Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence

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CRD summary
The authors concluded that clinical psychiatric and alcohol-related outcomes could be improved by supplementing treatment of alcohol dependence with psychiatric treatment for patients with co-occurring internalising disorders. The authors' conclusions reflect the evidence presented, but potential for language bias, no validity assessment and poor reporting of review methods mean that the reliability of the conclusions is unclear.

Authors' objectives
To evaluate the effects of supplementing treatment for alcohol dependence with a psychiatric treatment for patients with a co-occurring internalising disorder.

Searching
MEDLINE and PsycINFO databases were searched to June 2010 for articles in English published in peer-reviewed scientific journals; search terms were reported. Bibliographies of retrieved articles and reviews were searched for additional articles. Review authors searched their own resources and contacted laboratories.

Study selection
Randomised controlled trials (RCTs) that evaluated supplementary anxiety and depression treatment (psychosocial and pharmacological) compared to a control (placebo or therapy) in adult participants (aged 18 or older) being treated for alcohol dependence and with a co-occurring internalising disorder were eligible for inclusion. Studies were required to have follow-up assessments within one year of treatment and include sufficient data to enable calculation of effect sizes. Anxiety outcome measures had to be reported using a recognised tool. Alcohol-related outcomes included abstinence, frequency, intensity and quantity (definitions reported in the review).

Most of the included studies evaluated a pharmacological treatment. Other studies evaluated a psychosocial treatment. Half of the pharmacological treatment studies reported use of selective serotonin reuptake inhibitors (SSRIs). Other studies used buspirone, serotonin-norepinephrine reuptake inhibitors (SNDRIs) and tricyclic medication. All studies of psychosocial interventions used cognitive-behavioural therapy (CBT). Most studies included participants who were being treated for depression. Other studies were of people who were being treated for generalised anxiety disorder, panic disorder or social phobia. Most studies used a version of the Hamilton Rating Scale for measuring internalising outcomes; some studies used various other scales.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
The authors did not state that they conducted a validity assessment.

Data extraction
Data were extracted for the relevant outcomes and used to calculate effect size measures using Cohen's d for continuous outcomes and odds ratio (ORs) for dichotomous outcomes, together with corresponding 95% confidence intervals (CIs). Where possible, data were extracted on an intention-to-treat principle.

The authors did not report how many reviewers extracted data.

Methods of synthesis
Overall pooled effect sizes for alcohol and internalising disorder outcomes were calculated using a random-effects model. Studies were weighted to reflect sample size and variance. Heterogeneity was assessed using the Q statistic and the I² index. Where more than one internalising disorder outcome was reported, effect sizes were averaged for each measure to calculate a single summary effect size. The same principle was used for multiple alcohol outcomes.
Calculations were then adjusted to account for variance introduced through the multiple measures.

Subgroup analysis was conducted for the type of internalising disorder treated and type of treatment to examine the influence of more effective versus less effective internalising disorder treatment for alcohol outcomes. Publication bias was assessed by visual inspection of funnel plots and using methods by Egger and Begg. Duval and Tweedie trim-and-fill analysis was conducted.

**Results of the review**

Fifteen RCTs (1,310 participants) were included in the review.

**Internalising outcomes:** Overall there was a significant reduction in anxiety and depression following treatment of internalising disorders compared to placebo (effect size 0.32, 95% CI 0.17 to 0.47). There was no evidence of statistical heterogeneity for this analysis ($I^2=8\%$). Subgroup analysis reported a larger effect size for CBT than for pharmacological treatment ($p=0.032$) and for treatment of anxiety compared with depression ($p=0.044$). There was evidence of significant publication bias ($p<0.05$) and the trim-and-fill analysis estimated that the degree of bias was small.

**Alcohol outcomes:** Treatment of internalising symptoms significantly improved overall alcohol use (effect size 0.22, 95% CI 0.02 to 0.42), frequency (effect size 0.34, 95% CI 0.13 to 0.56) and quantity (effect size 0.36, 95% CI 0.16 to 0.56), but had no significant effect on abstinence or intensity. Heterogeneity was significant for the analysis of intensity ($I^2=53\%$). Subgroup analysis found no significant differences for alcohol outcomes for CBT compared with pharmacological treatment, anxiety compared with depression and for larger effect sizes compared with smaller effect sizes for internalising outcome. There was no evidence of publication bias.

**Authors’ conclusions**

The results indicated that clinical psychiatric and alcohol-related outcomes could be somewhat improved by supplementing treatment of alcohol dependence with psychiatric treatment for co-occurring internalising disorder.

**CRD commentary**

The review question was clearly stated with appropriate inclusion criteria. Some relevant sources were searched. The restriction to studies published in English risked language and publication biases. Formal assessment of publication bias found some evidence of publication bias for one analysis. It was unclear whether appropriate methods to reduce reviewer error and bias were used for study selection and data extraction. There was no validity assessment, so it was not possible to determine the reliability of the evidence presented. Some study details were reported. There were differences in outcome measures and pharmacological treatments between studies. Heterogeneity was assessed. Differences between studies in terms of outcome measures, co-occurring diagnosis and pharmacological treatments meant that pooling the results may not have been appropriate. The analysis by subgroup seemed reasonable.

The authors’ conclusions reflect the evidence presented, but potential for language bias, the lack of a validity assessment and the lack of reporting of review methods mean that the reliability of the conclusions is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that adding psychiatric treatment for co-occurring internalising disorders added clinically significant value to treatment of alcohol use disorders.

**Research:** The authors did not state any implications for research.

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