

Global Hepatitis Programme

Guideline development for Hepatitis C virus Screening, Care and Treatment in low- and middle-income countries

PICO 3: Care

A systematic review of interventions to reduce alcohol consumption among individuals with chronic HCV infection

**Conducted by the Burnet Institute, Melbourne and Health Protection Scotland, Glasgow
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PICO 3 (Care): Alcohol reduction interventions in chronic HCV

Centre for Disease Control and Prevention, Atlanta

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BACKGROUND

Alcohol consumption has been shown to accelerate the progression of liver disease among people with hepatitis C virus (HCV)(Asher et al, 2012). The impact of behavioural interventions to reduce consumption of alcohol among people with HCV is uncertain. The purpose of this review was to investigate the effectiveness of behavioural interventions to reduce alcohol consumption among people with HCV, in terms of HCV treatment outcomes, liver disease progression, and quality of life.

METHODS

Narrative review question: Are behavioural interventions targeting alcohol consumption effective among persons with chronic HCV infection?

PICO question:

Population: Individuals with chronic HCV infection

Intervention: Behavioural alcohol-reduction interventions

Comparison: No behavioural alcohol-reduction intervention

Outcomes: Reduction or cessation of alcohol intake, SVR, liver fibrosis, decompensated liver cirrhosis (DCC), hepatocellular carcinoma (HCC), quality of life, all-cause mortality

Study type/limits: Experimental studies published between 1994 and the present

Search strategy:

A systematic review was carried out using the following databases and information sources:

- Ovid MEDLINE, Ovid EMBASE, PsychINFO, LILACS, the Cochrane Library (CENTRAL and DARE) (without language restrictions)
- Reference lists of all relevant articles and reviews
- Relevant articles identified during the conduct of the other systematic reviews

Search terms included combinations of free text and medical subject heading terms (MeSH, Emtree) and are briefly summarized as: Hepatitis C/HCV AND alcohol intervention (see Appendix I).

Conduct of the review:

The review process followed the Cochrane methodology for conducting a systematic review and the PRISMA guidelines on reporting. The review was prospectively registered with the systematic

reviews registry PROSPERO (University of York). The review was undertaken by a primary and secondary reviewer. A third reviewer was consulted on any points of difference between the primary and secondary reviewer. Two reviewers assessed all search results, and included those studies that met population, intervention, comparison and at least one outcome criteria. The bibliographic records and abstracts were used to filter studies that clearly did not meet the inclusion criteria. Full articles were obtained and assessed to confirm eligibility of potentially relevant studies.

Quality appraisal:

Randomized controlled trials were assessed using the Cochrane Risk of Bias assessment tool, which grades studies as having a low, high, or unclear level of bias. Observational or prospective cohort studies were assessed using the Newcastle-Ottawa (N-O) checklist. N-O assesses each study in terms of the risk of bias in the representativeness of the study cohort, the comparability of the exposed and non-exposed participants, and the ascertainment of study outcomes.

Data extraction:

Data was extracted from each study by the primary reviewer and secondary reviewer acting independently. The third reviewer was consulted on points of disagreement between the primary and secondary reviewer.

Data was extracted to a standardised spread sheet recording:

- Study characteristics: country, study design, study objectives, funding source
- Study population: individuals with chronic HCV infection
- Participant details: age, sex, ethnicity
- Setting: primary/secondary/tertiary care, alcohol and drug services, harm reduction services
- Inclusion/exclusion criteria for study
- Sample size
- Intervention group: selection and characteristics of intervention group
- Intervention: duration of intervention, type of alcohol intervention (general advice, motivational interviewing (MI), cognitive-behavioural therapy (CBT)); delivered by clinician/alcohol or drug worker/psychologist/peer educator; year or time period of intervention; costs of delivery
- Comparison: selection and characteristics of comparison group

- Analysis: number offered intervention, number accepted intervention, reason for refusal, time to follow-up, loss to follow-up, study data collection method, statistical analysis, primary outcomes of study, secondary outcomes of study
- Results: Reduction or cessation of alcohol intake, SVR, liver fibrosis, DCC, HCC, quality of life, all-cause mortality

GRADE process:

The quality of the body of evidence for each outcome was assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology. GRADE rates the quality of evidence for each outcome of interest as high, moderate, low or very low, depending on a number of criteria. These include study design, study quality, study consistency (the similarity of estimates of effect across studies) and study directness (the extent to which the evidence is relevant to the population, intervention, and outcome of interest).

