Treatments for co-occurring depression and substance use in young people: A systematic review

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Short Title: Treatments for Youth Comorbidity: A Review

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Abstract

Background: Depression and problematic substance use represent two of the major social and health problems facing young people internationally. Frequently, these conditions co-occur and this co-occurrence is associated with greater functional impact, poorer treatment outcomes, and increased costs to both society and the individual.

Objective: This review aims to identify peer-reviewed published trials of interventions for co-occurring substance use and depression delivered to young people, describe these interventions, and critique the methodological quality of the studies.

Method: Eleven electronic databases were searched. The reference lists of relevant review papers were searched manually for additional studies not identified by the electronic database search.

Results: Initially, 1,976 studies were identified, of which 22 were classified as trial studies of youth-based treatment interventions for co-occurring substance use and depression. Ten of these studies met criteria for review. The majority (60%) utilised a pharmacotherapy component, but found it to be generally no better than placebo when both groups received adjunct counselling. Methodological quality of studies varied.

Conclusions: There is a dearth of trials of interventions for co-occurring depression and substance use disorders in young people. The limited data available is promising regarding the overall effectiveness of a psychological counselling approach. Given the importance of early intervention, and the difficulties faced when engaging youth in treatment, there is a need for further focussed effort amongst this group. This may require more innovative techniques in intervention design and implementation. Recent advances in Internet- and mobile phone-based therapies present a potential avenue for further research.

Keywords *adolescent, alcohol, co-occurring disorder, comorbidity, depression, substance use, systematic review, young people*

Introduction

Prevalence

Major depressive disorder (MDD) and problematic substance use are among the most significant public health concerns facing young people in the developed world. Recent epidemiological studies have indicated that approximately 15% of young adults meet criteria for lifetime MDD, while 13-22% meet criteria for a substance use disorder (SUD) [1-3]. Furthermore, comorbidity across the disorder classes is common [4, 5], with population-based surveys reporting one in four (26.6%) young people with current major depression, also met criteria for a 12-month SUD diagnosis, while amongst those with a 12-month SUD, one in five (18.1%) met criteria for current major depression [3]. Moreover, studies indicate that there has been a significant increase in the rates of depression amongst young people with SUDs in recent years [6].

The presence of co-occurring conditions increases the likelihood of treatment-seeking, as the risks of hospitalisation combine in those who have had more than one condition [7]. As such, prevalence rates for comorbidity in clinical samples tend to be even higher than those in population-based studies, ranging from 70 to 90% in substance use treatment services [8, 9]. Amongst this group, MDD is consistently found to be more prevalent than any other mental illness, with rates ranging from 24 to 50% [9-11]. In mental health settings, rates of problematic substance use in younger populations range from 11 to 71% [12, 13]. These rates vary depending on the treatment setting, informant, and method of assessment. Specific types of substances used tend to mirror the general population, with the most prevalent substance being alcohol [14].

Risks and harms of comorbidity

MDD and substance use comorbidity is a significant risk factor for a range of adverse outcomes and harms. Perhaps the most significant is that of suicide. In those with problematic alcohol use, depression is associated with increased suicidal ideation, ideation intensity, and behaviours [15-18]. Conversely, in depressed samples, alcohol use is associated with these same suicidal risk factors, in addition to the use of more lethal means of suicide [17, 19-22].

It has also been shown that in people receiving depression treatment, those with co-occurring problematic substance use have greater depressive symptomatology, higher rates of other concurrent mental disorders, an earlier age of onset of depression and poorer general functioning than those with depression alone [23, 24]. This

group also tends to attribute greater functional impairment to their illness [22]. Compared with individuals with depression only, those with co-occurring alcohol problems have impaired relationships with their spouses, as well as higher rates of divorce and living alone [24].

