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Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Cochrane systematic review

Review information

Review number: 63
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Abstract

Background
Problem alcohol use is common among illicit drug users and is associated with adverse health outcomes. It is also an important factor in poor prognosis among drug users with hepatitis C virus (HCV) as it impacts on progression to hepatic cirrhosis or opiate overdose in opioid users.

Objectives
To assess the effects of psychosocial interventions for problem alcohol use in illicit drug users (principally problem drug users of opiates and stimulants).

Search methods
We searched the Cochrane Drugs and Alcohol Group trials register (November 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 11, November 2011), PUBMED (1966 to 2011); EMBASE (1974 to 2011); CINAHL (1982 to 2011); PsycINFO (1872 to 2011) and reference list of articles. We also searched: 1) conference proceedings (online archives only) of the Society for the Study of Addiction (SSA), International Harm Reduction Association
Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: A Systematic Review

63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch... (IHRA), International Conference on Alcohol Harm Reduction (ICAHR), and American Association for the Treatment of Opioid Dependence (AATOD); 2) online registers of clinical trials, Current Controlled Trials (CCT), Clinical Trials.org, Center Watch and International Clinical Trials Registry Platform (ICTRP).

Selection criteria
Randomised controlled trials comparing psychosocial interventions with another therapy (other psychosocial treatment, including non-pharmacological therapies or placebo) in adult (over the age of 18 years) illicit drug users with concurrent problem alcohol use.

Data collection and analysis
Two review authors independently assessed risk of bias and extracted data from included trials.

Main results
Four studies, 594 participants, were included. Half of the trials were rated as having high or unclear risk of bias. They considered six different psychosocial interventions grouped into four comparisons: (1) cognitive-behavioural coping skills training versus 12-step facilitation (N = 41), (2) brief intervention versus treatment as usual (N = 110), (3) hepatitis health promotion versus motivational interviewing (N = 256), and (4) brief motivational intervention versus assessment-only group (N = 187). Differences between studies precluded any pooling of data. Findings are described for each trial individually:

- comparison 1: no significant difference;
- comparison 2: higher rates of decreased alcohol use at three months (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.19 to 0.54) and nine months (RR 0.16; 95% CI 0.08 to 0.33) in the treatment as usual group;
- comparison 3 (group and individual format): no significant difference;
- comparison 4: more people reduced alcohol use (by seven or more days in the past 30 days at 6 months) in the brief motivational intervention compared to controls (RR 1.67; 95% CI 1.08 to 2.60).

Authors’ conclusions
Very little evidence exists that there is no difference in the effectiveness between different types of interventions and that brief interventions are not superior to assessment only or treatment as usual. No conclusion can be made because of the paucity of the data and the low quality of the retrieved studies.

Plain language summary
Which talking therapies (counselling) work for drug users with alcohol problems?

What is problem alcohol use and what are psychosocial interventions?

Problematic use of alcohol means drinking above the recommended safe drinking limits. It can lead to serious alcohol problems or dependence. Excessive drinking in people who have problems with other drugs is common and often makes their problems worse as well as having serious health consequences for the person involved.

Psychosocial interventions are talking therapies that aim to identify an alcohol problem and motivate an individual to do something about it. They can be performed by staff with training in these approaches, for example doctor, nurse, counsellor, psychologist, etc. Talking therapies may help people cut down their drinking but the impact is not known in people who have problems with other drugs.

We wanted to do a review to see whether talking therapies have an impact on alcohol problems in drug users. In this review, we wanted to evaluate information from randomised trials in relation to the impact of talking therapies on alcohol drinking in adult (over the age of 18 years) users of illicit drugs (mainly opiates and stimulants).

This review found the following studies, and came to the following conclusions:

We found four studies that examined 594 people with drug problems. One study looked at cognitive-behavioural coping skills training versus 12-step facilitation. One study looked at brief intervention versus treatment as usual. One study looked at motivational interviewing (group and individual format) versus hepatitis health promotion. The last study looked at brief motivational intervention versus assessment only.

- The studies were so different that we could not combine their results to answer our question.
- It remains uncertain whether talking therapies affect drinking in people who have problems with other drugs because of the low quality of the evidence.
- It remains uncertain whether talking therapies for drinking affect illicit drug use in people who have problems with other drugs. There was not enough information to compare different types of talking therapies.
- Many of the studies did not account for possible sources of bias.
- More high-quality studies, such as randomised controlled trials, are needed to answer our question.

Background

Description of the condition
Problem alcohol use is common among illicit drug users and is associated with adverse health outcomes, which include physical, psychological and social implications (Srivastava 2008). NIDA (National Institute on Drug Abuse) meta-analyses of US clinical trials found alcohol use disorders (AUDs) in 38% and 45% of opiate- and stimulants-using treatment seekers, respectively (Hartzler 2010; Hartzler 2011). An earlier review of literature on the prevalence of 'heavy drinking' among drug users (Hernández-Cuadrado 2001) found a prevalence of 26%.
users enrolled in a methadone maintenance treatment (MMT) found prevalence rates of 13% to 25% (Ottomameli 1999). While more recent cross-sectional studies report prevalence from one-third up to 50% in this setting (Maremmani 2007; McCusker 2001).

Problem alcohol use is an expression that represents a spectrum of distinct drinking patterns (i.e. hazardous, harmful and dependent drinking). Hazardous drinking 'is likely to result in harm should present habits persist', while harmful drinking, which is an International Classification of Diseases - Tenth Revision (ICD-10) diagnosis (WHO 1993), 'causes harm to the health (physical or mental) of the individual' without the presence of dependence (Babor 2001). The term 'dependent drinkers' refers to individuals who meet criteria for the alcohol dependence syndrome under Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) or ICD-10 criteria (DSM-IV; WHO 1993).

Problem drug users are at high risk of liver disease resulting from hepatitis C virus (HCV) infection because of its high prevalence in this population (Smyth 1998). Problem alcohol use is an important factor in determining poor prognosis among people with HCV as it impacts on progression to hepatic cirrhosis, increased HCV-ribonucleic acid (RNA) levels or fatal opiate overdose in opiate users (Ostapowicz 1998; White 1999). Teplin 2007 noted that drug users have higher rates of mood, anxiety and personality disorders, all of which are exacerbated by alcohol use. In addition, there exists some evidence that alcohol may have a negative impact on outcomes of addiction treatment (Gossop 2000).

The emerging understanding of a high prevalence of problem alcohol use among current or former drug users, allied to the clear health implications of this problem for this population, necessitates a public health response to this issue.

**Description of the intervention**

Psychosocial interventions are best described as 'psychologically-based interventions aimed at reducing consumption behaviour or alcohol-related problems' (Kaner 2007), which exclude any pharmacological treatments. This term refers to a heterogeneous collection of interventions, which vary depending on their: (a) theoretical underpinnings (e.g. psychodynamic, behavioural, motivational), (b) duration or intensity (e.g. brief, extended), (c) setting (e.g. primary care based, inpatient), (d) mode of delivery (e.g. group, individual, web based) or (e) treatment goals (e.g. abstinence oriented, harm reduction). To date, many psychosocial interventions specifically designed to address problem alcohol use have been described. The most frequently used interventions include: motivational interviewing (MI), cognitive-behavioural therapy (CBT), psychodynamic approaches, screening and brief interventions (SBI), family therapy, drug counselling, 12-step programmes, therapeutic communities (TC) and vocational rehabilitation (VR).

- **MI** is a client-centred approach, but as opposed to its non-directive Rogerian origins, it is a directive therapy system. A central role is played by the client's motivation and readiness to change. Change within this approach is facilitated over a series of stages (Prochaska 1992). Relapse is not viewed as a failure to maintain healthy behaviour, but rather as a part of the process of change (Miller 2004).

- **CBT** draws upon the principles of learning theory. Change in addictive behaviour is approached through altering irrational assumptions, coping skills training or other behavioural exercises. This therapy often deals with the identification and prevention of triggers contributing to the drug use. Among the modern approaches utilising such behavioural techniques are relapse prevention (Marlatt 1996), contingency management (Budney 2001) or community reinforcement approach, which combines both contingency management and positive reinforcement for non-drinking behaviours (Hunt 1973).

- **Psychodynamic approaches** are based on the assumptions of psychoanalytic theory, which focuses on addressing the inner conflicts, childhood traumas or problematic relationship themes. They include a range of different methods designed to deal with the underlying conflicts (e.g. interpersonal therapy, supportive-expressive techniques, etc.) (Crits-Christoph 1999).

- **SBI** are time limited and therefore suitable for non-specialist facilities. Usually, the length and intensity of the intervention is determined by the levels of risky alcohol consumption (i.e. screening results). It can range from a couple of minutes to several sessions (three to six) of intervention. Each session includes provision of information and advice (Babor 2001). Increasingly, brief interventions (BIs) are based on the principles and techniques of MI, so that the distinction between these two modalities is blurred in this regard.

- **Family therapy**: the therapeutic change is achieved via intervening in the interaction between family members. Families are directly involved in a therapy session. The family therapist must be competent in eliciting the strengths and support of the wider family system. Frequently used family therapy models include multisystemic therapy, network therapy solution-focused brief therapy, etc. (CSAT 2004).

- **Drug counselling**: addiction is viewed as a chronic illness that has serious consequences to the health of the individual and social functioning, in consonance with the 12-step model. Recovery includes spiritual components and attendance at fellowship meetings as well. Primary focus of this approach is to help the patient attain abstinence by promoting behavioural changes including trigger avoidance, sport and other constructive activities. Both individual and group forms of drug counselling have been used in the largest collaborative cocaine treatment study (Crits-Christoph 1999).

- **12-step model**: emphasises powerlessness of an individual over the addiction, which is seen as a disease, and a need for a spiritual recovery. The foundations of this approach lie in the 12 steps and an accompanying document - 12 traditions (Alcoholics Anonymous 1939). The largest of all 12-step programmes is Alcoholics Anonymous (AA) and all other programmes evolved from it (e.g. Narcotics Anonymous, Al-Anon etc.). AA meetings, besides the 12 steps, utilise well-established therapeutic factors of group psychotherapy, such as group cohesiveness, interpersonal learning (i.e. sponsorship), peer pressure, etc.

- **TC** is a long-term (18 to 24 months), drug-free model of treatment, which usually runs in a residential form. This approach relies on community itself, as the main therapeutic factor, and also other factors, such as peer feedback, role-modelling or recapitulation of the primary family experience. Community has a high degree of autonomy, is democratic and each member has a clearly defined role and responsibilities within the structure of TC. A structured regimen of daily activities in
the TC often includes formal individual or group therapy sessions along with other educational and work activities (De Leon 2000).

- VR employment is seen as an important element of a successful rehabilitation from drug addiction and is often considered as one of its key indicators (Platt 1995). VR aims to increase the employability of drug users by developing their job interview skills or obtaining further qualifications. A necessary part of increasing ex-users' access to the job market is linking with potential employers and addressing their concerns and prejudices related to drug users. An example of VR for unemployed MMT patients is the customised employment supports model (Blankertz 2004).

**How the intervention might work**

Substantial evidence has described the value of psychosocial interventions in treating problem alcohol use.

A review by Raistrick 2006 presented data on the effectiveness of many such interventions, including screening, further assessment, BIs, more intensive treatments that can still be considered 'brief' and alcohol-focused specialist treatments. They reported mixed evidence on longer-term effects of BIs and whether extended BIs add anything to the effects of simple BI.

The Mesa Grande project, which reviewed 361 controlled clinical trials (CCTs) (a three-year update), found BIs to be the most strongly supported psychosocial treatment effective in treating AUDs (Miller 2002). These findings are supported by an Australian systematic review that found BIs to be effective in reducing alcohol consumption for drinkers without dependence or those with a low level of dependence (Shand 2003). Another meta-analysis found positive effect of BIs to be evident at the follow-up points of three, six and 12 months, and these results were more apparent when dependent drinkers were excluded (Moyer 2002). Indeed, dependent drinkers have been excluded from much of the research indicating that they are possibly unsuitable for BI and should be routinely referred to specialist treatment (Raistrick 2006).

While BIs are generally delivered across a range of settings, primary care has an important role in delivery of BIs for problem alcohol use among problem drug users. BIs are well suited to primary care owing to their feasibility, they can be delivered in general settings by non-specialist staff in a short period of time, and they can also be delivered to patients not actively seeking treatment (Kaner 2007; Raistrick 2006).

The benefits of primary care-based interventions for people with problem alcohol use have been demonstrated by a Cochrane review (Kaner 2007), although the authors have reported considerable variation in trials and the effect of BIs appeared equivocal among women. Another systematic review of brief, multi-contact behavioural counselling among adult patients attending primary care found a reduction of 13% to 34% in average of drinks per week (Whitlock 2004).

In conclusion, brief psychosocial interventions are feasible and potentially highly effective components of an overall public health approach to reducing problem alcohol use, although considerable variation in effectiveness trials exists and problem drug users from primary care settings are under-represented in these trials (Kaner 2007; Whitlock 2004).

Because BIs have been developed and evaluated mainly in conventional general practice settings, it is not clear whether they can be effectively applied to excessive drinking among illicit drug users, or whether new forms of intervention need to be developed and evaluated. Could the 'advice-giving' form of BI be effective in illicit drug users or are motivational techniques, in which the impetus for change comes from the user, more likely to be effective in this population?