RESULTS

The literature search identified 1109 unique citations. An initial review excluded 171 citations from consideration and subsequent screening by title and abstract excluded a further 920 citations which did not meet requirements for population, intervention and at least one outcome (Figure 1).

Eighteen abstracts advanced to full text review. Of these, six studies (Asher et al., 2012, John-Baptiste et al., 2009, Lang et al., 2003, McDonald et al., 2012, Nguyen et al., 2007, Plebani et al., 2010) were excluded as they were observational studies which did not include an intervention, despite examining a variety of outcomes for hepatitis C and relating them to alcohol use.

A further six studies (Curcio et al., 2010, Groessl et al., 2011, Knott et al., 2006, Le Lan et al., 2012, Rifai et al., 2006, Evon et al., 2010) were excluded because the intervention comprised of a general integrated health promotion in which alcohol reduction may have been included, but was not reported or evaluated separately. One study (Zule et al., 2009) was excluded by population as the participants were drawn from a group of People Who Inject Drugs (PWID) rather than from a group of those infected with Hepatitis C.

Five studies were assessed as meeting the PICO criteria. Two of these studies were randomized control trials (RCT) and three were cohort studies. Table 1 provides a summary of the characteristics

and outcomes of each and a Cochrane Risk of Bias assessment. A GRADE Evidence Profile of collated results can be found in Table 2.

Among 135 veterans in Minneapolis and Portland with chronic HCV who reported heavy drinking (s), Dieperink et al. (2012) conducted a randomised control trial of Motivational Enhancement Therapy (MET). MET is an adaptation of Motivational Interviewing (MI) devised by Miller and Rollnick and is a short-term intervention specifically tailored to addiction. This was compared to an educational control condition where individuals were informed of positive strategies on sleep, hygiene, nutrition, diet, stress management, fitness and exercise. Both groups received 4 sessions of each intervention, with no loss to follow-up reported. Alcohol consumption outcomes were measured using self-reported mean drinking days per month. Both groups decreased their drinking at 6 months follow-up, with the MET intervention resulting in a significantly greater reduction in mean drinking days in the previous month than the EDU. Data from this study was only available in abstract form and no additional data could be obtained after contacting the authors at this point.

Drumwright et al. (2011) conducted a randomised control trial of a group behavioural intervention among a group of HCV antibody-positive PWID. Participants attended six 2-hour professional-led sessions which stressed the dangers of alcohol use and the benefits of reducing consumption. The control condition attended an equal number of group sessions which facilitated a general discussion of the experiences and identities of PWID. Alcohol consumption outcomes were measured using the AUDIT score (see Appendix 2) of alcohol related harms and dependence, and also includes an alcohol consumption sub-score. The proportion of participants achieving abstinence from alcohol increased from baseline in both groups by 22.7%. However, this was achieved in both arms of the study, with the alcohol specific intervention conferring no unique benefit to any outcomes. Given the small number of studies meeting the PICO, and the heterogeneity across those studies, meta-analysis was not carried out.

Proeschold-Bell et al. (2012) conducted a 24-week integrated treatment for alcohol and other medical issues for a cohort of 53 individuals with chronic HCV. All participants reported some level of alcohol consumption at baseline, with 44% reporting abstinence at six months' follow-up.

Dieperink et al. (2010) assessed the benefits of a one-off brief alcohol counselling intervention among a cohort of 47 patients with chronic HCV with a DSM-IV diagnosis of alcohol abuse or

dependence. They reported a significant decrease both in mean drinking days (in the previous month) and mean quantity consumed on those days at one to two months follow-up.

Watson et al. (2007) also assessed the impact of a one-off brief alcohol intervention delivered by HCV professionals, this time among a cohort of 17 chronic Hep C patients who were receiving opioid maintenance treatment (OMT). At one month follow-up participants reported a significant reduction in mean alcohol consumption per day. Table 3 offers a summary of the characteristics and outcomes of these studies, considered as indirect evidence.

