A Systematic Review of Integrated Treatments for Depression and Substance Use in Young People

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Introduction

Both depression and substance misuse represent two of the major social and health problems facing young people worldwide[1,2]. Frequently, these conditions co-occur and this co-occurrence is associated with high rates of:

- Suicidal ideation and behaviours;
- Attrition, relapse and poor treatment response;
- Treatment service dependency;
- Functional impairment [3].

Integrated treatment approaches have been found to produce better outcomes than parallel or sequential approaches to co-occurring disorders in both young people and adults [6].

Due to systemic barriers, integrated treatment services for comorbidity in young people have been lacking. As a result, there has been a recent increase in debate regarding how best to address this gap [4].

Aims

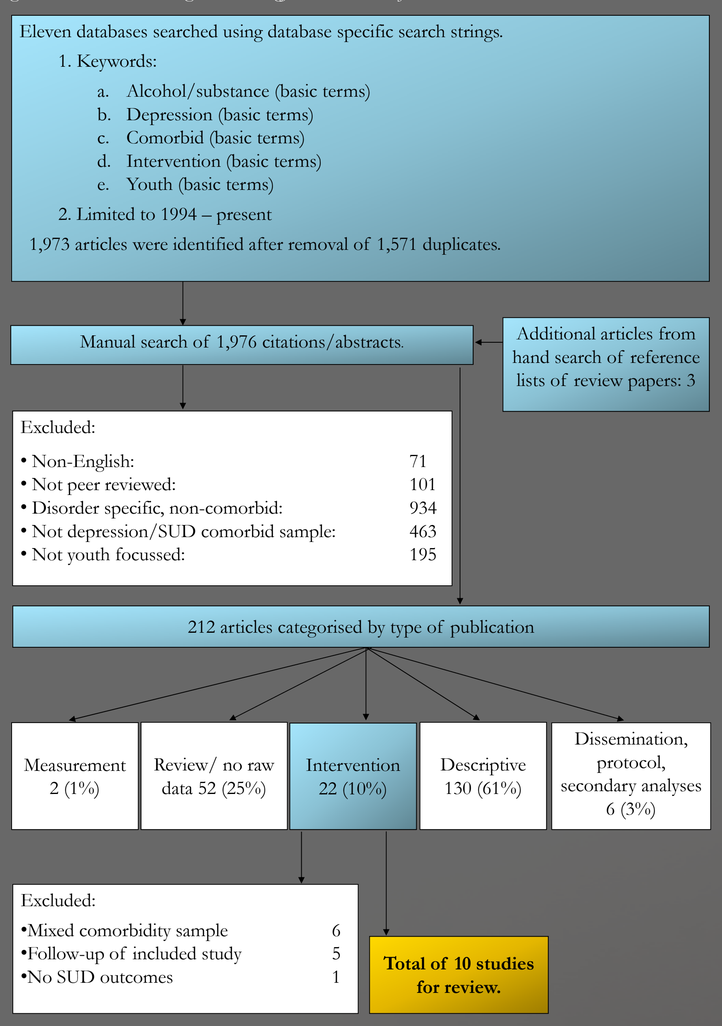
This systematic review aims to:

(1) identify published evaluation studies of interventions aimed at improving substance use and depression outcomes in comorbid young people;
(2) describe and critique their methodology; and
(3) identify opportunities for future intervention.

Method

Figure 1 summarizes the systematic search strategy.

Figure 1. Flowchart indicating search strategy and article classification



Effect sizes were calculated for common, primary outcome measures for controlled trials.

Results

Table 1 presents the key characteristics and outcome data of the studies reviewed. Of the studies identified, psychological treatment trials showed the most promise. Overall, those trials utilising a pharmacological component showed few, if any, between-group differences for either disorder. However, within-group improvement was often found for both intervention and control groups, this was pertinent as in most cases both groups received adjunct counselling as part of the trial. This within-group effect was also observed amongst each of the uncontrolled trials, each of which utilised a form of psychological counselling.

Table 1. Characteristics of evaluation studies of integrated treatments for co-occurring depression and substance use in young people