**Why it is important to do this review**

The described evidence of a high prevalence and serious consequences of problem alcohol use among illicit drug users highlights an opportunity for a Cochrane systematic review in this population. The question being asked in this review is important also because there are no other systematic reviews published that could help answer it.

Two narrative literature reviews have dealt with this question to date. The older of these reviews discussed six reports of four studies among methadone patients and saw some promise in the contingency management procedures (Bickel 1987). A more recent review described implications of combining behavioural and pharmacological treatments, that are effective in treating either alcohol- or drug-use disorders alone, for the treatment of people who have both of these disorders (Arias 2008). While pointing to the paucity of research specifically focused on the treatment of people with co-occurring alcohol and other substance use disorders, the reviews concluded that successful treatment must take into account both alcohol- and drug-use disorders. Additionally, one narrative review on treating people seeking therapy primarily for alcohol problems, who also use other drugs, concurred in this idea (Miller 1996).

Cochrane reviews have so far examined the effectiveness of psychosocial interventions for stimulant, opiate and alcohol use disorders (Amato 2011; Amato 2011b; Knapp 2007; Lui 2008; Mayet 2004; Minozzi 2011). Although other reviews and review protocols targeted poly-drug use, they concentrated either on specific populations, for example women and adolescents, or particular interventions, such as case management and MI, but not on 'alcohol-specific' interventions (Dalsbo 2010; Hesse 2007; Smedslund 2011; Smith 2006; Terplan 2007; Thomas 2008). None of the published reviews on psychosocial interventions examined the effectiveness of alcohol-specific interventions in problem drug users. The main problem driving the lack of good studies in this area seems to flow from the administrative separation of drug from alcohol problems. This separation has led researchers to focus on one or the other but not on both. In the US, the National Institutes of Health (NIH) plan to correct this separation by forming a new institute that covers both drugs and alcohol – the proposed National Institute of Substance Use and Addiction Disorders (NIH 2012).

The lack of systematic evaluation, together with the anticipated differences in the responsiveness of problem drug users to psychosocial interventions, provides additional reasons for conducting this review. In another words, results of reviews on the effectiveness of this type of intervention among the general population might not be applicable to specific patient groups,
Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...

such as drug users, because they may have different responsiveness to psychosocial interventions (Nilsen 2010). Several factors could possibly influence the responsiveness of drug users to treatment interventions, for example stability of drug use, engagement with the service, concurrent personality disorders, etc. For example, evidence suggests that drug users with antisocial personality disorder are more likely to respond to rewarding than to punitive approaches (Messina 2003), and the use of more intensive psychosocial interventions is recommended in those who achieved sufficient degree of stability and compliance with service regimen (Pilling 2010).

Objectives
To determine the effectiveness of psychosocial interventions targeting problem alcohol use versus other treatments in illicit drug users. Especially the effectiveness on reducing alcohol consumption.

Methods
Criteria for considering studies for this review
Types of studies
Randomised controlled trials (RCTs) and CCTs.

Types of participants
Adult (≥ 18 years) problem drug users attending a range of services (i.e. community, inpatient or residential (including opiate substitution treatment)). Problem drug use was defined by European Monitoring Centre for Drugs and Drug Addiction, as 'injecting drug use or long-duration/regular use of opioids, cocaine and/or amphetamines' (EMCDDA 2008, p. 10). This definition included other similar terms too, for example substance use, misuse, abuse, dependence or addiction.

Only studies that defined participants as problem drug and alcohol users at randomisation were included. Studies with problem drug users without concurrent problem alcohol use were excluded. People whose primary drug of use was alcohol were excluded from this review.

Types of interventions
Experimental interventions: any psychosocial intervention that is described by the study’s author as such, compared to:
Control interventions: other psychosocial interventions that will allow for comparisons between different types of interventions (e.g. CBT, contingency management, family therapy, etc.), standard care, no intervention, waiting list, placebo/or any other non-pharmacological therapy (including moderate drinking, assessment only).

We intended to exclude studies comparing psychosocial with pharmacological treatments. However, trials with two psychosocial arms and pharmacological arms were exempted from this rule.

Types of outcome measures
Primary outcomes 1. Alcohol use (reduction or stabilisation) as measured by either biological markers or self-report tests.

Secondary outcomes 1. Illicit drug use (changes in illicit drug use) as measured by either biological markers or self-report tests.
2. Engagement in further treatment (i.e. drop-out rates, utilisation of health services).
3. Alcohol-related problems or harms as represented by physical or mental health outcomes associated with problem alcohol use. We planned to pool the results from individual trials if sufficient number of studies used a measure of alcohol problems and the included studies utilised similar instruments to measure their outcomes. However, this was not possible and the secondary outcomes are described for individual trials only.

We intended to examine the sustained benefit of the intervention at three, six and 12 months through the subgroup analyses. However, insufficient information precluded this type of analysis.

Search methods for identification of studies
Electronic searches
We searched the following electronic databases (search date: 22 Nov 2011):
1. MEDLINE (PubMed) (1966 to Nov 2011);
2. CINAHL (EBSCO Host) (1982 to Nov 2011);
3. the Cochrane Central Register of Controlled Trials (CENTRAL)(The Cochrane Library, Issue 11, Nov 2011);
4. PsycINFO (ProQuest) (1872 to Nov 2011);
5. EMBASE (Elsevier, EMBASE.com) (1974 to Nov 2011);

* All trials from the CDAG Specialized Register can be found in The Cochrane Library by doing a search on SR-ADDICTN.

Databases were searched using a strategy developed incorporating the filter for the identification of RCTs (Higgins 2011), combined with selected MeSH terms and free-text terms relating to alcohol use. Electronic searches were conducted by the CDAG Group’s Trials Search Co-ordinator (databases 1-3, 5-6) and the first author of the review (4). The MEDLINE search strategy was translated into the other databases using the appropriate controlled vocabulary as applicable. Since the initial
search yielded several RCTs, we continued to search the databases with the RCT filter. Results of the electronic searches were collated into a single EndNote database.

The search strategies for all databases are shown in Appendix 1, Appendix 2, Appendix 3, Appendix 4 and Appendix 5. In addition, we searched for ongoing clinical trials and unpublished studies via Internet searches on the following sites:

1. www.controlled-trials.com (search date: 5 Apr 2012)
2. www.clinicaltrials.gov (search date: 30 Mar 2012)

Searching other resources
We searched also:

1. reference lists of articles considered eligible based on full report screening and other relevant papers;
2. conference proceedings (online archives only) of the Society for the Study of Addiction, International Harm Reduction Association, International Conference on Alcohol Harm Reduction and American Association for the Treatment of Opioid Dependence;
3. contacted investigators and relevant trial authors seeking information about unpublished or incomplete trials.

All searches included non-English language literature and studies with English abstracts were assessed for inclusion. When considered likely to meet inclusion criteria, abstracts were translated.

Data collection and analysis

Selection of studies
Two review authors (JK, CAF) independently screened titles and abstracts and selected studies potentially relevant to the review. Differences between selection lists were resolved by discussion with a third and fourth review author with respective thematic and methodological expertise (WC, COG). Full-text copies of each potentially relevant paper were obtained, as well as full reports of references with inadequate information in order to definitively determine relevance.

Two review authors (JK, CAF) independently re-evaluated whether studies were eligible for the review or not, according to the inclusion criteria. A second opinion on several studies was sought from the third author (COG) or an independent expert (S Minozzi, M Trivela). One review author (JS) inspected citations rejected during the screening on title and abstract and screening on full report. The processes of abstract screening, study selection and data extraction were facilitated with the Epip Reviewer 4 software.

Data extraction and management
Two review authors (JK, CAF) independently extracted data from the full-text reports using electronic version of an amended data extraction form of the Cochrane Drug and Alcohol review group (CDAG). Disagreements were resolved by mutual discussion. A third review author (JS) inspected the extracted outcomes after the two review authors had independently completed data extraction.

Assessment of risk of bias in included studies
The 'Risk of bias' assessments for RCTs and CCTs in this review were performed using the criteria recommended by the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). The recommended approach for assessing risk of bias in studies included in Cochrane review is a two-part tool addressing five specific domains (namely, sequence generation, allocation concealment, blinding, incomplete outcome data and other issues). The first part of the tool involves describing what was reported to have happened in the study. The second part of the tool involves assigning a judgement relating to the risk of bias for that entry in terms of high, low or unclear risk of bias. To make these judgements we used the criteria indicated by the Cochrane Handbook for Systematic Reviews of Interventions adapted to the addiction field. See table in Appendix 6 for details.

The domains of sequence generation and allocation concealment (avoidance of selection bias) were addressed in the tool by a single entry for each study.

Blinding of participants and providers was not possible for the kind of intervention. Blinding of outcome assessor (avoidance of detection bias) was considered separately for objective outcomes (e.g. drop-out, substance use measured by urine analysis, subjects relapsed at the end of follow-up, subjects engaged in further treatments) and subjective outcomes (e.g. duration and severity of signs and symptoms of withdrawal, patient self-reported use of substance, side effects, social functioning as integration at school or at work, family relationship, etc.).

Incomplete outcome data (avoidance of attrition bias) was considered for all outcomes except for the drop-out from the treatment, which is very often the primary outcome measure in trials on addiction. It was assessed separately for results at the end of the study period, and for results at follow-up.

Measures of treatment effect
The results were not pooled in a meta-analysis owing to a substantial clinical and statistical heterogeneity. For continuous data, mean differences (MD) between the intervention and comparator groups with 95% confidence intervals (CI) were calculated. Dichotomous outcomes were presented as risk ratios (RR), with 95% CIs.
Unit of analysis issues
The meta-analysis was not performed, therefore unit-of-analysis error was not an issue. Only one multi-arm trial was included in the review and it was not used more than once in any of the comparisons.

Dealing with missing data
Four authors of original studies were contacted by email for missing data (April 2012) and reminded after two weeks. To date, two study authors have responded and provided additional information.

Assessment of heterogeneity
Investigations of heterogeneity were not conducted owing to the low number of included studies.

Assessment of reporting biases
The potential for reporting bias was planned to be further explored by funnel plots if more than 10 RCTs were included; however, this was not possible because only four RCTs were found.

Data synthesis
A formal meta-analysis was not possible owing to substantial differences between studies; there were no two studies similar enough to be considered for pooling. Results of included studies are reported individually for each trial, re-expressed as RRs for dichotomous outcomes and MDs for continuous outcomes, and reported with 95% CIs. A fixed-effect model was used because there was only one study for each comparison.

Subgroup analysis and investigation of heterogeneity
Investigations of heterogeneity were not conducted. If sufficient information had been available, the following subgroup analyses were planned:

1. types of psychosocial interventions (e.g. motivational vs. behavioural or BIs);
2. length of the interventions (short, medium, extended).

The following subgroup analyses were also anticipated, but not performed:

1. sustained benefit at six and 12 months after intervention;
2. gender differences;
3. single-drug (alcohol) versus poly-drug focused interventions;
4. single-drug (alcohol) versus poly-drug focused interventions, which also address other health-related behaviours.

Sensitivity analysis
If sufficient information had been available, sensitivity analyses were planned according to the methodological quality criteria used for study inclusion:

- studies with a high risk of bias were to be excluded from the analysis; this decision was to be based on a pre-defined cut-off score (i.e. studies judged to be at high risk of bias for three and more risk items, including selection bias, were to be excluded);
- a separate sensitivity analysis was to be performed excluding CCTs.

Consumer participation
Consumer participation in the preparation of the protocol and the review itself was sought by: a) the first review author (JK), who is a member of the Cochrane Consumers Network, b) the Consumers network was approached to assist with a plain language summary of the review, and c) one of the co-authors of this review (EK) contributed to consumer consultation during the protocol and review development, as he was a practicing clinician in a healthcare facility with a high prevalence of this problem.

Results

Description of studies
See Characteristics of included studies and Characteristics of excluded studies tables.

Results of the search
Electronic searches yielded 7207 abstracts for review, and six additional records were identified through searching other sources. Duplicates were removed (by S. Mitrova) and 5523 references were excluded on the basis of title and abstract; 25 reports were acquired in full text for more detailed evaluation; 18 full-text reports were excluded and seven reports were included (describing four RCTs). No additional studies were found through reference checking. The process and results of study identification are outlined in a flow diagram (Figure 1) according to the PRISMA statement (Moher 2009).

Included studies
Four studies (594 participants) were eligible for this review. The studies assessed the effectiveness of six psychosocial interventions: CBT, 12-step facilitation (TSF), BI, hepatitis health promotion (HHP), MI and brief motivational intervention (BMI).

Type of psychosocial intervention and setting
1. CBT versus TSF in an outpatient clinic (Carroll 1998).
2. BI versus treatment as usual in an outpatient clinic with/out opioid substitution treatment (Feldman 2011).
3. MI (group) versus HHP in an opioid substitution clinic (Nyamathi 2010).
4. MI (single) versus HHP in an opioid substitution clinic (Nyamathi 2010).
5. BMI versus assessment only in a needle exchange programme (Stein 2002a).

Countries in which the studies were conducted: three studies were conducted in USA and one in Switzerland.

Duration of the trials: range from four to 12 weeks (plus various follow-ups), mean 7.5 weeks. Between one and 16 sessions were offered to participants, mean 5.5 (from 15 minutes to 16 hours of treatment time).

Participants: 594 problem drug users*: 33% were female. Mean age was 38.3 years.