In addition to these studies, which involve interventions amongst people with HCV, two Cochrane reviews offer summaries of evidence for brief alcohol interventions for non-HCV populations. Kaner et al. (2009) found that amongst 5860 hazardous or dependent drinkers across 22 studies, HCV screening followed by brief intervention, compared with no intervention, significantly reduced mean weekly alcohol consumption from 313g per week by 38.42g per week. Klimas et al. (2012) investigated the efficacy of psychosocial interventions for drinkers with concurrent illicit drug use. Amongst 594 participants across 4 studies, alcohol-focused interventions resulted in significant reductions in alcohol consumption at 3 months (RR 0.32, 95%CI 0.19 to 0.54) and 9 months (RR 0.16, 95%CI 0.08 to 0.33) compared to treatment as usual.

CONCLUSIONS

Despite a limited number of relevant studies, there is moderate evidence that alcohol reduction interventions can reduce alcohol consumption among people living with chronic HCV. However, a significant limitation for data analysis was the heterogeneity of the interventions and comparison groups across the studies. Also, whilst alcohol-targeted interventions reduced consumption in each study, participants in the two RCT comparison groups also received varying broad support and reduced their drinking. The heterogeneity of the intervention and comparison groups makes it difficult to draw any firm conclusions about the effect of specific alcohol-focused interventions for this population.

Implications for clinical practice

Alcohol reduction interventions for chronic HCV patients could encourage abstinence or reduce the number of drinking days per month. However, there is no data on whether longer-term important outcomes including treatment response, morbidity, mortality and quality of life are affected by alcohol reduction interventions.

Implications for research

Additional research is required to assess medium to long term impacts of behavioural interventions in this population, and further, to determine whether alcohol reduction interventions have any impact on other important outcomes including morbidity, mortality, and quality of life. Measuring alcohol consumption is complex and different instruments are used across studies making comparisons and synthesis of the evidence difficult. Future research should consider using validated and standardised tools for measuring alcohol consumption where possible.