Similarly, amongst those receiving substance use treatment, those with comorbid depression have been found to report more substance-related problems, and a poorer quality of life [25]. This group also reports poorer treatment outcomes [26, 27], higher rates of poly-drug use [28], and increased rates of early relapse [29, 30]. There have been mixed findings regarding rates of treatment dropout [31]. The limited available research suggests that co-occurring substance use is associated with reduced treatment adherence for depression treatment [32], while the inverse is true for co-occurring depression in substance use treatment [33].

One proposed mechanism explaining the high rates of depression in individuals with problematic substance use is ‘self-medication’ [34], that is, substances being used in an attempt to medicate mental health symptoms [35]. However, this often only proves a temporary solution as co-occurring depression and SUDs have consistently been associated with significantly larger treatment use and costs compared with any condition in isolation [36]. Curran and colleagues [37] reported that primary psychiatric patients generally—and depressed patients specifically—with a co-occurring substance use comorbidity had a significantly more emergency department visits than primary psychiatric patients without this comorbidity. Conversely, patients with SUDs generally and co-occurring depression had significantly more emergency department visits [38] and hospital admissions [39] than patients without this comorbidity. Longitudinal studies, have indicated that depressed outpatients with SUDs incur consistently higher health care costs overall than other non-comorbid outpatients [40], and the same was true among substance use treatment outpatients with co-occurring depression [41].

Current state of comorbid treatment

There is an intuitive propensity, on the part of the medical profession, to view individual conditions in isolation and a historic tendency to segregate treatment for different diagnostic groupings based upon primacy [8, 42]. However, there are practical difficulties in reliably diagnosing primary and secondary conditions [43]. Furthermore, once both conditions are established, the relationship between them is often one of mutual influence, with each condition maintaining or exacerbating the other, thus rendering the primary/secondary distinction immaterial [44]. Instead, comorbidity experts advocate for the focus of treatment to be on functional impairment and distress caused by the conditions, as opposed to diagnostic sub-type classification, or the model

of aetiology [45]. Indeed, recent evidence highlights the importance of treating depression and substance use disorders concurrently [46].

Concurrent, integrated treatments for adults with co-occurring disorders have begun to emerge and expand over the last decade with encouraging results [47-51]. A recent meta-analysis identified 14 double-blind, randomized controlled trials (RCTs) for the treatment of depression and comorbid SUDs in general adult samples [52]. This study revealed a modest (i.e. 0.38) pooled effect size of antidepressant treatment, but maintained concomitant therapy directly targeting the substance use was also indicated. The therapies available to this group include motivational interviewing (MI), cognitive-behavioural therapy (CBT), contingency management, relapse prevention, case management, and skills training [53]. However, the tendency to exclude those with problematic substance use from clinical trials of psychiatric disorders [54-56] has limited findings and made inference difficult [57-59].

The importance of targeted youth approaches

Given the high prevalence rate and the myriad of adverse outcomes associated with comorbidity, early intervention in young people is fundamental to averting the development of more severe, ingrained morbidity [60]. Yet the proportional gap between those in need of treatment and those receiving it is widest amongst this group [61, 62]. In a recent national survey, Reavley and colleagues [63] found that although more than one in four young people between the ages of 16 and 24 experienced a 12-month mental disorder, less than 25% of these affected youth accessed health services in a 12-month period. This gap was widest amongst those with SUDs. These figures compared to one in five of the general population experiencing a disorder, with just over one in three of those seeking treatment.

The reasons for this discrepancy are complex. There is a suggestion that perceived stigmatisation among individuals with mental health disorders may be a component in this lack of health service utilisation [64-67]. Others have suggested motivations for behaviour and behavioural change in young people are likely to differ from those of adults which can lead to a reluctance to seek treatment, especially by way of traditional avenues [68-70]

These plausible explanations aside, a major reason for this shortfall is potentially due to the lack of applicable youth-based treatments and services [71]. Services have been slow to acknowledge that this phase of life has evolved with a unique culture, and thus requires treatment models that differ substantially from those suitable

for children and older adults [72]. Traditionally, in addition to the problem of historical separation of substance use and mental health services [55], attention has been further split between the child and adult mental health system services [71, 73]. The attempts of child and adult-based services to provide for older adolescents and young adults have been largely unsuccessful, failing to engage and provide access to this high risk group [71]. Consequently, due to this systemic weak point many of those with the greatest need fail to receive treatment, and the ability of transition-age youth with depression and problematic substance use to successfully adopt adult roles and responsibilities is at serious risk [73-75].