*one multi-arm trial included 122 participants (Carroll 1998); however, only two psychosocial arms (N = 41) were considered for this review.

See Characteristics of included studies table for more detailed information.

Excluded studies
Thirty studies did not meet the criteria for inclusion in this review, for more information see Characteristics of excluded studies table.

The grounds for exclusion were: type of intervention not in the inclusion criteria (no studies); type of participants not in the inclusion criteria (23 studies); type of outcomes not in the inclusion criteria (six studies); study design not in the inclusion criteria (one study).

Risk of bias in included studies
Summary results across studies for each domain, see Figure 2 and Figure 3. See Characteristics of included studies table for more detailed information.

Allocation (selection bias)
Random sequence generation
Random sequence generation was judged as adequate in two studies (for one of them this was based on unpublished information from email communication with the study authors), and unclear in the remaining trials.

Allocation concealment
Only one study was judged being at low risk of bias, one was judged at high risk of bias and the remaining at unclear risk of bias.

Blinding (performance bias and detection bias)
Objective outcomes
- abstinence or use of substance measured by patients with negative urine-tests, or breathalysers: participants and personnel were not blinded in all studies for the kind of interventions, and objective outcomes were not reported in the trials. They were used as an additional measure to confirm abstinence in two studies.

Subjective outcomes
- abstinence or use of substance as measured by self-reported or interviewer-administered questionnaires: participants and personnel were not blinded in all studies for the kind of interventions; two studies (50%) specified that outcome assessors were blinded and were judged to be at low risk of bias. Two studies reported that the outcome assessor was not blinded and were judged at high risk of bias; for one of them this is unpublished information from email communication with the study authors.

Incomplete outcome data (attrition bias)
End of study outcomes
- (except retention in treatment): only one study measured this type of outcome and it was judged as high risk because the drop-out rates were not balanced across all groups in the trial (e.g. “the psychotherapy groups had significantly lower retention rates than the medication groups” (Carroll 1998).

Follow-up outcomes
- (except retention in treatment): three studies were judged to be at low risk of bias because there were few patients (less than 10%) withdrawn from the studies, or there was a high rate of drop-out but percentages were balanced across intervention groups and reasons for withdrawn were provided, or authors performed an intention to treat (ITT) analysis. One study was judged to be at high risk of bias because of a high drop-out rate, which was unbalanced across groups.

Effects of interventions
Meta-analysis of all included studies was not possible. The results were summarised according to the type of psychosocial intervention, with comparisons of quantitative data where possible. The included studies used different questionnaires to measure their outcomes and for many of them the authors did not report the post-treatment/follow-up scores or they did not state what was considered to represent mild, moderate and severe categories. This prevented comparison of results across studies. One study had three arms, in this case they were entered into two separate comparisons (group and single format), so they were not counted twice. See Characteristics of included studies table for more detailed information.
We present the effects of the interventions by comparisons examined in the primary studies. Primary outcome was alcohol use or abstinence and secondary outcome was illicit drug use or abstinence. Other secondary outcomes were planned at the protocol stage of the review: engagement in further treatment (i.e. drop-out rates, utilisation of health services) and alcohol-related problems or harms. These are not reported here because they were not measured in the identified trials.

1. **Cognitive-behavioural coping skills training versus 12-step facilitation**

   **Continuous outcomes**

   1.1.1 Alcohol abstinence as maximum number of weeks of consecutive alcohol abstinence during treatment
   
   One study, 41 participants (Carroll 1998), MD 0.40 (95% CI -1.14 to 1.94), the difference was not statistically significant, see Analysis 1.1.

   1.1.2 Illicit drug abstinence as maximum number of weeks of consecutive abstinence from cocaine during treatment
   
   One study, 41 participants (Carroll 1998), MD 0.80 (95% CI -0.70 to 2.30), the difference was not statistically significant, see Analysis 1.1.

   1.2.1 Alcohol abstinence as number achieving three or more weeks of consecutive alcohol abstinence during treatment
   
   One study, 41 participants (Carroll 1998), RR 1.96 (95% CI 0.43 to 8.94), the difference was not statistically significant, see Analysis 1.2.

   1.2.2 Illicit drug abstinence as number achieving three or more weeks of consecutive abstinence from cocaine during treatment
   
   One study, 41 participants (Carroll 1998), RR 1.10 (95% CI 0.42 to 2.88), the difference was not statistically significant, see Analysis 1.2.

   1.2.3 Alcohol abstinence during follow-up year
   
   One study, 41 participants (Carroll 1998), RR 2.38 (95% CI 0.10 to 55.06), the difference was not statistically significant, see Analysis 1.2.

   1.2.4 Illicit drug abstinence as abstinence from cocaine during follow-up year
   
   One study, 41 participants (Carroll 1998), RR 0.39 (95% CI 0.04 to 3.98), the difference was not statistically significant, see Analysis 1.2.

2. **Brief intervention versus treatment as usual**

   **Continuous outcomes**

   2.1.1 Alcohol use as AUDIT scores at three months
   
   One study, 110 participants (Feldman 2011), MD 0.10 (95% CI -2.96 to 3.16), the difference was not statistically significant, see Analysis 2.1.

   2.1.2 Alcohol use as AUDIT scores at nine months
   
   One study, 110 participants (Feldman 2011), MD 1.50 (95% CI -1.74 to 4.74), the difference was not statistically significant, see Analysis 2.1.

   2.1.3 Alcohol use as number of drinks per week at three months
   
   One study, 110 participants (Feldman 2011), MD 2.40 (95% CI -4.59 to 9.39), the difference was not statistically significant, see Analysis 2.1.

   2.1.4 Alcohol use as number of drinks per week at nine months
   
   One study, 110 participants (Feldman 2011), MD -1.70 (95% CI -8.93 to 5.53), the difference was not statistically significant, see Analysis 2.1.

   **Dichotomous outcomes**

   2.2.1 Alcohol use as decreased alcohol use at three months
   
   One study, 110 participants (Feldman 2011), RR 0.32 (95% CI 0.19 to 0.54), the difference was statistically significant (P < 0.0001) in favour of treatment as usual, see Analysis 2.2.

   2.2.2 Alcohol use as decreased alcohol use at nine months
   
   One study, 110 participants (Feldman 2011), RR 0.16 (95% CI 0.08 to 0.33), the difference was statistically significant (P < 0.0001) in favour of treatment as usual, see Analysis 2.2.

3. **Motivational interviewing (group) versus hepatitis health promotion**

   **Continuous outcomes**

   3.1.1 Alcohol use (unpublished) as number of standard drinks consumed per day over the last 30 days
   
   One study, 147 participants (Nyamathi 2010), MD -0.40 (95% CI -2.03 to 1.23), the difference was not statistically significant, see Analysis 3.1.

   3.1.2 Illicit drug use (unpublished) as frequency of drug use (as measured by Addiction Severity Index - ASI drug)
One study, 147 participants (Nyamathi 2010), MD 0.00 (95% CI -0.03 to 0.03), the difference was not statistically significant, see Analysis 3.1.

3.1.3 Illicit drug use (unpublished) as a composite drug score (frequency*severity for all drugs taken)
One study, 151 participants (Nyamathi 2010), MD 0.00 (95% CI -0.42 to 0.42), the difference was not statistically significant, see Analysis 3.1.

This study reported an additional outcome as a change score for: daily drug use since baseline (past 30 days and six-month recall). We do not report this calculated variable here because authors provided us with unpublished results of two original variables that fed into this aggregate variable. Moreover, the published article reported scores for this variable as a mean change between assessment scores together with standard errors (SEs), which would have to be transformed into standard deviations (SDs).

Dichotomous outcomes
3.2.1 Alcohol use as greater than 50% reduction in number of standard drinks consumed per day over the last 30 days
One study, 166 participants (Nyamathi 2010), RR 1.10 (95% CI 0.82 to 1.48), the difference was not statistically significant, see Analysis 3.2.

3.2.2 Alcohol abstinence as abstinence from alcohol over the last 30 days
One study, 166 participants (Nyamathi 2010), RR 0.88 (95% CI 0.49 to 1.58), the difference was not statistically significant, see Analysis 3.2.

4. Motivational interviewing (single) versus hepatitis health promotion
Continuous outcomes
4.1.1 Alcohol use (unpublished) as number of standard drinks consumed per day over the last 30 days
One study, 155 participants (Nyamathi 2010), MD -0.10 (95% CI -1.89 to 1.69), the difference was not statistically significant, see Analysis 4.1.

4.1.2 Illicit drug use (unpublished) as frequency of drug use (as measured by Addiction Severity Index - ASI drug)
One study, 155 participants (Nyamathi 2010), MD 0.00 (95% CI -0.03 to 0.03), the difference was not statistically significant, see Analysis 4.1.

4.1.3 Illicit drug use (unpublished) as a composite drug score (frequency*severity for all drugs taken)
One study, 157 participants (Nyamathi 2010), MD -0.10 (95% CI -0.46 to 0.26), the difference was not statistically significant, see Analysis 4.1.

This study reported an additional outcome as a change scores for: daily drug use since baseline (past 30 days and six-month recall). We do not report this calculated variable here because authors provided us with unpublished results of two original variables which fed into this aggregate variable.

Dichotomous outcomes
4.2.1 Alcohol use as greater than 50% reduction in number of standard drinks consumed per day over the last 30 days
One study, 177 participants (Nyamathi 2010), RR 0.92 (95% CI 0.68 to 1.26), the difference was not statistically significant, see Analysis 4.1.

4.2.2 Alcohol abstinence as abstinence from alcohol over the last 30 days
One study, 177 participants (Nyamathi 2010), RR 0.97 (95% CI 0.56 to 1.67), the difference was not statistically significant, see Analysis 4.1.

5. Brief motivational intervention versus assessment only
Continuous outcomes
5.1.1 Alcohol use as number of days in the past 30 days with alcohol use at one month
One study, 187 participants (Stein 2002a), MD -0.30 (95% CI -3.38 to 2.78), the difference was not statistically significant, see Analysis 5.1.

5.1.2 Alcohol use as number of days in the past 30 days with alcohol use at six months
One study, 187 participants (Stein 2002a), MD -1.50 (95% CI -4.56 to 1.56), the difference was not statistically significant, see Analysis 5.1.

Dichotomous outcomes
5.2.1 Alcohol use as 25% reduction of drinking days in the past 30 days
One study, 187 participants (Stein 2002a), RR 1.23 (95% CI 0.96 to 1.57), the difference was not statistically significant, see Analysis 5.2.

5.2.2 Alcohol use as 50% reduction of drinking days in the past 30 days
One study, 187 participants (Stein 2002a), RR 1.27 (95% CI 0.96 to 1.68), the difference was not statistically significant, see Analysis 5.2.
5.2.3 Alcohol use as 75% reduction of drinking days in the past 30 days
One study, 187 participants (Stein 2002a), RR 1.21 (95% CI 0.84 to 1.75), the difference was not statistically significant, see Analysis 5.2.

5.2.4 Alcohol use as one or more drinking days' reduction in the past 30 days
One study, 187 participants (Stein 2002a), RR 1.12 (95% CI 0.91 to 1.38), the difference was not statistically significant, see Analysis 5.2.

5.2.5 Alcohol use as seven or more drinking days' reduction in the past 30 days
One study, 187 participants (Stein 2002a), RR 1.67 (95% CI 1.08 to 2.60), the difference was statistically significant in favour of BI (P = 0.02), see Analysis 5.2.

Other analyses
The following subgroup analyses were planned at the protocol stage of this review:
- type of psychosocial intervention (e.g. motivational vs. behavioural or BIs);
- length of the intervention (short, medium, extended);
- sustained benefit at six and 12 months after intervention;
- gender differences;
- single-drug (alcohol) versus poly-drug focused interventions;
- single-drug (alcohol) versus poly-drug focused interventions which also address other health-related behaviours;
- studies with low and unclear risk of bias.

None of the planned subgroup analyses were performed because there were not enough data/studies and high/unclear risk of bias in the included trials. Sensitivity analysis, assessment of heterogeneity and assessment of reporting biases were not performed for the same reasons.

Discussion
Summary of main results
Four studies involving 594 participants were included in this review. The studies assessed the effectiveness of six psychosocial interventions: CBT, TSF, BI, HHP, MI and BMI.

There was significant clinical and reporting heterogeneity among the included studies, which precluded meta-analysis. The outcomes were analysed only in single studies. Comparing different psychosocial interventions, there was only one study for each comparison. Most of the comparisons were not statistically significant, except for decreased alcohol use at three months (RR 0.32; 95% CI 0.19 to 0.54) and nine months (RR 0.16; 95% CI 0.08 to 0.35) in the Feldman 2011 study. Surprisingly, these results favoured the control intervention. This could be interpreted in the light of the main limitations of this study, namely, the standard intervention provided to the control group was 'too strong' to enable reasonable comparison with the intervention group, and the intervention group had a high proportion of people with alcohol addiction who received the 15-minute-long brief alcohol intervention. This is in contradiction to the manual for BIs, which states that people with alcohol addiction should not receive BI, but should be referred to a specialised, more intensive treatment (Babor 2001). Evidence from other systematic reviews examining the general population indicates that BI is effective for harmful/hazardous use, but not for dependence (Moyer 2002; Raistrick 2006). Finally, participants receiving BMI were significantly more likely to reduce their alcohol use by seven or more days in the past 30 days at six months' follow-up, compared to control group (RR 1.67; 95% CI 1.08 to 2.60).