FIGURES AND TABLES

Identification

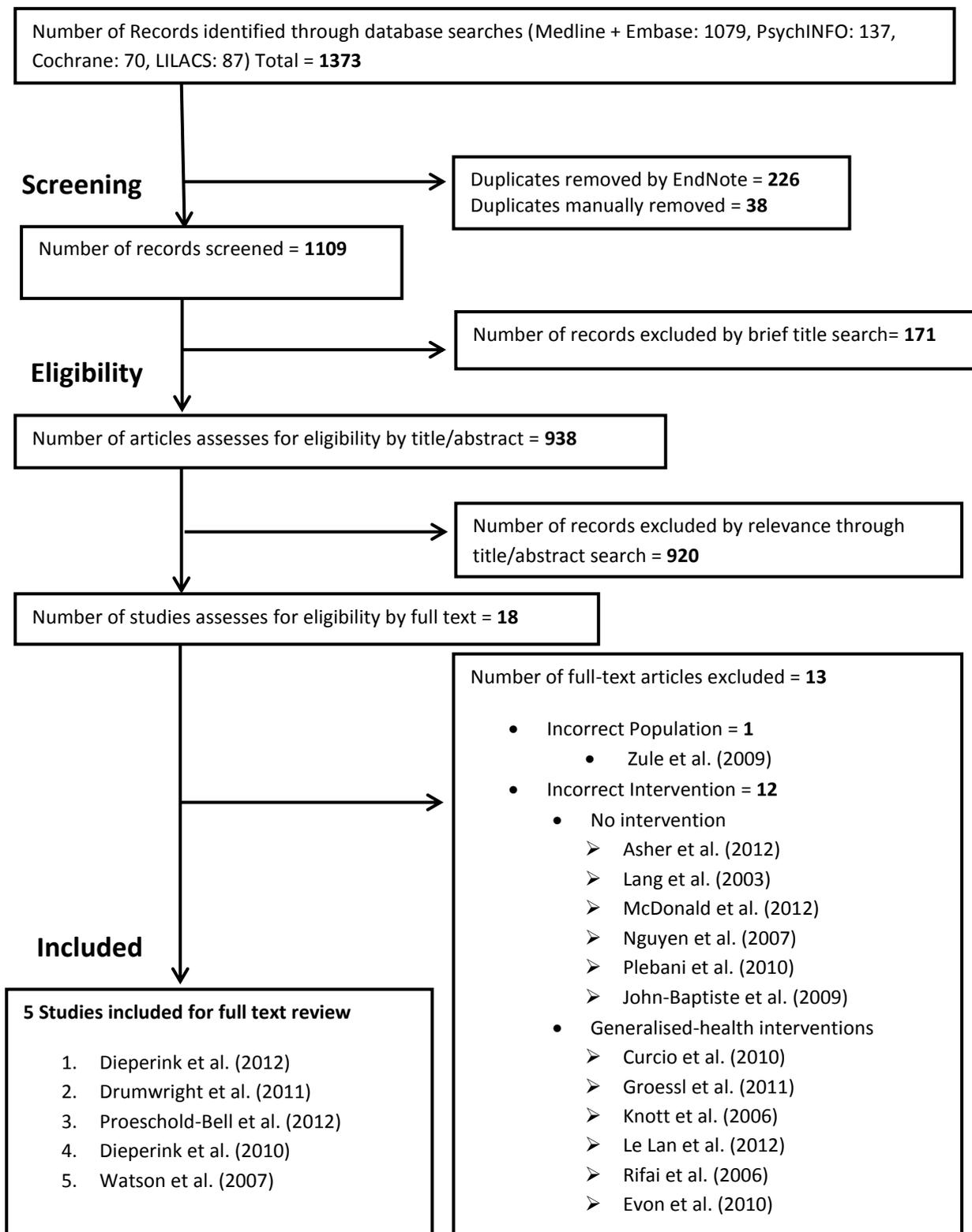


Figure 1: Flowchart for Systematic Review

Table 1: Results from included studies

STUDYNO.1	Dieperink et al. (2012) - Randomized Controlled trial of Motivational Enhancement Therapy to Reduce Alcohol in Patients with Chronic Hepatitis C.
PARTICIPANTS	<p>Setting: Not specified</p> <p>Location: Minneapolis and Portland, USA</p> <p>Study period: Data Presented in 2012</p> <p>Sample: 135 chronic Hep C infected Minneapolis and Portland Veterans</p> <p>Study inclusion criteria: Alcohol Consumption: 7+ drinks daily in past fortnight or weekly heavy drinking or DSM-IV alcohol use disorder</p> <p>Study exclusion criteria: Cocaine, methamphetamine or opioid dependence in preceding 6 months, CNS trauma, significant cognitive impairment, dementia, encephalopathy, acute psychiatric instability</p> <p>Study population characteristics: 95.6% men, 68.1% white Participation rate not stated</p>
METHODS	<p>Study type: Randomised Controlled Trial (single-blind)</p> <p>Duration: Six Months follow up</p> <p>Loss to follow-up: Not stated</p> <p>Type of comparison: between-groups</p> <p>Data Analysis: Mixed-effects model</p>
INTERVENTIONS	<p>Experimental: 4 sessions of Alcohol targeted Motivational Enhancement Therapy (MET)</p> <p>Comparison: 4 sessions generalised health Educational Control Condition (EDU)</p>
OUTCOMES	Mean drinking days in past month at 6 months follow up.
NOTES	Conference Abstract only
INTERVENTION ARM	8.4 mean drinking days in past month at follow up, from 20.0 at baseline
CONTROL ARM	12.9 mean drinking days in past month at follow up, from 20.3 at baseline
EFFECT SIZE	P=0.042. Cohen's d=.40
COCHRANE RISK OF BIAS ASSESSMENTS	<p>Sequence generation? UNCLEAR</p> <p>Allocation concealment? UNCLEAR</p> <p>Blinding? YES</p> <p>Incomplete outcome data addressed? UNCLEAR</p> <p>Free of selective reporting? YES</p> <p>Free of other bias? YES</p> <p>Summary Assessments Outcome: LOW RISK OF BIAS (on basis of abstract alone)</p>