As young populations differ from adults in a number of fundamentally important ways, which are likely to affect treatment utilisation, adherence, and outcomes [76-79], simply replicating adult-oriented treatments for young people is likely to be inadequate. This group requires specialized treatment to meet their unique developmental and engagement needs [80-82].

Objectives

In light of these issues, this systematic review aims to: (1) identify published studies evaluating interventions aimed at improving depression and problematic alcohol use outcomes in young people, with these co-occurring conditions; (2) describe and critique the methodology of identified studies; and (3) pinpoint opportunities for future intervention.

Method

Sample

The search was limited to publications from 1994 to March 2012. This starting date was selected as the Diagnostic and Statistical Manual underwent major revision in 1993 and the DSM-IV was published [83, 84]. Rather than specify an arbitrary age range prior to the search procedure, which may have led to a failure to detect good quality intervention studies, the search strategy used general search terms pertaining to the term 'youth'.

Search strategy

Figure 1 summarizes the systematic search including databases used, the search terms employed, the exclusion criteria, and classification of included studies. Consistent with methods detailed in the *Cochrane Collaboration's Handbook: Systematic Reviews of Health Promotion and Public Health Interventions* [85] and

PRISMA statement for systematic reviews [86], the search strategy comprised two steps. First, consultation with an experienced archivist identified eleven relevant electronic databases to search: Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CCRCT), EMBASE, ERIC, MEDLINE, Project Cork, PsycINFO, PubMed, Scirus, Scopus, and Web of Science. Electronic databases were searched individually with specific search strings as this method is deemed more effective at identifying relevant articles than a simultaneous search using generic search terms [85]. Keyword search terms used were as follows: youth (young, adolesc*, juvenile, “emerging adult”), comorbid* (co-occur*, “dual diagnosis”), intervention (treat*, therap* trial*, random*), “substance use” (alcohol, “drug depend*”, “drug abuse”, substance) and depression (depress*, mood).

The combined searches of the eleven databases located 3,544 articles. After automatic and manual removal of 1,571 duplicates, 1,973 articles remained.

The second step in the search process involved a manual search of the reference lists of relevant review papers ($n = 52$) identified in step one. This process identified three additional studies [87-89], not captured by the primary search.

Classification of studies

A three-step process was used to classify the abstracts of the 1,976 identified studies.

Step 1: Identification of studies for exclusion. Papers were excluded if they were:

- i) Not in English ($n = 71$);
- ii) Not peer-reviewed (e.g., books/posters) ($n = 101$);
- iii) Disorder specific, non-comorbidity populations ($n = 934$)
- iv) Not a comorbid depression/problematic substance use sample ($n = 463$)
- v) Not youth focussed ($n = 195$)

Step 1 excluded 1,764 articles.

Step 2: Classification of studies. The remaining studies ($n = 212$) were classified as either intervention studies or one of four other criteria:

- i) *interventions* – evaluations or trials of youth-based intervention approaches targeting co-occurring depression and problematic substance use ($n = 22$);

- ii) *measurement* – articles detailing the development and/or testing of measurement instruments ($n = 2$);
- iii) *descriptive* – data-based descriptive, analytical research such as epidemiological studies, prevalence/incidence studies, treatment rates, and correlates ($n = 130$);
- iv) *dissemination/adoption, protocols and secondary analyses* – studies reviewing and describing development of interventions, evaluating approaches for improving delivery of these interventions or using secondary data from intervention studies ($n = 6$);
- v) *reviews* – literature reviews, non-data-based articles, and comments ($n = 52$).