Overall completeness and applicability of evidence
The identified studies are not sufficient to address all objectives of this review. All included studies were conducted in US and Switzerland, which limits their applicability to other contexts. A substantial proportion of participants in the included studies had significant problems with alcohol (e.g. a diagnosis of abuse or dependence), which may have impacted on the effectiveness of the short-term therapies offered to them. These people may require more intensive interventions, as BIs have been shown to be effective among people with less severe alcohol problems (Raistrick 2006). Only one study examined a longer type of intervention (i.e. 16 sessions); however, it included only 41 participants and reported their outcomes in a way that precluded comparison with other studies (Carroll 1998).

How do the results of this review fit into the context of current practice? This review selected a very narrow clinical question that was limited to a very specific population of patients or clients. Although the size of this population is not negligible, it is highly unlikely that all of the patients of a treatment service in a real-life setting will have both of the conditions selected as the eligibility criteria for this review. These stringent eligibility criteria strengthened the internal validity of the review; however, with an inevitable detriment to its external validity. A typical clinician in an actual treatment clinic would normally deal with a mixture of problem drug users who may or may not have other concurrent conditions or co-morbidities. To manage this demanding patient workload, they may want to consider other studies, which did not meet the eligibility criteria of our review (see Characteristics of excluded studies table).

Quality of the evidence
Key methodological limitations
Methodological quality of the included studies was generally considered as low.
Half of the studies failed to describe random sequence generation and allocation concealment satisfactorily, with one trial being judged as high risk of allocation concealment. Two studies had low risk of bias on sequence generation. None of the studies were double blinded owing to the type of intervention assessed (psychosocial). For risk of bias related to incomplete outcome data, end-of-study outcomes were assessed in one trial only, and this was judged to be at high risk of bias. Three studies were judged to be at low risk of bias related to incomplete outcome data at follow-up, and one was judged as unclear risk.

Regarding the risk of bias at an outcome level, we could not assess the objective outcomes (alcohol/drug use measured by breathalysers or urine-analysis) because they were used only as an additional measure to check for accuracy of the self-reported alcohol/drug use in two studies, and therefore their scores were not reported in the primary studies. Two studies did not use objective measures of outcomes at all. For subjective outcomes (alcohol/drug use measured by self-reports), two studies were judged at unclear or high risk of detection bias. Sensitivity analysis, including or excluding studies at high risk of bias, was not performed owing to a small number of identified studies. Similarly, it was impossible to pool the data for illicit drug use outcomes or any other anticipated secondary outcomes (e.g. physical or psychological health).

### Indirectness of evidence

Studies providing indirect evidence about our research question, for example trials that included illicit drug users with and without a concurrent problem alcohol use, were not included in this review. Other sources of indirectness, for example interventions, outcomes or comparators, were not identified.

### Inconsistency of results

We identified only small unexplained heterogeneity or inconsistency in the results. One trial found the control intervention to be more beneficial than the experimental intervention on a calculated, dichotomised outcome. Most studies did not find significant, or found only a small, differences in effectiveness between the compared interventions on their primary outcomes.

### Potential biases in the review process

There is a small chance that we missed some trials during the identification of relevant studies. We did not limit our searches to studies published in English; however, studies in non-English languages may have been missed because they are commonly less indexed in the selected databases. Unpublished studies may also have been missed. Unpublished studies are likely to have negative results, which is why they are not published. None of the authors who were contacted for information about unpublished or ongoing trials provided this information. Owing to a small number of included studies, we did not conduct the funnel plot for publication bias. The major limitation of the review process was that most trials did not provide enough published data, or data in a form that could be extracted for meta-analysis. Although all four authors were emailed, only two responded and provided further data. Furthermore, we could not include a number of potentially relevant studies, because they involved drug users without problem alcohol use in their samples.

### Agreements and disagreements with other studies or reviews

Comparison of our review with other studies or reviews is complicated by the fact that we did not perform any meta-analysis and therefore do not have any aggregated results to allow this type of comparison. As described in the background section, two narrative literature reviews dealt with our research question to date (Arias 2008; Bickel 1987). Similarly to our work, these reviews were unable to identify evidence to answer our question or to conduct a meta-analysis. Subsequently, they based their conclusions on evidence coming from a mixed type of studies (e.g. case studies, RCTs) or studies that included illicit drug users without a concurrent problem alcohol use. We excluded this type of studies (see Characteristics of excluded studies). Furthermore, the review by Arias 2008 discussed 14 reports/studies about treatment of co-occurring alcohol and cocaine/opioid dependence, two of which were included in our review.

This review is unintentionally tapping into a sensitive controversy regarding the requirement of providing ancillary counselling services to patients in opioid substitution treatments. The questions are: do additional services provided to patients in MMT improve their outcomes? Does adding any psychosocial support to standard maintenance treatments yield additional benefits?

There are a number of ways to answer this question. While previous studies (Amato 2011; Gossop 2006; McLellan 1993; Schwartz 2012) answered this question by providing evidence of effectiveness of these interventions for general/mixed conditions/outcomes, which were based on mixed populations with or without concurrent alcohol problems, or based on mixed types of interventions (i.e. pharmacological plus psychosocial), we focused on a single type of intervention and a ‘pure’ population where all participants had both alcohol and drug problems. This may be one of the reasons why our review found such a small number of studies. Nevertheless, our findings concur with the weakness of the evidence base to answer this important question, as reported in a previous Cochrane review (Amato 2011).

Another important question is: what constitutes standard maintenance/outpatient treatment? It appears that all standard treatments contain some type of psychosocial support, which varies considerably, and this makes it difficult to evaluate the added value of additional services. This was true for studies included in our review and, in addition, the process of assessment or quick feedback following the assessment, or both, resulted in improved alcohol outcomes among the participants.

### Authors’ conclusions

#### Implications for practice
Based on the weak evidence identified in this review, we cannot recommend using or ceasing psychosocial interventions for problem alcohol use in illicit drug users. In addition, no reliable conclusions can be made from these data regarding the effectiveness of different types of psychosocial interventions for the target condition. Similarly to other conditions, problem alcohol use has better prospects for a successful treatment if approached early. Evidence from the general population suggests that we need to focus on early detection and intervention as well as try to influence more established alcohol patterns of use. Early interventions are not implemented into routine care, especially in the settings where there is a potential for impact owing to high exposure, such as primary health care. Notwithstanding the clear benefit and feasibility of such early interventions (Kaner 2007), systematic reviews of the literature show that their integration into primary care is variable (2% to 93%) (e.g. Anderson 2004; Williams 2011), and a similar variation has been documented in state-level approaches to addressing problem alcohol use in opioid treatment programmes (Harris 2010). In addition, challenges to successful integration of alcohol-related interventions for problem drug users into general medical care were reported (Klimas 2012).

Given the high rates of co-occurrence of alcohol and drug problems, integration of alcohol- and drug-orientated interventions appears as a logical action, but in light of this review remains without an evidence base.

Implications for research

This review emphasises the need for RCT to test the effectiveness of psychosocial interventions in reducing problem alcohol use in illicit drug users. We recommend trials of robust methodology, which are reported well to allow for critical appraisal. For researchers planning an RCT in this area, we recommend to design their study as follows (according to the EPICOT format for research recommendations on the effects of treatments, see Brown 2006).

- **E** Evidence (what is the current state of the evidence?): the current evidence is limited to four RCTs conducted in outpatient/community setting, two of them with an accompanying opioid substitution treatment. More RCTs are needed.
- **P** Population (what is the population of interest?): adults, including younger adults, who are identified as problem drug users with a concurrent and confirmed problem alcohol use; people in or out of a formal addiction treatment.
- **I** Intervention (what are the interventions of interest?): psychosocial intervention, that is talking therapy or counselling (e.g. MI, CBT, contingency management, family therapy, BI, etc.).
- **C** Comparison (what are the comparisons of interest?): treatment as usual, no intervention, waiting list, other psychosocial interventions; pharmacological treatments (alone, or in combination with psychosocial treatments); interventions of different type, length and intensity.
- **O** Outcome (what are the outcomes of interest?): reduction in/abstinence from alcohol or drug use, or from both. In order to be able to combine outcomes of future trials with our current data, outcome measures of future trials should include formal validated instruments, for example AUDIT questionnaire. Objective measures of these outcomes should be used in conjunction to self-reports wherever possible, for example breathalysers, urine-analysis.
- **T** Time stamp (date of literature search): 22 November 2011.

Acknowledgements

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Contributions of authors

JK: designing and coordinating the review, writing and re-drafting the protocol and full review.
WC, CAF, COG: contributing to design of the review and commenting on drafts.
LG, JS: providing methodological advice and commenting on review drafts.
GB, EK, CD: commenting on review drafts.

Declarations of interest

The authors declare that they have no competing interests.

Differences between protocol and review

The protocol intended to exclude studies comparing psychosocial with pharmacological treatments. However, trials with two psychosocial arms and pharmacological arms were exempted from this rule in the review. The subgroup/sensitivity analyses, anticipated in the protocol, were not conducted owing to a lack of studies. Wording of the primary and secondary outcome measures from the protocol was simplified for ease of presentation, as follows:

1. reduction and/or stabilisation of alcohol use = alcohol use or abstinence;
2. illicit drug use outcomes (changes in illicit drug use) = illicit drug use or abstinence.

New references have been added to the Background sections: Description of the condition and Why is it important to do this review, to reflect recent developments in the field. Text in the sections: Experimental interventions and Types of participants...
was reduced to exclude examples. The Newcastle-Ottawa scale for assessing the quality of non-randomised studies (NOS) was removed from the review as it was not used because observational studies were not included in the review.

**Published notes**

**Characteristics of studies**

**Characteristics of included studies**

**Carroll 1998**

<table>
<thead>
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<th>Methods</th>
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<tbody>
<tr>
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<td>years of alcohol misuse - lifetime</td>
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<td>primary route of administration: nasal 11%, smoking 84%, intravenous 5%</td>
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<td>previous treatment: alcohol 32%, drugs 58%</td>
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### Interventions

Description of the experimental and control interventions:
The trial included 5 treatment arms: CBT plus disulphiram; TSF plus disulphiram; CM plus disulphiram; CBT plus no medication; TSF plus no medication. We considered only the latter 2 psychosocial arms. CBT was based on Marlatt's relapse prevention model and TSF was adapted from that used in Project MATCH and was grounded in the concept of substance dependence as a spiritual and medical disease.

Route of delivery: treatments were manual-guided, 4 doctoral-level psychologists conducted CBT, 2 masters-level clinicians conducted TSF.

Number of participants allocated to each group: 25 in CBT plus no medication; 19 in TSF plus no medication.

Duration of the intervention: 12 weeks, 16 individual sessions.

Duration of follow-up: 12 weekly assessments within-treatment, and at 1, 3, 6, 12 months.

Country of origin, setting: a non-profit substance abuse treatment centre (APT foundation) affiliated with Yale University in New Haven, Connecticut.

### Outcomes

1.1.1 Alcohol abstinence as maximum number of weeks of consecutive alcohol abstinence during treatment
1.1.2 Illicit drug abstinence as maximum number of weeks of consecutive abstinence from cocaine during treatment
1.2.1 Alcohol abstinence as number achieving 3 or more weeks of consecutive alcohol abstinence during treatment
1.2.2 Illicit drug abstinence as number achieving 3 or more weeks of consecutive abstinence from cocaine during treatment
1.2.3 Alcohol abstinence during follow-up year
1.2.4 Illicit drug abstinence as abstinence from cocaine during follow-up year

### Notes

All sessions were recorded and checked and rated for the accuracy and fidelity of the intervention.

"Subjects also met weekly with an independent clinical evaluator who collected urine specimens, assessed cocaine and alcohol use and monitored other clinical symptoms."

"Patients were paid $25 for each follow-up interview, with a $10 increase for each consecutive interview they attended, to encourage more complete data collection. In addition, patients were paid a $5 bonus for attending an interview within 28 days of the target interview date."

- Only 39 subjects completed the full 12-week treatment (compliant treatment completers)
- Participants in the pharmacological arms stayed longer in treatment (patients were not blind to their intervention)
- The specific type of self-report questionnaires not reported in the primary paper (1998), only in the follow-up paper
- Results are reported as No. of weeks of continuous abstinence
- The follow-up report (2000) does not provide any end-point scores (only results of the Random effects regression model)
- Use of cocaine and alcohol were strongly associated with each other during treatment, particularly for the subjects assigned to disulphiram.