STUDY NO.2	Drumwright et al. (2011) - Predictors and effects of alcohol use on liver function among young HCV-infected injection drug users in a behavioural intervention
PARTICIPANTS	<p>Setting: Not specified Location: Baltimore, Maryland; New York City, New York; Seattle, Washington Study period: April 2002 – May 2004 Sample: 334 Hep C antibody positive PWID, aged 18-35 Inclusion Criteria: None specified Exclusion: HIV+ 75% men, 55.8% white Participation rate: 630 enrolled, 418 randomised. 355 completed at least one follow-up (10 insufficient data)</p>
METHODS	<p>Study type: Randomised control trial Duration: Six Months follow up Lost to follow up: 13.6% of randomised (n=57) did not complete any follow-up. Type of comparison: between groups Data Analysis: Univariate and multivariate logistic regression</p>
INTERVENTIONS	<p>Experimental: six 2-hour professional led sessions stressing dangers of alcohol use and benefits held over 3 weeks Comparison: six 2-hour professional-led discussions on injecting drug user lives and identities</p>
OUTCOMES	<ol style="list-style-type: none"> 1. Overall Alcohol Use Disorders Identification Test (AUDIT, see Appendix II) score at 6 months follow-up; 2. Specific AUDIT score for alcohol consumption at 6 months follow-up; 3. Abstinence from alcohol.
EFFECT SIZE	<ol style="list-style-type: none"> 1. AUDIT score: AOR=0.99 (95% CI 0.96, 1.01); 2. AUDIT (consumption only): AOR=1.03 (95% CI 0.94, 1.13); 3. Abstinence from alcohol increased by 22.7% in both groups.
COCHRANE RISK OF BIAS ASSESSMENTS	<p>Sequence generation? UNCLEAR Allocation concealment? UNLEAR Blinding? UNCLEAR Incomplete outcome data addressed? YES Free of selective reporting? YES Free of other bias? YES</p> <p>Summary Assessments Outcome: LOW RISK OF BIAS</p>

STUDY NO.3	Proeschold-Bell et al.(2012) - An integrated Alcohol Abuse and Medical Treatment Model for Patients with Hepatitis C
PARTICIPANTS	<p>Setting: Medical Clinic Location: Durham, NC. USA Study period: February 2009 – March 2010 Sample: 53 Participants, 18+ years old , Chronic Hep C Inclusion Criteria: Some degree of alcohol consumption (unspecified levels) Exclusion: No other 60.4% men, 30.2% White, 5.7% Multiracial or other, 4.1% Hispanic, 64.2% Black or African American Participation rate: 53 of 60 recruited received intervention (88%)</p>
METHODS	<p>Study type: Prospective Cohort Study Duration: Six Months follow up Lost to follow-up: 45 of 53 (85%) followed up at six months Type of comparison: Post versus pre intervention Data Analysis: Logistic regression analysis</p>
INTERVENTIONS	<p>Experimental: 24-week integrated alcohol and medical treatment targeting both alcohol use and HCV health. Comparison: Post-intervention versus baseline</p>
OUTCOMES	Abstinence from alcohol at six months
INTERVENTION ARM	44% abstinence reported at six months compared to 20.8% at baseline
EFFECT SIZE	AOR 3.36 (95%CI 2.62-4.10), p<0.01
NEWCASTLE-OTTAWA SCORE	4 out of maximum 9 points
COCHRANE RISK OF BIAS ASSESSMENTS	<p>Sequence generation? NO Allocation concealment? NO Blinding? NO Incomplete outcome data addressed? YES Free of selective reporting? YES Free of other bias? YES</p> <p>Summary Assessments Outcome: HIGH RISK OF BIAS</p>

STUDY NO.4	Dieperink et al. (2010) - Significant Reductions in Drinking Following Brief Alcohol Treatment in a Hepatitis C Clinic
PARTICIPANTS	<p>Setting: Hepatitis C Clinic Location: Minneapolis, VA. USA Study period: February 2003 – April 2004 Sample: 47 Participants- Chronic Hep C and attending Hep C clinic Alcohol Consumption Criteria: Diagnosis of alcohol abuse or dependence Exclusion: No other mentioned 100% men, 62% White, 2% Native American, 2% Asian, 4% Hispanic, 19% Black or African American, 11% Unknown ethnicity Participation rate: N/A (retrospective study)</p>
METHODS	<p>Study type: Retrospective cohort study Duration: 1-2 months (follow up) Lost to Follow-up: N/A Type of comparison: Post-intervention versus baseline. Data Analysis: Chi-Square tests, two-tailed t-tests</p>
INTERVENTIONS	<p>Experimental: One Brief Alcohol Counselling session by HCV clinician. Comparison: Post-Intervention versus baseline</p>
OUTCOMES	<p>Mean Drinking days in last month (17.3 baseline vs 10.6 follow-up) Mean Quantity (standard 14g drink) consumed on drinking day (9.5 baseline vs. 5.5 follow-up)</p>
EFFECT SIZE	<p>Mean difference in drinking days: -6.7 days; p<0.001 Mean difference in quantity consumed on drinking day: -4.0 standard drinks; p<0.001</p>
NEWCASTLE-OTTAWA SCORE	4 out of maximum 9 points
COCHRANE RISK OF BIAS ASSESSMENTS	<p>Sequence generation? NO Allocation concealment? NO Blinding? NO Incomplete outcome data addressed? YES Free of selective reporting? YES Free of other bias? YES</p> <p>Summary Assessments Outcome: HIGH RISK OF BIAS</p>

