sentence: "We assessed cluster-RCTs using the variation of the RoB 2 tool for cluster-RCTs and the special issues to be considered as described in Chapter 23 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022; Eldridge 2021)".

In Unit of analysis issues, we added the following sentence explaining how we handled cluster-randomised trials: "We analysed cluster-RCTs according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022). If results did not control for clustering, we contacted the trialists to request an estimate of the intracluster correlation coefficient (ICC). If we were unable to obtain an ICC from the trialists, we imputed ICC from other cluster-RCTs included in the review".

In Summary of findings and assessment of the certainty of the evidence, we specified that we assessed the certainty of evidence also for the secondary outcome withdrawal symptoms, as this is important for decision-making.

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