### Risk of bias table

<table>
<thead>
<tr>
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<th>Authors' judgement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Not enough information provided; e.g. &quot;Of the 122 randomised subjects, 117 initiated the treatment&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated</td>
</tr>
<tr>
<td>Bias</td>
<td>Authors' judgement</td>
<td>Support for judgement</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear</td>
<td>Objective measures used rather as an accuracy check than an outcome (urine specimens and Brethalyser tests conducted by a blinded evaluator)</td>
</tr>
<tr>
<td>Objective outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Within-study assessments: &quot;Independent clinical evaluator who collected urine specimens, assessed cocaine and alcohol use; the evaluator saw patients in an office physically separated from the therapy offices and instructed patients not to disclose detail of their therapist of treatment&quot;</td>
</tr>
<tr>
<td>Subjective outcomes</td>
<td></td>
<td>Follow-up assessments (2000 paper): &quot;Patients were assessed at face-to-face follow-up interviews conducted 1, 3, 6 and 12 months after the 12-week termination point by an independent clinical evaluator who was blind to both psychotherapy and pharmacotherapy condition&quot;</td>
</tr>
</tbody>
</table>
| Incomplete outcome data (attrition bias)       | High risk          | Within-treatment assessments (1998): "Assignment to disulphiram was associated with significantly better retention in treatment". The psychotherapy groups had significantly lower retention rates than the medication groups: "subjects assigned to disulphiram treatment were retained significantly longer than those assigned to no medication (8.4 versus 5.8 weeks. F= 8.7, p< 0.05)". Retention rates:  
  - CBT/disulphiram group (mean 8.8 weeks)  
  - CM/disulphiram (8.4 weeks)  
  - TSF/disulphiram (8.0)  
  - CBT/no medication (6.3)  
  - TSF/no medication (5.3)  
  "However, such analyses, ..., are confounded by differences among the treatments in retention"

Only 30% completed treatment, however: "Subjects who remained in treatment the full 12 weeks/16 sessions (n=39) did not differ from those who did not start treatment or dropped out (n=83) in terms of gender, race, employment status, route of administration, presence of lifetime affective, anxiety or antisocial personality disorder, but those who met criteria for a nonASP Axis II disorder, were significantly more likely to complete treatment than these who did not (48.1% versus 23.1%)"

Comments:  
1) baseline characteristics provided for the ITT sample (N = 122), but  
2) rates of consecutive abstinence provided for the exposed sample (N = 117)  
3) it is not known whether missing outcome data were balanced in numbers across intervention groups, because group breakdowns for drop-outs are not provided.  
4) psychotherapy groups (CBT, TSF) differed significantly at baseline: for frequency of alcohol use; and medication groups had lower baseline cocaine use
<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete outcome data (attrition bias) Follow up</td>
<td>High risk</td>
<td>All groups had a comparable number of follow-up data points. However, number of drop-outs not reported for each group separately. &quot;It is possible that poorer-functioning subjects who dropped out of treatment early were under-represented in the follow-up data, inflating outcomes in all groups&quot;. &quot;Participants who completed more sessions had better outcomes during follow-up&quot;</td>
</tr>
</tbody>
</table>

**Feldman 2011**

**Methods**

Study design: RCT

Recruitment modality of participants: for 1 year, participation in the study was proposed systematically to each adult outpatient who was treated for opioid or cocaine dependence

**Participants**

Number of participants: 110

Gender: 72.3% male

Age (mean ± SD): 35 ± 7.8 years

Condition: problem alcohol use based on questions from the AUDIT questionnaire, i.e. excessive drinking (7 ≤ AUDIT score < 13 for men and 6 ≤ AUDIT score < 13 for women); and alcohol dependence (score > 13); 43.8% were classified as excessive drinkers and 56.2% as alcohol dependents

Other relevant information: opiate dependence treatment with methadone substitution (56.2%) or diacetyl morphine (heroin treatment; 12%); no opioid substitution and treatment for opiate or cocaine dependence (31.7%)

Most patients with cocaine dependence or with opiate dependence also had tobacco or cannabis dependence. Most patients had 1 or more concomitant psychiatric disorders (mood disorder, 35.6%; personality disorder, 34%; anxiety disorders, 14.7%; psychotic disorders, 9.4%). "Diagnoses were established according to the criteria of the ICD-10) by a resident and a senior psychiatrist"
| Interventions | Description of the experimental and control interventions: the intervention group was BI and the control group was TAU.  
(1) BI: BI was delivered in 1 session, based on WHO guidelines, delivered by a trained staff (4 hours' training). The intervention group received the same TAU as controls. The outpatient staff consisted of a psychiatrist, general practitioner, psychologist, nurse, and social worker  
(2) TAU: "The control group received TAU in addition to AUDIT and score feedback. TAU refers to outpatient pharmacological and psychosocial treatment. Maintenance treatment with methadone or heroin included medical and psychiatric follow-up, primary health care, psychosocial interventions, and administration of opiate treatments in a clinical setting. Psychosocial treatment included medical and psychiatric follow-up, primary health care, psychosocial interventions, and, if necessary, administration of pharmacotherapy in a clinical setting"  
Number of participants allocated to each group: 60 in BI, 52 in TAU  
Duration of the intervention (mean ± SD): 16 ± 4.7 minutes  
Duration of follow-up: 3 and 9 months  
Country of origin, setting: specialised outpatient clinic in the Division of Substance Abuse of the University Hospitals of Geneva, Switzerland |
| Outcomes | 2.1.1 Alcohol use as AUDIT scores at 3 months  
2.1.2 Alcohol use as AUDIT Scores at 9 months  
2.1.3 Alcohol use as number of drinks per week at 3 months (number of glasses of alcohol per week, 1 glass: 10 g of alcohol; wine = 100 mL; beer = 250 mL; spirits = 25 mL)  
2.1.4 Alcohol use as number of drinks per week at 9 months  
2.2.1 Alcohol use as decreased alcohol use at 3 months  
2.2.2 Alcohol use as decreased alcohol use at 9 months  
2.2.3 and 2.2.4 Increased or unchanged alcohol use at 3 and 9 months (i.e. reverse of the above) |
| Notes | The patients in both groups were already in treatment for opioid or cocaine dependence before study inclusion. Patients allocated to BI received this intervention 2 or 3 weeks after AUDIT screening  
The WHO manual recommends to refer patients with alcohol dependence to specialist treatment without providing BI  
All screened patients received feedback that explained the meaning of their AUDIT score  
Almost 40% of the sample was lost to follow-up  
More participants had success (decreased alcohol use) in control group than intervention. Strong effect of TAU in the control group |
<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: &quot;The randomisation scheme was drawn by a statistician, who used the Web site [<a href="http://www.randomizer.org/">http://www.randomizer.org/</a>]. A random permuted block method was used, with blocks of 4 patients&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: &quot;The sequence was concealed from all investigators with numbered opaque sealed envelopes prepared by the statistician and handed over to the physician in charge of the study&quot;</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) Objective outcomes</td>
<td>Unclear risk</td>
<td>Not available, objective measures not used</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) Subjective outcomes</td>
<td>High risk</td>
<td>Not stated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unpublished information: &quot;There is no blinding assessment&quot;</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) End of Study outcomes</td>
<td>Unclear risk</td>
<td>Not available. The study did not assess outcomes at the time of the study end</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) Follow up</td>
<td>Low risk</td>
<td>Modified ITT analysis (multiple imputation, random assumption) At T0 - 1 person not included in analysis because of data-entry errors, both in both control and intervention group Number of drop-outs and reasons: &quot;Of the BI group, 59.3% completed the last observation and of the control group, 58.8% completed it&quot; Intervention (T0 = 51, T3 = 29, T9 = 30) Control (T0 = 59, T3 = 30, T9 = 35) No reasons provided for drop-outs, but regression showed no differences: &quot;Logistic regressions showed that the - Type of drinker- and - Treatment group - did not explain the missingness of data&quot; &quot;Hence, these variables displayed no particular pattern, meaning that the data for excessive drinkers and for alcohol-dependent patients, as well as for the control group and the intervention group, were equally likely to be missing&quot; Comment: dichotomous outcomes: 40% of participants dropped out, but the observed event risk was 10% to 20% (control), and 60% to 80% (intervention)</td>
</tr>
</tbody>
</table>

**Nyamathi 2010**

**Methods**

Study design: RCT open label, 3 arms
Recruitment modality of participants: flyers displayed in 5 methadone treatment sites
| Participants | Number of participants: 256  
Gender: 59.2% male  
Age (mean ± SD): 51.2 ± 8.4 years  
Condition: reported moderate-to-heavy alcohol use based on questions from the ASI. Methadone maintenance treatment was an inclusion criterion (minimum 3 months)  
Other relevant information: fair/poor health: 60.4%  
Depressive symptoms: 80.8%  
Poor emotional well-being: 67.5%  
Ethnicity: African-American: 45.1%; white: 18.8, Latino: 26.7, Other: 9.4, Education: high school graduate 58%  
Partnered: 54.3%  
Employed: 17.3%  
Recent alcohol use at baseline (Mean number standard drinks last 30 days): 0-40: 25.1; 41-89: 24.7; 90-180: 26.7; 180+: 23.5  
Marijuana use in past 30 days: 16%  
IDU in past 30 days: 40%  
Smoke > 1 pack/day: 56.1%  
Self-help program in past 30 days: 21.2%  
Social support: primarily from drug users 12.6%; primarily non-drug users 48.6%, both: 34.9% |
| Interventions | Description of the experimental and control interventions: (1) nurse-led HHP group sessions; (2) MI delivered in group sessions (MI-group), and (3) MI delivered 1-on-1 sessions (MI-single).  
(1) HHP: didactic style, also interactive as the group raised questions. Delivered by a nurse and hepatitis-trained research assistant. Sessions based on "The comprehensive health seeking and coping paradigm (CHSCP; Nyamathi, 1989), originally adapted from Lazarus and Folkman's (1984) stress and coping paradigm and Schlotfeldt's (1981) health seeking paradigm". Staff trained on the integration of the CHSCP into their education delivery.  
Focus: progression of HCV infection and the culturally-sensitive strategies that infected individuals can adopt to prevent or reduce accumulated damage to liver functioning. Strategies included: discussing the dangers of alcohol use on hepatitis (cognitive factors), discussing ways to avoid alcohol and other drugs, eating a balanced diet, dangers of reinfection of HCV by IDU, receiving unsafe tattoos and piercing, having unprotected sexual behaviour, and being consistent in engaging in other health-related behaviours. Additional health promoting activities: enhancing coping, such as seeking positive social support, getting support from religion and building self-esteem when afflicted with a history of drug and alcohol addiction. The HHP was directed by a detailed protocol.  
(2) MI-group: focus: alcohol, risky behaviours, MI spirit; by trained MI specialists, i.e. a PhD-prepared psychologist conducted primarily the MI-group sessions. Content of the individual and group sessions was identical, guided by a detailed protocol and biweekly meetings with the investigator and therapists. The average number of participants was 6 (range 5 to 7)  
(3) MI-single: focus: alcohol, risky behaviours, MI spirit; a MSW-prepared researcher conducted primarily the individual MI sessions  
Number of participants allocated to each group: HHP: N = 87; MI group: N = 79; MI single: N = 90  
Duration of the intervention: 3 x 60-minute sessions, spaced 2 weeks apart  
Duration of follow-up: 6 months  
Country of origin, setting: 5 methadone treatment sites in Los Angeles and Santa Monica, USA |
### Outcomes

3.1.1 Alcohol use (unpublished) as number of standard drinks consumed per day over the last 30 days
3.1.2 Illicit drug use (unpublished) as frequency of drug use (as measured by ASI drug)
3.1.3 Illicit drug use (unpublished) as a composite drug score (frequency * severity for all drugs taken)
3.2.1 Alcohol use as > 50% reduction in number of standard drinks consumed per day over the last 30 days
3.2.2 Alcohol abstinence as abstinence from alcohol over the last 30 days

Outcomes 4.1.1 to 4.2.2 refer to the individual (single) format of MI

### Notes

- 6 participants reported no alcohol use at baseline
- A total of 86.7% of participants completed all 3 sessions and 91.3% completed the 6-month follow-up
- The sessions were open; i.e. participants who had not completed their 3 sessions with their original cohort could complete with a later cohort.
- The original protocol describes HHP as a control intervention (UCG)
- Means (SD) of outcomes measures (ASI, TLFB) are not provided for any of the outcomes; baseline scores are not provided either

### Risk of bias table
<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation               | Low risk           | Quote: "This study was a randomised controlled trial"
Unpublished information: "As participants were enrolled, they were systematically assigned to each of the three arms. In terms of randomisation, we used random assignment using a random number table" |
| Allocation concealment                   | High risk          | Masking: open label                                                                   |
| Source of information: published protocol of the trial |
| Blinding of outcome assessment           | Unclear risk       | Not available, objective measures not used                                             |
| Objective outcomes                       |                    |                                                                                       |
| Blinding of outcome assessment           | High risk          | Masking: open label                                                                   |
| Subjective outcomes                      |                    | Source of information: published protocol of the trial                                 |
| Incomplete outcome data (attrition bias) | Unclear risk       | Not available. The study did not assess outcomes at the time of the study end         |
| End of Study outcomes                    |                    |                                                                                       |
| Incomplete outcome data (attrition bias) | Low risk           | Comment:                                                                              |
| Follow up                                 |                    | All analyses were ITT; however, it is not stated which method of data imputation was used for ITT analysis |
|                                           |                    | Missing data balanced across groups                                                   |
|                                           |                    | Comparability of all 3 arms assessed at baseline                                       |
|                                           |                    | Number of drop-outs and reasons:                                                      |
|                                           |                    | • MI-S (90), 86% completed all sessions, 9% lost to follow-up                          |
|                                           |                    | • MI-G (79), 85% completed all sessions, 10% lost to follow-up                         |
|                                           |                    | • HHP (87), 89% completed all sessions, 7% lost to follow-up                           |
|                                           |                    | Unpublished information: "The 6 reported abstainers were distributed as follows: 2 in MI-Single, 3 in MI-Group and 1 in HHP. No one was excluded from the final regression model based on ethnicity. The statement was erroneously carried over from preliminary modelling. However, since ethnicity was not important in that modelling, it was not included in the final model and there was no need to exclude anyone based on ethnicity. The 6 abstainers were excluded from the logistic regression analysis. "A missing value for drug-using partners caused an additional case to be omitted (actually there were 248 cases in the regression model rather than 249. Two subjects had missing values for drug-using partners)" |

**Stein 2002a**

**Methods**

Study design: RCT

Recruitment modality of participants: study was advertised at 3 NEP sites using posters and NEP volunteers offered all clients referral cards. NEP clients called a study telephone to be screened by a research assistant at a separate research site in hospital. During the initial study visit, all NEP clients presented their study cards (received at NEP). Between February 1998 and October 1999
Participants

Number of participants: 187  
Gender: 119 male (63.6%)  
Age: mean 36.2 years  
Condition: problem alcohol use, i.e. AUDIT-positive (> 8) active IDUs. "Current alcohol abuse or dependence diagnosis was ascertained using the SCID interview. 159 (85.0%) met DSM-IV criteria for current alcohol abuse or dependence (80% for abuse, 70% for dependence)."