STUDY NO.5	Watson <i>et al.</i> (2007) - Hazardous alcohol consumption and other barriers to antiviral treatment among hepatitis C positive people receiving opioid maintenance treatment.
PARTICIPANTS	<p>Setting: Hospital Drug Health Service</p> <p>Location: Sydney, Australia</p> <p>Study period: Data presented in 2007</p> <p>Sample: 17 Chronic Hepatitis C participants, receiving opioid maintenance treatment</p> <p>Inclusion Criteria: Drinking more than half the limit set by the National Health and Medical Research Council (NHMRC) – MEN 20g/day and/or 30g in any session, WOMEN 10g/day and/or 20g in any session.</p> <p>Exclusion: No other</p> <p>Demographics not stated</p> <p>Participation rate: 17 of 20 followed up</p>
METHODS	<p>Study type: Prospective Cohort Study</p> <p>Duration: One month (follow-up)</p> <p>Lost to follow-up: 3 of 20 (15%)</p> <p>Type of comparison: Post intervention versus baseline</p> <p>Data Analysis: Paired t-test</p>
INTERVENTIONS	<p>Experimental: One Brief Alcohol intervention</p> <p>Comparison: Post-intervention versus baseline</p>
OUTCOMES	<p>Alcohol consumption reduced by mean of 3.1g/day</p> <p>No relative change given; baseline consumption greater than 20g/day in men, 10g/day in women, exact mean consumption not specified</p>
EFFECT SIZE	<p>Mean difference -3.1g/day, p=0.003</p>
NEWCASTLE-OTTAWA SCORE	<p>3 out of a maximum of 9 points</p>
COCHRANE RISK OF BIAS ASSESSMENTS	<p>Sequence generation? NO</p> <p>Allocation concealment? NO</p> <p>Blinding? NO</p> <p>Incomplete outcome data addressed? YES</p> <p>Free of selective reporting? YES</p> <p>Free of other bias? YES</p> <p>Summary Assessments Outcome: HIGH RISK OF BIAS</p>

Table 2: GRADE Evidence Summary - Effect of alcohol reduction interventions among persons with chronic HCV

Outcomes (Follow up)	No of participants (Studies)	Quality of the Evidence (GRADE)	Relative Effect (95% CI)	Anticipated absolute effects	
				Risk without intervention	Risk difference with alcohol reduction intervention
Alcohol consumption:					
Measure One: Mean Drinking Days in preceding month (at 6 months)	135 (1 RCT)	Moderate ¹	Cohen's D = 0.40 (21% reduction in mean drinking days, no CI available)	20 mean drinking days per month	A reduction of 4.2 mean drinking days per month
Measure Two: Overall AUDIT score (at 6 months)	334 (1 RCT)	Moderate ¹	OR 0.99 (0.96-1.01)	Baseline data not available	
Measure Three: AUDIT - alcohol consumption score only (at 6 months)	334 (1 RCT)	Moderate ¹	OR 1.03 (0.94-1.13)	Baseline data not available	
Measure Four: Achieved abstinence (at 6 months)	53 (1 observational study)	Low	OR 3.36 (2.62-4.10)	208 per 1000 abstinent	232 per 1000 increased abstinence
Measure Five: Mean quantity of alcohol consumed on a drinking day during preceding month (at 1 month)	64 (2 observational studies)	Very Low ²	Pool RR cannot be calculated from data. Risk difference estimates: 3.1g EtOH/day (1 study, p<0.01); 56g EtOH/day (1 study, p<0.001)	Range from 20g to 133g EtOH/day	Range from 3.1g less alcohol consumed on drinking day to 56g less alcohol consumed on drinking day
SVR	No data				
Morbidity	No data				
Mortality	No data				
Quality of Life	No data				

¹Assessed moderate GRADE evidence given some imprecision in measuring outcome

²This outcome (drinking days/month) downgraded quality of evidence due to imprecision of outcome measurement, and inadequate level of detail in study data to estimate comparative effect sizes and pooling data across observational studies.