Study	Conditions	Sample, eligibility	Age range (% male)	Depression outcomes	Substance use outcomes	Conclusions
Controlled trials						
Cornelius et al [5] (RCT)	CBT/MET+Fluoxetine vs CBT/MET+ Placebo	N = 50; MDD, AUD	15-20 (44%)	HAM-D, *d* = 0.27 BDI, *d* = 0.14	TLFB-Q (alc), *d* = 0.57 TLFB-F (alc), *d* = 0.12	Fluoxetine did not improve outcomes above that of placebo for either disorder. The role of CBT/MET or placebo effects are unclear.
Cornelius et al [6] (RCT)	CBT/MET+ Fluoxetine vs CBT/MET+ Placebo	N = 70; MDD, CUD	14-24 (67%)	HAM-D, *d* = -0.57 BDI, *d* = -0.1	TLFB-Q (alc), *d* = -0.02 TLFB-F (alc), *d* = 0.11 TLFB-F (can), *d* = 0.25	Fluoxetine did not improve outcomes above that of placebo for either disorder. The role of CBT/MET or placebo effects are unclear.
Cornelius et al [7] (CT)	CBT/MET vs Naturalistic care	N = 118; MDD, AUD	15-20 (49%)	HAM-D, *d* = -1.28*** BDI, ES -1.14***	TLFB-Q (alc), *d* = -0.34 TLFB-F (alc), *d* = -0.38	CBT/MET therapy was associated greater improvement in depressive symptoms and alcohol-related symptoms at the two-year follow-up compared to naturalistic care.
Deas et al [8] (RCT)	CBT+Sertraline vs CBT+Placebo	N = 10; MDD, AUD	14-18 (80%)	HAM-D, *d* = 0.33	TLFB-Q (alc), *d* = -0.13 TLFB-F (alc), *d* = 0.03	Sertraline did not improve outcomes above that of placebo for either disorder. The role of CBT or placebo effects are unclear.
Findling et al [9]	Fluoxetine vs Placebo	N = 34; MDD, SUD	12-17 (85%)	BDI, *d* = 0.35 CDRS, *d* = 0.42	Urine toxicology, non significant	Fluoxetine did not improve outcomes above that of placebo.
Hides et al [10] (CT)	SC+CBT/MI vs SC	N = 88; likely MDD, SUD	16-25 (44%)	BDI, *d* = -0.17 CESD-R, *d* = -0.51* BDI, *d* = 0.28 CDRS, *d* = -0. 1	TLFB-Q (alc), *d* = 0.0 TLFB-F (alc), *d* = 0.08 TLFB-Q (can), *d* = -0.57* TLFB-F (can), *d* = -0.23 TLFB-Q (alc), *d* = -0.11 TLFB-F (alc), *d* = -0.2 TLFB-Q (can), *d* = -0.35 TLFB-F (can), *d* = 0.1	CBT/MI in combination with SC may accelerate short-term treatment gains.
Riggs et al [11] (RCT)	CBT+ Fluoxetine vs CBT+Placebo	N = 126; MDD, SUD	13-19 (67%)	CESD-R, *d* = -0.78* CGI-I, RR 1.08	TLFB-F (sub), *d* = -0.07	Fluoxetine+CBT had greater efficacy than placebo+ CBT on one but not both depression measures. SUD symptoms reduced overall, but not between groups. The role of CBT effects is unclear.
Uncontrolled trials						
Cornelius et al [12]	Standard psychotherapy +Fluoxetine	N = 13; MDD, AUD	15-19 (23%)			Preliminary evidence of the long-term therapeutic effects of fluoxetine and psychotherapy.
Curry et al [13]	Family and coping skills CBT	N = 13; DD, SUD	14-18 (54%)			Preliminary evidence for the feasibility and effectiveness of the integrated CBT intervention.
Hides et al [14]	MI/CBT+ Mindfulness	N = 60; MDD, SUD	15-25 (57%)			Preliminary evidence for the effectiveness of the integrated CBT intervention.

Significant difference between intervention and control p<*0.001****, p<*0.02***, p<*0.05**. d = *Cohen's* d *(effect size);* RR = *risk ratio;. RCT = randomised controlled trial; CT = controlled trial. BDI = Beck Depression Inventory; HAM-D = Hamilton Depression scale; CDRS-R = Children's Depression Rating Scale; CGI-I = Clinical Global Impressions-Improvement Scale; CESD-R = Center for Epidemiologic Studies Depression Scale – Revised; TLFB = Time-Line Follow-Back (Q – quantity, F – frequency; alc – alcohol, can – cannabis, O – other drugs, S - substance). MDD = major depressive disorder; DD = depressive disorder; CUD = cannabis use disorder; AUD = alcohol use disorder; SUD = substance use disorder; SC = standard care; CBT = cognitive behavioural therapy; MET =motivational enhancement therapy; MI = motivational interviewing.*

Table 2. Methodological adequacy

Study	Selection bias	Design bias	Confounders	Blinding	Data collection	Withdrawals/ dropout
Cornelius et al [5]	Moderate	Strong	Moderate	Strong	Strong	Strong
Cornelius et al [6]	Moderate	Strong	Strong	Strong	Strong	Strong
Cornelius et al [7]	Moderate	Moderate	Moderate	Moderate	Strong	Moderate
Deas et al [8]	Weak	Strong	Strong	Strong	Strong	Strong
Findling et al [9]	Moderate	Strong	Strong	Strong	Strong	Moderate
Hides et al [10]	Moderate	Moderate	Moderate	Strong	Strong	Moderate
Riggs et al [11]	Moderate	Strong	Strong	Strong	Strong	Strong
Cornelius et al [12]	Weak	Moderate	Moderate	Weak	Strong	Moderate
Curry et al [13]	Moderate	Weak	Moderate	Weak	Moderate	Moderate
Hides et al [14]	Moderate	Weak	Strong	Moderate	Strong	Moderate

Table 2 summarises the methodological adequacy of the 10 studies. Methodological quality of studies varied, particularly in relation to age-appropriateness of therapy, design, sample size, and follow-up rates. Statistical techniques employed for the analysis of study outcomes were generally appropriate.

Conclusions

Overall, there is a scarcity of evidence-based intervention trials for treating co-occurring depression and substance misuse in young people in an integrated way. More importantly, the studies that do exist are predominantly pharmacotherapy feasibility trails which do not adequately assess the role of counselling components. These studies consistently failed to find medication to be any more effective than placebo when both groups also receive counselling therapy.

The few studies which do specifically look to evaluate psychological therapies showed the most promising results, but rarely had adequate methodology to draw clear conclusions. No randomised controlled trials of this kind were found.

Further development and evaluation of fully integrated psychological interventions for co-occurring depression and substance misuse in young people is required.

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