Other relevant information:
- mean education: 11.5 years  
- ethnicity: 162 (86.6%) Caucasian  
- most frequently injected drug: heroin for 141 (75.4%) subjects, cocaine for 15 (8.0%), heroin and cocaine for 31 (16.6%)  
- 120 (64.1%) participants visited the NEP at least once a month  
- mean AUDIT score at screening was 22.2.  
- 159 (85.0%) met DSM-IV criteria for current alcohol abuse or dependence (80% for abuse, 70% for dependence)  
- mean ± SD number of drinking days in the past 30 days prior to baseline assessment: 12.0 ± 10.3  
- 71.4% of quantities on all drinking days exceeded conventional criteria defining heavy alcohol consumption (5+ drinks for men and 3+ drinks for women)  
- mean ± SD drinks per drinking days 7.3 ± 5.8

Interventions

Description of the experimental and control interventions: (1) brief MI and (2) control group  
(1) MI: focus on alcohol use and HIV risk-taking  
Goals: to assess the degree to which the patient engages in hazardous drinking; to identify relationships between alcohol consumption and alcohol-related negative consequences including HIV risk behaviour; to identify goals for behaviour change and any barriers to change  
- Included a written change plan, designed to reduce the link between alcohol consumption and hazardous behaviours that may lead to negative consequences of drinking, including HIV risk behaviour  
- Interventionist trained by studying the manual and watching MI tapes from Project MATCH  
- Standard delivery of the MI protocol  
- Adherence monitoring by: an MI checklist completed by the therapist after each session and audiotapes of sessions were randomly reviewed by a supervisor trained in MI  
(2) Control: assessment only, approximately 3 hours  
Number of participants allocated to each group: 95 in MI, 92 in control group  
Duration of the intervention: 2 therapist sessions, 1 month apart; 1st session: 60 minutes, 2nd session: 30 to 45 minutes  
Duration of follow-up: 1 and 6 months  
Country of origin, setting: NEP clients, study site: Rhode Island Hospital in Providence, USA
### Outcomes

5.1.1 Alcohol use as number of days in the past 30 days with alcohol use at 1 month
5.1.2 Alcohol use as number of days in the past 30 days with alcohol use at 6 months
5.2.1 Alcohol use as 25% reduction of drinking days in the past 30 days
5.2.2 Alcohol use as 50% reduction of drinking days in the past 30 days
5.2.3 Alcohol use as 75% reduction of drinking days in the past 30 days
5.2.4 Alcohol use as 1 or more drinking days' reduction in the past 30 days
5.2.5 Alcohol use as 7 or more drinking days' reduction in the past 30 days

Secondary outcome: number of days in the past 30 days with IRRB - defined as answer to 1 question: have you used needles etc. after someone else? (reported only for a subset of 109 participants in the 2002b paper)

### Notes

Study retention: 96.8% at 6 months

Control and MI subjects received identical research assessments at baseline, 1 and 6 months

- at baseline and 1 month later, both MI and control group received a list of referrals for substance abuse and medical treatment
- patients in the control group spent approximately 3 total hours (assessment time) with research staff, "the assessment included sections on demographics, drug and alcohol use, drug and alcohol treatment, health-related quality of life, attitudes and experiences with alcohol and HIV risk behavior"
- the assessment control group also experienced meaningful reduction in alcohol use
- 6-month follow-up: 11 subjects were interviewed in prison and 6 were interviewed by telephone
- total reimbursement: $90 with $20 given at baseline, $30 at the 1-month interview and $40 at the final interview
- 65 (34.8%) participants reported 4 or fewer drinking days at baseline: their maximum possible decrease in drinking days at follow-up is 4 or less (i.e. floor and ceiling effects)
- change in heroin use was not associated with change in alcohol use
- the association between change in IRRB days and change in alcohol use days was not statistically significant

The paper reporting IRRB outcomes (Stein 2002b) was included in another Cochrane review (Meader 2010), therefore it was not considered for this review

### Risk of bias table
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</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>Unclear risk</td>
<td>Not enough information provided: “Following the baseline interview subjects were assigned to treatment conditions using a randomisation schedule created with permuted blocks of eight assignments.” &quot;After randomisation, the research interventionist saw participants assigned to MI...”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated how the randomisation schedule was prepared: “This method ensured that the treatment groups were balanced in number to within four patients throughout the trial. The data manager prepared the randomisation schedule before the first patient enrolled”</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Not available. Objective measures used rather as an accuracy check than an outcome: &quot;During the initial study visit, all NEP subjects presented their study cards (received at NEP), underwent blood alcohol level testing (to ensure subjects were not inebriated, BAL &lt; 0.04)”</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>&quot;At each follow-up assessment, research assistants were blinded to the treatment condition of the subject; the interventionist did not perform research assessments”</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Not available. The study did not assess outcomes at the time of the study end</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>&quot;We conducted an intent-to-treat analysis using a conservative 'worst case scenario' strategy in which observations with missing follow-up data were assigned the maximum value of 30 drinking days, a data imputation approach which tends to minimize observed reductions in mean drinking days across time To ensure that our substantive results were not sensitive to missing observations (there were no condition differences in missing data) we replicated our analyses using observations with complete data (n = 181), and using other imputation strategies (e.g. mean substitution, regression estimation and ‘best case scenario’). All imputation strategies resulted in substantively consistent findings. To evaluate the adequacy of random assignment, we used t- and x2-tests to compare treatment groups with respect to background characteristics and baseline measures of drinking behaviours and alcohol problems” Number of drop-outs and reasons: There were no study withdrawals: 93 of 95 in the MI group received both MI sessions: 2 people missed their second session. 6-month follow-up data were available for 96.8% (N = 181) of the 187 randomly assigned subjects. 3 subjects in each treatment arm were lost to follow-up at 6 months</td>
</tr>
</tbody>
</table>

**Footnotes**


**Characteristics of excluded studies**

*Abou-Saleh 2008*
<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alessi 2007</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol and drug use not an inclusion criterion</td>
</tr>
<tr>
<td>Andreasson 2002</td>
<td>Participants not in the inclusion criteria: participants had alcohol dependence only</td>
</tr>
<tr>
<td>Azrin 1994</td>
<td>Participants not in the inclusion criteria: participants were not problem drug users and concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Azrin 1996</td>
<td>Participants not in the inclusion criteria: participants were not problem drug users and concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Baker 2005</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Baker 2006</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Ball 2007</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Bennett 2002</td>
<td>Study design not in the inclusion criteria: not an RCT</td>
</tr>
<tr>
<td>Bernstein 2005</td>
<td>Outcome not in the inclusion criteria: alcohol use was not measured, because the intervention focused on drug use and the participants were not reported to have problem alcohol use at randomisation</td>
</tr>
<tr>
<td>Black 2011</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol and drug use not an inclusion criterion</td>
</tr>
<tr>
<td>Bowen 2006</td>
<td>Study design not in the inclusion criteria: not an RCT</td>
</tr>
<tr>
<td>Brown 2007</td>
<td></td>
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<tr>
<td>Study Reference</td>
<td>Reason for exclusion</td>
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<tr>
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</tr>
<tr>
<td>Burling 2001</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Chermack 2002</td>
<td>Study design not in the inclusion criteria: not an RCT</td>
</tr>
<tr>
<td>Cohen 1982</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion for all subjects randomised into trial. Quote: &quot;Approximately one-third of all the active alcoholics [n=105] were assigned to each of the three study groups (1983, p864; 1982, p360).&quot; Comment: it is highly probable that non-alcoholics were randomised into trial. Operative alcoholics (N = 105) versus all subjects randomised into trial (N = 127)</td>
</tr>
<tr>
<td>Daeppen 2010</td>
<td>Participants not in the inclusion criteria: concurrent problem drug use not an inclusion criterion. Only 10% to 11% participants smoked cannabis once per week</td>
</tr>
<tr>
<td>Darker 2011</td>
<td>Study design not in the inclusion criteria: not an RCT</td>
</tr>
<tr>
<td>Drapkin 2008</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Drumright 2011</td>
<td>Study design not in the inclusion criteria: not an RCT. A secondary analysis of 2 RCTs that did not have concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Forsberg 2011</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Gruber 2008</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Marsden 2006</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>O'Farrell 2008</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
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</tr>
<tr>
<td>Sanson-Fisher 2010</td>
<td>Participants not in the inclusion criteria: participants were eligible if they had alcohol dependence diagnosis with or without comorbid drug diagnosis</td>
</tr>
<tr>
<td>Staiger 2009</td>
<td>Study design not in the inclusion criteria: not an RCT</td>
</tr>
<tr>
<td>Van Der, 1995</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion. Alcohol was used only by 149 of the 166 participants in the 90 days prior to initial presentation</td>
</tr>
<tr>
<td>Worden 2010</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion. Additionally, 46.6% reported alcohol as their primary drug (review exclusion criterion)</td>
</tr>
<tr>
<td>Zule 2007</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
<tr>
<td>Zule 2009</td>
<td>Participants not in the inclusion criteria: concurrent problem alcohol use not an inclusion criterion</td>
</tr>
</tbody>
</table>

**Footnotes**

RCT: randomised controlled trial.

**Characteristics of studies awaiting classification**

**Footnotes**

**Characteristics of ongoing studies**

**Footnotes**

**Summary of findings tables**

**Additional tables**

**References to studies**

**Included studies**

**Carroll 1998**


**Feldman 2011**

*Feldman N, Chatton A, Khan R, Khazaal Y, Zullino D. Alcohol-related brief intervention in patients treated for opiate or...*

Nyamathi 2010
Published and unpublished data

Stein 2002a
Published data only (unpublished sought but not used)

Excluded studies
Abou-Saleh 2008

Alessi 2007

Andreasson 2002

Azrin 1994

Azrin 1996

Baker 2005

Baker 2006

Ball 2007

Bennett 2002

Bernstein 2005

Black 2011

Bowen 2006

Brown 2007

Burling 2001

Chermack 2002

Cohen 1982

Daeppen 2010

Darker 2011

Drapkin 2008

Drumright 2011

Forsberg 2011
Forsberg LG, Ernst D, Sundqvist K, Farbring CA. Motivational Interviewing delivered by existing prison staff: a randomized controlled study of effectiveness on substance use after release. Substance Use and Misuse 2011;46(12):1477-85.