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APPENDICES

Appendix 1: Search Syntax

1. OVID Medline and Embase - 1079 references

- 1 exp Hepatitis C/
- 2 Hepatitis C.ti,ab.
- 3 HCV.ti,ab.
- 4 exp alcohol liver cirrhosis/ or exp alcohol abstinence/ or exp alcohol consumption/ or exp alcohol/ or exp alcohol liver disease/ or exp alcohol abuse/
- 5 alcohol.ti,ab.
- 6 drink*.ti,ab.
- 7 exp drinking/ or exp drinking behavior/
- 8 exp binge drinking/
- 9 exp intervention study/
- 10 exp therapy effect/ or exp group therapy/ or exp cognitive therapy/ or exp behavior therapy/
- 11 exp *therapy/
- 12 (intervention adj6 alcohol).ti,ab.
- 13 (therapy adj6 alcohol).ti,ab.
- 14 exp clinical evaluation/ or exp evaluation/
- 15 (evaluation adj6 alcohol).ti,ab.
- 16 exp drug dependence treatment/
- 17 (treatment adj6 alcohol).ti,ab.
- 18 exp psychotherapy/
- 19 CBT.ti,ab.
- 20 motivational interviewing.ti,ab.
- 21 exp motivational interviewing/
- 22 exp counseling/
- 23 exp patient counseling/
- 24 1 or 2 or 3
- 25 4 or 5 or 6 or 7 or 8
- 26 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
- 27 24 and 25 and 26
- 28 limit 27 to yr="1994 -Current"

2. PsychINFO – 137 references

- 1 exp hepatitis/
- 2 hepatitis c.mp.
- 3 HCV.mp.
- 4 exp Alcohols/
- 5 exp Alcohol Drinking Patterns/ or exp Drinking Behavior/ or exp Binge Drinking/
- 6 alcohol.mp.
- 7 drink*.mp.

- 8 exp Intervention/
- 9 (intervention adj6 alcohol).ti,ab.
- 10 exp Treatment/
- 11 (treatment adj6 alcohol).ti,ab.
- 12 exp Evaluation/ or exp Program Evaluation/
- 13 (evaluation adj6 alcohol).ti,ab.
- 14 exp Motivational Interviewing/
- 15 exp Brief Psychotherapy/ or exp Psychotherapy/ or exp Family Therapy/ or exp Counseling/ or exp Counseling Psychology/
- 16 exp Cognitive Therapy/ or exp Group Psychotherapy/ or exp Cognitive Behavior Therapy/
- 17 1 or 2 or 3
- 18 4 or 5 or 6 or 7
- 19 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
- 20 17 and 18 and 19
- 21 limit 20 to yr="1994 -Current"

3. Cochrane Database – 70 references

- 1 MeSH descriptor: [Hepatitis C] explode all trees
- 2 hepatitis c;ti,ab,kw (word variations have been searched)
- 3 HCV: ti,ab,kw (word variations have been searched)
- 4 MeSH descriptor: [Alcohols] explode all trees
- 5 Alcohol:ti,ab,kw (word variations have been searched)
- 6 MeSH descriptor: [Alcohol drinking] explode all trees
- 7 MeSH descriptor: [Drinking behaviour] explode all trees
- 8 MeSH descriptor: [Intervention Studies] explode all trees
- 9 MeSH descriptor: [Cognitive Therapy] explode all trees
- 10 MeSH descriptor: [Psychoanalytic Therapy] explode all trees
- 11 MeSH descriptor: [Behavior Therapy] explode all trees.
- 12 therapy near/6 alcohol:ti,ab,kw (word variations have been searched)
- 13 intervention near/6 alcohol:ti,ab,kw (word variations have been searched).
- 14 MeSH descriptor: [Evaluation Studies as Topic] explode all trees.
- 15 evaluation near/6 alcohol:ti,ab,kw (word variations have been searched).
- 16 CBT:ti,ab,kw (word variations have been searched)
- 17 MeSH descriptor: [counselling] explode all trees
- 18 #1 or #2 or #3
- 19 #4 or #5 or #6 or #7
- 20 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17
- 21 #18 and #19 and #20

4. LILACS Database – 87 References

Hepatitis C/HCV AND Alcohol AND Intervention/therapy

Appendix 2: The Alcohol Use Disorders Identification Test

The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written.