Gruber 2008

Marsden 2006

O'Farrell 2008

Sanson-Fisher 2010

Staiger 2009

Van Der, 1995

Worden 2010

Zule 2007

Zule 2009

Studies awaiting classification

Ongoing studies

Other references

Additional references

Alcoholics Anonymous 1939

Amato 2011

Amato 2011b

Anderson 2004

Arias 2008

Babor 2001

Bickel 1987

Blankertz 2004

Brown 2006

Budney 2001

Crits-Christoph 1999

**CSAT 2004**


**Dalsbø 2010**


**De Leon 2000**


**DSM-IV**


**EMCDDA 2008**


**Gossop 2000**


**Gossop 2006**


**Harris 2010**


**Hartzler 2010**


**Hartzler 2011**


**Hesse 2007**


**Higgins 2011**


**Hunt 1973**


**Kaner 2007**


**Klimas 2012**

Knapp 2007

Lui 2008

Maremmani 2007

Marlatt 1996

Mayet 2004

McCusker 2001

McLellan 1993

Meader 2010

Messina 2003

Miller 1996

Miller 2002

Miller 2004

Minozzi 2011

Moher 2009

Moyer 2002

NIH 2012
Nilsen 2010

Ostapowicz 1998

Ottomanelli 1999

Pilling 2010

Platt 1995

Prochaska 1992

Raistrick 2006

Schwartz 2012

Shand 2003

Smedslund 2011

Smith 2006

Smyth 1998
Smyth BP, Keenan E, O'Connor JJ. Bloodborne viral infection in Irish injecting drug users. Addiction 1998;93(11):1649-56. [0965-2140: (Print)]

Srivastava 2008

Teplin 2007

Terplan 2007

Thomas 2008

White 1999
Whitlock 2004

WHO 1993

Williams 2011

Other published versions of this review
Classification pending references

AERC 2010

Amato 2008c

Anderson 1993

Babor 1994

Campbell 2000

Fiellin 2000

Joseph 1985

NOS

Sobell 2000

Data and analyses

1 Cognitive-behavioural coping skills training (CBT) versus 12-step facilitation (TSF)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Continuous outcomes</td>
<td>1</td>
<td></td>
<td>Subtotals only</td>
<td></td>
</tr>
<tr>
<td>1.1.1 Alcohol abstinence as maximum number of weeks of consecutive alcohol abstinence during treatment</td>
<td>1</td>
<td>41</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.40[-1.14, 1.94]</td>
</tr>
<tr>
<td>1.1.2 Illicit drug abstinence as maximum number of weeks of consecutive abstinence from cocaine during treatment</td>
<td>1</td>
<td>41</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.80[-0.70, 2.30]</td>
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</tbody>
</table>
1.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2.1 Alcohol abstinence as number achieving 3 or more weeks of consecutive alcohol abstinence during treatment</td>
<td>1</td>
<td>41</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.96[0.43, 8.94]</td>
</tr>
<tr>
<td>1.2.2 Illicit drug abstinence as number achieving 3 or more weeks of consecutive abstinence from cocaine during treatment</td>
<td>1</td>
<td>41</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.10[0.42, 2.88]</td>
</tr>
<tr>
<td>1.2.3 Alcohol abstinence during follow-up year</td>
<td>1</td>
<td>41</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>2.38[0.10, 55.06]</td>
</tr>
<tr>
<td>1.2.4 Illicit drug abstinence as abstinence from cocaine during follow-up year</td>
<td>1</td>
<td>41</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.39[0.04, 3.98]</td>
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2 Brief intervention (BI) versus treatment as usual

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<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
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<tr>
<td>2.1 Continuous outcomes</td>
<td>1</td>
<td>110</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>Subtotals only</td>
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<tr>
<td>2.1.1 Alcohol use as AUDIT scores at 3 months</td>
<td>1</td>
<td>110</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.10[-2.96, 3.16]</td>
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<tr>
<td>2.1.2 Alcohol use as AUDIT Scores at 9 months</td>
<td>1</td>
<td>110</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>1.50[-1.74, 4.74]</td>
</tr>
<tr>
<td>2.1.3 Alcohol use as number of drinks per week at 3 months</td>
<td>1</td>
<td>110</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>2.40[-4.59, 9.39]</td>
</tr>
<tr>
<td>2.1.4 Alcohol use as number of drinks per week at 9 months</td>
<td>1</td>
<td>110</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-1.70[-8.93, 5.53]</td>
</tr>
<tr>
<td>2.2 Dichotomous outcomes</td>
<td>1</td>
<td>41</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>2.2.1 Alcohol use as decreased alcohol use at 3 months</td>
<td>1</td>
<td>110</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.32[0.19, 0.54]</td>
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<tr>
<td>2.2.2 Alcohol use as decreased alcohol use at 9 months</td>
<td>1</td>
<td>110</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.16[0.08, 0.33]</td>
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</table>

3 Motivational interviewing(group) (MI-G) versus hepatitis health promotion (HHP)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Continuous outcomes</td>
<td>1</td>
<td>147</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>Subtotals only</td>
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<tr>
<td>3.1.1 Alcohol use as number of standard drinks consumed per day over the last 30 days</td>
<td>1</td>
<td>147</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-0.40[-2.03, 1.23]</td>
</tr>
<tr>
<td>3.1.2 Illicit drug use as frequency of drug use (as measured by Addiction Severity Index - ASI drug)</td>
<td>1</td>
<td>147</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.00[-0.03, 0.03]</td>
</tr>
<tr>
<td>3.1.3 Illicit drug use as a composite drug score (frequency*severity for all drugs taken)</td>
<td>1</td>
<td>151</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.00[-0.42, 0.42]</td>
</tr>
<tr>
<td>3.2 Dichotomous outcomes</td>
<td>1</td>
<td>166</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>3.2.1 Alcohol use as greater than 50% reduction in number of standard drinks consumed per day over the last 30 days</td>
<td>1</td>
<td>166</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.10[0.82, 1.48]</td>
</tr>
<tr>
<td>3.2.2 Alcohol abstinence as abstinence from alcohol over the last 30 days</td>
<td>1</td>
<td>166</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.88[0.49, 1.58]</td>
</tr>
</tbody>
</table>

4 Motivational interviewing (single) (MI-S) versus hepatitis health promotion (HHP)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
</table>
### 4.1 Continuous outcomes

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as number of standard drinks consumed per day over the last 30 days</td>
<td>1</td>
<td>155</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-0.10[-1.89, 1.69]</td>
</tr>
<tr>
<td>I illicit drug use as frequency of drug use (as measured by Addiction Severity Index - ASI drug)</td>
<td>1</td>
<td>155</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>0.00[-0.03, 0.03]</td>
</tr>
<tr>
<td>I illicit drug use as a composite drug score (frequency*severity for all drugs taken)</td>
<td>1</td>
<td>157</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-0.10[-0.46, 0.26]</td>
</tr>
</tbody>
</table>

### 4.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as greater than 50% reduction in number of standard drinks consumed per day over the last 30 days</td>
<td>1</td>
<td>177</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.92[0.68, 1.26]</td>
</tr>
<tr>
<td>Alcohol abstinance as abstinence from alcohol over the last 30 days</td>
<td>1</td>
<td>177</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>0.97[0.56, 1.67]</td>
</tr>
</tbody>
</table>

### 5.1 Continuous outcomes

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as number of days in the past 30 days with alcohol use at 1 month</td>
<td>1</td>
<td>187</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-0.30[-3.38, 2.78]</td>
</tr>
<tr>
<td>Alcohol use as number of days in the past 30 days with alcohol use at 6 months</td>
<td>1</td>
<td>187</td>
<td>Mean Difference(IV, Fixed, 95% CI)</td>
<td>-1.50[-4.56, 1.56]</td>
</tr>
</tbody>
</table>

### 5.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as 25% reduction of drinking days in the past 30 days</td>
<td>1</td>
<td>187</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.23[0.96, 1.57]</td>
</tr>
<tr>
<td>Alcohol use as 50% reduction of drinking days in the past 30 days</td>
<td>1</td>
<td>187</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.27[0.96, 1.68]</td>
</tr>
<tr>
<td>Alcohol use as 75% reduction of drinking days in the past 30 days</td>
<td>1</td>
<td>187</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.21[0.84, 1.75]</td>
</tr>
<tr>
<td>Alcohol use as 1 or more drinking days' reduction in the past 30 days</td>
<td>1</td>
<td>187</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.12[0.91, 1.38]</td>
</tr>
<tr>
<td>Alcohol use as 7 or more drinking days' reduction in the past 30 days</td>
<td>1</td>
<td>187</td>
<td>Risk Ratio(M-H, Fixed, 95% CI)</td>
<td>1.67[1.08, 2.60]</td>
</tr>
</tbody>
</table>

### Figures

**Figure 1**
Study flow diagram.

Figure 2
Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Sources of support

Internal sources
- No sources of support provided

External sources
- Cochrane Training Fellowship (No. CTF/2010/9) from Health Research Board, Ireland

Feedback

Appendices

1 PubMed search strategy
MEDLINE (via PubMed)
Tuesday, November 22, 2011 (2656 hits):

Search terms to locate drug abuse:
1. "Substance-Related Disorders"[MeSH]
3. #1 or #2

**Search terms to identify drugs:**
4. "heroin"[mh] OR heroin[tiab]
5. narcotic*[tiab]
7. "Street Drugs"[MeSH]
8. "Designer Drugs"[MeSH]
9. #4 or #5 or #6 or #7 or #8

**Search terms to identify alcohol:**
10. alcohol*[tiab]
11. binge*[tiab] OR drink*[tiab]
12. alcoholism[MeSH]
13. alcoholic Intoxication[MeSH]
14. "Drinking behavior"[MeSH]
15. #10 or #11 or #12 or #13 or #14

**Search terms to locate interventions:**
16. psychotherapy[MeSH]
18. "brief intervention"*[tiab]
19. "early intervention"*[tiab]
20. "minimal intervention"*[tiab]
22. "cognitive therapy"*[tiab]
23. "family therapy"*[tiab]
24. "social skill"*[tiab]
25. "stress management training"*[tiab]
26. "supportive expressive therapy"*[tiab]
27. neurobehavioral*[tiab]
28. "coping skill"*[tiab]
29. "self-control training"*[tiab]
30. "social support"[MeSH]
31. "relaxation techniques"[MeSH]
32. "case management"[MeSH]
33. #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32

**Search terms to locate randomised controlled trials**
34. randomised controlled trial[pt]
35. controlled clinical trial[pt]
36. random*[tiab]
37. placebo*[tiab]
38. drug therapy[sh]
39. trial*[tiab]
40. groups*[tiab]
41. #34 or #35 or #36 or #37 or #38 or #39 or #40
42. Animals[mh] NOT Humans[mh]
43. #41 NOT #42
44. #3 AND #9 AND #15 AND #33 AND #43

**2 CENTRAL (CLIB) search strategy**

**The Cochrane Library**

**Issue 11, Nov 2011 (1736 hits)**

#1. MeSH descriptor Substance-Related Disorders explode all trees
#2. ((stimulant* or polydrug* or drug* or substance) near/3 (abuse* or abusing or depend* or addict* or disorder* or intoxicat* or misus* or use*)):ti,ab
#3. (#1 OR #2)
#4. (abuse* or abusing or depend* or addict* or depend* or overdos* or withdraw* or abstain* or abstinen* or disorder* or intoxicat* or misus*):ti,ab,kw
#5. use*:ti,ab
#6. (#4 OR #5)
#7. MeSH descriptor Narcotics explode all trees
#8. (heroin or morphine* or diacetylmorphine or morfín* or narcotic* or methadone):ti,ab,kw
#9. MeSH descriptor Methadone explode all trees
#10. (Opioid* or opiate* or opium):ti,ab,kw
#11. MeSH descriptor Amphetamine explode all trees
#12. (amphetamine* or dextroamphetamine* or methamphetamine or Methylamphetamine*):ti,ab,kw
#13. MeSH descriptor Methamphetamine explode all trees
#14. (ecstasy or MDMA or hallucogen*):ti,ab,kw
#15. MeSH descriptor Hallucinogens explode all trees
#16. MeSH descriptor Street Drugs explode all trees
#17. MeSH descriptor Cocaine explode all trees
#18. (crack or cocaine):ti,ab,kw
#19. MeSH descriptor Cannabis explode all trees
#20. (cannabis or marijuana or marihuana or Hashish):ti,ab,kw
#21. (Lysergic Acidic Diethylamide):ti,ab,kw
#22. (LSD):ti,ab,kw
#23. (benzodiazepine* or barbiturate* or ketamine or solvent or inhalant):ti,ab,kw
#24. (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25. (#6 AND #24)
#26. (#3 OR #25)
#27. (alcohol*):ti,ab,kw
#28. (binge or drink*):ti,ab
#29. MeSH descriptor Drinking Behavior explode all trees
#30. MeSH descriptor Alcoholism explode all trees
#31. MeSH descriptor Alcoholic Intoxication explode all trees
#32. (#27 OR #28 OR #29 OR #30 OR #31)
#33. MeSH descriptor Psychotherapy explode all trees
#34. (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*):ti,ab,kw
#35. (social near/2 skill*):ti,ab
#36. (coping near/2 skill):ti,ab
#37. MeSH descriptor Counseling explode all trees
#38. (behavi* near/2 therap*):ti,ab
#39. MeSH descriptor Reinforcement (Psychology) explode all trees
#40. (brief near intervention):ti,ab
#41. (early near intervention):ti,ab
#42. (minimal near intervention):ti,ab
#43. (cognitive near therapy):ti,ab
#44. (family near therapy):ti,ab
#45. (stress near management near training):ti,ab
#46. (supportive near expressive near therapy):ti,ab
#47. MeSH descriptor Social Support explode all trees
63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Cochr...
63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...

[41x814]63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...

4 CINAHL search strategy

CINAHL (via EBSCO)

Tuesday, November 22, 2011 (127 hits)

S01. MH "Substance Use Disorders"

S02. TX(drug N3 addict*) or TX(drug N3 dependen*) or TX(drug N3 abuse*) or TX(drug N3 misus*) or TX(drug N3 use*)

S03. TX(substance N3 addict*) or TX(substance N3 dependen*) or TX(substance N3 abuse*) or TX(substance N3 misus*)

S04. S1 or S2 or S3

S05. TX(addict* OR overdos* OR intoxicat* OR abstin* OR abstain OR withdraw* OR abus* OR misus* OR disorder* OR dependen* OR use*)

S06. MH "Heroin"

S07. MH "Narcotics"

S08. MH "Designer Drugs"

S09. TX(polydrug or opioid or opiate or opium or hallucinogen or cocaine or benzodiazepine* or amphetamine*or "anti-anxiety-agents" or barbiturate* or "lysergic acid" or ketamine or cannabis or marihuana or hashish or inhalant* or solvent or steroid* or methadone or morphine)

S10. TI ecstasy or TI mdma or AB ecstasy or AB mdma

S11. S6 or S7 or S8 or S9 or S10

S12. S5 and S11

S13. S4 or S12

S14. TI alcohol* or AB alcohol*

S15. TI drink* or TI binge or AB drink* or AB binge

S16. MH "Alcoholism"

S17. MH "Alcoholic Intoxication"

S18. (MH "Drinking Behavior+")

S19. S14 or S15 or S16 or S17 or S18

S20. MH "Clinical Trials+

S21. PT Clinical trial

S22. TI clinic* N1 trial* or AB clinic* N1 trial*

S23. TI ( singl* or doubl* or trebl* or tripl* ) and TI ( blind* or mask* )

S24. AB ( singl* or doubl* or trebl* or tripl* ) and AB ( blind* or mask* )

S25. TI randomi?ed control* trial* or AB randomi?ed control* trial*

S26. MH "Random Assignment"

S27. TI random* allocat* or AB random* allocat*

S28. MH "Placebos"

S29. TI placebo* or AB placebo*

S30. MH "Quantitative Studies"

S31. S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30

S32. S13 and S19 and S31

S33. S13 and S19 and S31

Limiters - Exclude MEDLINE records; Human

5 PsycINFO search strategy

PsycINFO (via ProQuest)
63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...

Tuesday, November 22, 2011 (706 hits)

1. (all(AB(psychotherapy*) OR TI,AB(psychosocial*) OR TI,AB("behaviour therapy") OR TI,AB("behavior therapy") OR TI,AB(reinforcement) OR TI,AB(motivation*) OR TI,AB(contingent*) OR TI,AB(advice) OR TI,AB(biofeedback) OR TI,AB(community) OR TI,AB(stimulation) OR TI,AB(education*) OR SU("psychotherapy") OR (TI,AB(incentive*) OR TI,AB(voucher))))

2. (TI,AB,IF(alcohol*) OR (TI,AB,IF(binge) OR TI,AB,IF(drink*)) OR SU(alcoholism) OR SU("alcohol intoxication") OR SU("alcohol drinking patterns"))

3. (IF("heroin") OR IF("morphine") OR IF("narcotics") OR (TI,AB(drug) OR TI,AB(polydrug) OR TI,AB(substance) OR TI,AB(opioid) OR TI,AB(opiate) OR TI,AB("hallucinogenic drugs") OR IF("psychedelic drugs") OR IF("Lysergic Acid Diethylamide") OR TI,AB(LSD) OR TI,AB(cocaine) OR TI,AB(benzodiazepine*) OR TI,AB("amphetamine") OR TI,AB("anti-anxiety-agents") OR TI,AB(barbiturate*) OR TI,AB(ketamine) OR TI,AB("cannabis") OR TI,AB("marihuana") OR TI,AB(hashish) OR TI,AB(opium) OR TI,AB("inhalant abuse") OR TI,AB(solvent) OR TI,AB(steroid*) OR TI,AB("methadone") OR TI,AB(ecstasy) OR TI,AB("methyleneoxyamphetamine") OR (IF(street drug*) OR IF(designer drug*)))

4. (SU("drug abuse") OR (IF(addict* OR abus* OR dependen*) OR cabs(overdose) OR cabs(intoxicat*) OR cabs(abstin*) OR cabs(abstain) OR cabs(withdrawal) OR cabs(abuse) OR cabs(use) OR cabs(misuse) OR cabs(disorder*) OR IF("drug addiction")))

5. SU(treatment effectiveness evaluation)

6. SU(clinical trials)

7. SU(mental health program evaluation)

8. SU(placebo)

9. TI,AB(placebo*)

10. AB(randomly)

11. TI,AB(random*ed)

12. TI,AB(trial)

13. TI,AB((singl* OR doubl* OR trebl* OR tripl*) W/3 (blind* OR mask* OR dummy))

14. TI,AB((control*) W/3 (trial* OR study OR studies OR group*))

15. TI,AB(factorial*)

16. TI,AB(allocat*)

17. TI,AB(assign*)

18. TI,AB(volunteer*)

9 AND 6 AND 7 AND 8 AND 9 AND 10 AND 11 AND 12 AND 13 AND 14 AND 15 AND 16 AND 17 AND 18

20. 1 AND 2 AND 3 AND 4 AND 19

21. 20 AND (po.exact("human")

**6 Criteria for risk of bias in RCTs and CCTs**

<table>
<thead>
<tr>
<th>Item</th>
<th>Judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>The investigators describe a random component in the sequence generation process such as: random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimisation</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>The investigators describe a non-random component in the sequence generation process such as: odd or even date of birth; date (or day) of admission; hospital or clinic record number; alternation; judgement of the clinician; results of a laboratory test or a series of tests; availability of the intervention</td>
</tr>
<tr>
<td></td>
<td>Unclear risk</td>
<td>Insufficient information about the sequence generation process to permit judgement of low or high risk</td>
</tr>
<tr>
<td>2. Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based, and pharmacy-controlled, randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes</td>
</tr>
<tr>
<td>Risk Level</td>
<td>Risk Description</td>
<td>Example of High Risk</td>
</tr>
<tr>
<td>------------</td>
<td>------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>High risk</td>
<td>Investigators enrolling participants could possibly foresee assignments because one of the following method was used: open random allocation schedule (e.g. a list of random numbers); assignment envelopes without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure</td>
<td>Insufficient information to permit judgement of low or high risk This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definitive judgement</td>
</tr>
<tr>
<td>Unclear risk</td>
<td>No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding</td>
<td>No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding</td>
</tr>
<tr>
<td>Low risk</td>
<td>Objective outcomes. Subjective outcomes.</td>
<td>Low risk</td>
</tr>
<tr>
<td>Low risk</td>
<td>No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding</td>
<td>No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding</td>
</tr>
<tr>
<td>High risk</td>
<td>Insufficient information to permit judgement of low or high risk (e.g. number randomised not stated, no reasons for missing data provided; number of drop-out not reported for each group)</td>
<td>Insufficient information to permit judgement of low or high risk (e.g. number randomised not stated, no reasons for missing data provided; number of drop-out not reported for each group)</td>
</tr>
</tbody>
</table>

Graphs
1. Cognitive-behavioural coping skills training (CBT) versus 12-step facilitation (TSF)
63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...

1.1 Continuous outcomes

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CBT Mean SD</th>
<th>Total 23</th>
<th>TSF Mean SD</th>
<th>Total 18</th>
<th>Weight IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carroll 1998</td>
<td>2.2 3</td>
<td>23</td>
<td>18 2</td>
<td>18</td>
<td>0.40 [-1.14, 1.94]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>23</td>
<td>18 100.0%</td>
<td>0.40 [1.14, 1.94]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.51$ (P = 0.61)

1.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CBT Events Total</th>
<th>TSF Events Total</th>
<th>Weight M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carroll 1998</td>
<td>23 5</td>
<td>23 2</td>
<td>18 100.0% 1.96 [0.42, 0.88]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>23 5</td>
<td>18 100.0% 1.96 [0.42, 0.88]</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.51$ (P = 0.61)

2 - Brief intervention (BI) versus treatment as usual
### 2.1 Continuous outcomes

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>BI Mean</th>
<th>SD Total</th>
<th>Control Mean</th>
<th>SD Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
<th>Heterogeneity</th>
<th>Test for overall effect (P = 0.95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as AUDIT scores at 3 months</td>
<td>Feldman 2011</td>
<td>14.9</td>
<td>7.2</td>
<td>59</td>
<td>14.9</td>
<td>9.9</td>
<td>51</td>
<td>100.0%</td>
<td>0.10 [-2.96, 3.16]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>0.10 [-2.96, 3.16]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use as AUDIT scores at 9 months</td>
<td>Feldman 2011</td>
<td>13.8</td>
<td>8.7</td>
<td>59</td>
<td>12.3</td>
<td>8.8</td>
<td>51</td>
<td>100.0%</td>
<td>1.50 [-1.74, 4.74]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>1.50 [-1.74, 4.74]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use as number of drinks per week at 3 months</td>
<td>Feldman 2011</td>
<td>15.4</td>
<td>17.6</td>
<td>59</td>
<td>13</td>
<td>19.5</td>
<td>51</td>
<td>100.0%</td>
<td>2.40 [4.59, 9.39]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>2.40 [4.59, 9.39]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use as number of drinks per week at 9 months</td>
<td>Feldman 2011</td>
<td>14.7</td>
<td>17.5</td>
<td>59</td>
<td>16.4</td>
<td>20.7</td>
<td>51</td>
<td>100.0%</td>
<td>-1.70 [-9.53, 5.53]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>-1.70 [-9.53, 5.53]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 2.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>BI Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>M-H, Fixed, 95% CI</th>
<th>Heterogeneity</th>
<th>Test for overall effect (P = 0.50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use as decreased alcohol use at 3 months</td>
<td>Feldman 2011</td>
<td>13</td>
<td>59</td>
<td>35</td>
<td>51</td>
<td>100.0%</td>
<td>0.32 [0.13, 0.64]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>0.32 [0.13, 0.64]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>13</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use as decreased alcohol use at 9 months</td>
<td>Feldman 2011</td>
<td>7</td>
<td>59</td>
<td>37</td>
<td>51</td>
<td>100.0%</td>
<td>0.16 [0.03, 0.33]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>59</td>
<td>100.0%</td>
<td>0.16 [0.03, 0.33]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>7</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for sub-group differences: Ch^2 = 2.28, df = 1 (P = 0.13), P = 55.6%

### 3 - Motivational interviewing(group) (MI-G) versus hepatitis health promotion (HHP)

---

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63 Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users: Coch...
4.2 Dichotomous outcomes

### 4.2.1 Alcohol use as greater than 50% reduction in number of standard drinks consumed per day over the last 30 days

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>M-H</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>M-H</th>
<th>Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Namasti 2010</td>
<td></td>
<td>41</td>
<td>98</td>
<td>43</td>
<td>87</td>
<td>100.0%</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>90</td>
<td></td>
<td>87</td>
<td>100.0%</td>
<td>0.82 (0.66, 1.26)</td>
</tr>
<tr>
<td>Total events</td>
<td></td>
<td>41</td>
<td></td>
<td>43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.52$ (P = 0.61)

### 4.2.2 Alcohol abstinence as abstinence from alcohol over the last 30 days

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>M-H</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>M-H</th>
<th>Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Namasti 2010</td>
<td></td>
<td>20</td>
<td>98</td>
<td>20</td>
<td>87</td>
<td>100.0%</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>90</td>
<td></td>
<td>87</td>
<td>100.0%</td>
<td>0.97 (0.86, 1.07)</td>
</tr>
<tr>
<td>Total events</td>
<td></td>
<td>20</td>
<td></td>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.12$ (P = 0.91)

---

5 - Brief motivational intervention (BMI) versus assessment only

### 5.1 Continuous outcomes

#### 5.1.1 Alcohol use as number of days in the past 30 days with alcohol use at 1 month

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>M-H</th>
<th>Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein 2002a</td>
<td>-0.30 (3.38, 2.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>-0.30 (3.38, 2.76)</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.13$ (P = 0.85)

#### 5.1.2 Alcohol use as number of days in the past 30 days with alcohol use at 6 months

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>M-H</th>
<th>Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein 2002a</td>
<td>-1.50 (4.56, 1.56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>-1.50 (4.56, 1.56)</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect $Z = 0.96$ (P = 0.34)
5.2 Dichotomous outcomes

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>BMI</th>
<th>Control</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2.1 Alcohol use as 25% reduction of drinking days in the past 30 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stein 2002a</td>
<td>61</td>
<td>95</td>
<td>48</td>
<td>92</td>
<td>1.23 [0.99, 1.57]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>61</td>
<td></td>
<td>48</td>
<td>92</td>
<td>1.23 [0.99, 1.57]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect $Z = 1.85$ ($P = 0.10$)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

| 5.2.2 Alcohol use as 50% reduction of drinking days in the past 30 days |
| Stein 2002a       | 65  | 95      | 42    | 92     | 1.27 [0.96, 1.70] |
| Subtotal (95% CI) |     |         |       |        |             |                   |
| Total events      | 65  |         | 42    | 92     | 1.27 [0.96, 1.70] |
| Heterogeneity: Not applicable |
| Test for overall effect $Z = 1.06$ ($P = 0.30$) |

| 5.2.3 Alcohol use as 75% reduction of drinking days in the past 30 days |
| Stein 2002a       | 40  | 95      | 32    | 92     | 1.21 [0.84, 1.76] |
| Subtotal (95% CI) |     |         |       |        |             |                   |
| Total events      | 40  |         | 32    | 92     | 1.21 [0.84, 1.76] |
| Heterogeneity: Not applicable |
| Test for overall effect $Z = 1.02$ ($P = 0.31$) |

| 5.2.4 Alcohol use as 1 or more drinking days’ reduction in the past 30 days |
| Stein 2002a       | 68  | 95      | 57    | 92     | 1.12 [0.91, 1.38] |
| Subtotal (95% CI) |     |         |       |        |             |                   |
| Total events      | 68  |         | 57    | 92     | 1.12 [0.91, 1.38] |
| Heterogeneity: Not applicable |
| Test for overall effect $Z = 1.08$ ($P = 0.28$) |

| 5.2.5 Alcohol use as 7 or more drinking days’ reduction in the past 30 days |
| Stein 2002a       | 39  | 95      | 22    | 92     | 1.67 [1.08, 2.60] |
| Subtotal (95% CI) |     |         |       |        |             |                   |
| Total events      | 39  |         | 22    | 92     | 1.67 [1.08, 2.60] |
| Heterogeneity: Not applicable |
| Test for overall effect $Z = 2.29$ ($P = 0.02$) |