1. How often do you have a drink containing alcohol?

0 points - Never

1 point - Monthly or less

2 points - 2 to 4 times a MONTH

3 points - 2 to 3 times a WEEK

4 points - 4 or more times a week

Questioner may skip to Questions 9 and 10 if reply to Question 1 is never, or if both answers to Q 2 and 3 are 0.

2. How many drinks containing alcohol do you have on a typical day when you are drinking?

0 points - 1 or 2 drinks

1 point - 3 or 4 drinks

2 points - 5 or 6 drinks

3 points - 7 or 8 or 9 drinks

4 points - 10 or more drinks

3. How often do you have six or more drinks on one occasion?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

AUDIT-C Score /12 (complete full questionnaire if score is 3 or more)

4. How often during the last year have you found that you were not able to stop drinking once you had started?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?

0 points - Never

1 point - Less than monthly

2 points - Monthly

3 points - Weekly

4 points - Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?

0 points - No, never

2 points - Yes, but not in the last year

4 points - Yes, during the last year

10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?

0 points - No, never

2 points - Yes, but not in the last year

4 points - Yes, during the last year

The Alcohol Use Disorders Identification Test

(AUDIT) Score = /40

Scores of 8 or more are considered an indicator of hazardous and harmful alcohol use.

Appendix 3: Newcastle-Ottawa Scale

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE FOR COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

- 1) Representativeness of the exposed cohort
 - a) truly representative of the average _____ (describe) in the community *
 - b) somewhat representative of the average _____ in the community *
 - c) selected group of users eg nurses, volunteers
 - d) no description of the derivation of the cohort
- 2) Selection of the non exposed cohort
 - a) drawn from the same community as the exposed cohort *
 - b) drawn from a different source
 - c) no description of the derivation of the non exposed cohort
- 3) Ascertainment of exposure
 - a) secure record (eg surgical records) *
 - b) structured interview *
 - c) written self report
 - d) no description
- 4) Demonstration that outcome of interest was not present at start of study
 - a) yes *
 - b) no

Comparability

- 1) Comparability of cohorts on the basis of the design or analysis
 - a) study controls for _____ (select the most important factor) *
 - b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

- 1) Assessment of outcome
 - a) independent blind assessment *
 - b) record linkage *
 - c) self report
 - d) no description
- 2) Was follow-up long enough for outcomes to occur
 - a) yes (select an adequate follow up period for outcome of interest) *
 - b) no
- 3) Adequacy of follow up of cohorts
 - a) complete follow up - all subjects accounted for *
 - b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) *
 - c) follow up rate < ____ % (select an adequate %) and no description of those lost
 - d) no statement

Appendix 4: Cochrane Collaboration's tool for assessing risk of bias

Domain	Description	Review authors' judgement
Sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to Allow an assessment of whether it should produce comparable groups.	Was the allocation sequence adequately generated?
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Was allocation adequately concealed?
Blinding of participants, personnel and outcome assessors <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Was knowledge of the allocated intervention adequately prevented during the study?
Incomplete outcome data <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Were incomplete outcome data adequately addressed?
Selective outcome reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Are reports of the study free of suggestion of selective outcome reporting?
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Was the study apparently free of other problems that could put it at a high risk of bias?

Appendix 5: GRADE approach to assessing the quality of evidence across studies

Quality of Evidence (summary score)	Study Design	Downgrading Factors	Upgrading Factors
<p>High (4) =Further research is very unlikely to change our confidence in the estimate of effect.</p>	<p>Randomized trials or valid accuracy studies for diagnostic tests begin with a score of High (4)</p>	<p>Study Limitations:</p> <p>-1 Serious</p> <p>-2 Very serious</p>	
<p>Moderate (3) = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</p>		<p>Consistency:</p> <p>-1 Serious</p> <p>-2 Very serious</p>	<p>Large effect</p> <p>+1 Large</p> <p>+2 Very large</p>
<p>Low (2) = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</p>	<p>Observational studies or indirect accuracy studies for diagnostic tests begin with a score of low (2).</p>	<p>Directness:</p> <p>-1 Serious</p> <p>-2 Very serious</p>	<p>Plausible confounding would change the effect</p> <p>+1</p>
<p>Very low (1) = Any estimate of effect is very uncertain.</p>		<p>Precision:</p> <p>-1 Serious</p> <p>-2 Very serious</p> <p>Publication Bias:</p> <p>-1 Serious</p> <p>-2 Very serious</p>	<p>Dose-response gradient</p> <p>+1 if Present</p>