Twenty-five per cent of the articles not excluded in step 1 ($n = 53$) were classified a second time by a blinded second rater (M.T.) to cross-check the classifications conducted originally by the first author (M.D.). The articles excluded in step 1 were not cross-checked because they were deemed not relevant for the review. Agreement between co-authors was 92%. Discrepancies were discussed and resolved. Due to high agreement between co-raters, cross-checking more than 25% of article classification was deemed unnecessary.

Step 2 excluded 190 articles.

Step 3: Identification of relevant studies. Of the 22 intervention articles identified, six used a mixed sample of various internalising and externalising comorbidities [10, 88-92]. These were excluded as they did not present specific depression assessments and/or outcomes. Five follow-up and case study papers from a single cohort study [93-97] were linked with the original paper as per Higgins and Green [85]. Finally, one paper reported no substance use outcomes [98].

Step 2 excluded 12 articles, leaving a total of 10 studies for review.

Figure 1. Search strategy.

Data extraction from studies

The criteria used for data extraction from studies were adapted from the *Cochrane Collaboration's Handbook: Systematic Reviews of Health Promotion and Public Health Interventions* [85]. These criteria relate to the intervention sample (including diagnosis, size, age range, percentage male), type of intervention (length, design, follow-up period, age-appropriateness), outcomes, and conclusions reached.

Methodological critique of intervention studies

The *Dictionary for the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies* [99, 100] was used to test the methodological quality of the studies. This tool has been validated in previous studies [101]. Sections A to F (A = selection bias; B = design/allocation bias; C = confounders; D = blinding; E = data collection methods; and F = withdrawals and drop-outs) were coded weak, moderate, or strong, consistent with the component rating scale of the dictionary [99]. For Sections G (intervention integrity) and H (analysis), descriptive information was recorded, guided by the tool's recommendations. Due to a degree of interpretation required by the assessment tool this was coded twice by two blind raters (M.D., M.T.). Agreement between co-authors was 88%. Discrepancies were discussed and resolved.

Data analysis

In order to understand the direction and magnitude of mean differences, effect sizes were calculated using the *d*-index [102] for commonly used, primary outcome measures using the following formula:

$$d = C_p \left[\frac{(M_{\text{post};T} - M_{\text{pre};T}) - (M_{\text{post};C} - M_{\text{pre};C})}{SD_{\text{pre},pooled}} \right]$$

Where $M_{\text{post};T}$ and $M_{\text{post};C}$ represent the mean post-intervention scores for treatment and control groups respectively. $M_{\text{pre};T}$ and $M_{\text{pre};C}$ represent the mean treatment and control baseline scores respectively, and $SD_{\text{pre},pooled}$ represents the pooled baseline standard deviation, calculated as per Walter and Yao [103]:

$$SD_{\text{pre},pooled} = \sqrt{\frac{(n_T - 1)SD^2_{\text{pre},T} + (n_C - 1)SD^2_{\text{pre},C}}{n_T + n_C - 2}}$$

Where n_T and n_C represent the sample size of treatment and control populations respectively. The above *d*-calculation was deemed the most unbiased estimate of effect size across studies [104, 105]. This effect size

formula was based on that of Becker [106]. However, an error in Becker's formula has been found to potentially underestimate the sampling variance, particularly when sample size is small [107]. C_p corrects for this error:

$$C_p = 1 - \frac{3}{4df - 1}$$

In studies without a control condition the simplified version of the formula was used:

$$d = C_p \left[\frac{(M_{\text{post}} - M_{\text{pre}})}{SD_{\text{pre}}} \right]$$

Where follow-up intervals existed, effect size was calculated using baseline and follow-up data. Where available, odds ratios, or risk ratios were extracted from papers.

A meta-analytic approach was explored, but deemed inappropriate, given the small number of studies and the heterogeneity of study quality and design, outcome measures, and follow-up rates. For this reason we chose to report the results in a systematic review.

Results

Intervention type and setting

Table 1 presents the extracted data of these studies. Of the 10 articles identified for review, three of these were uncontrolled trials [87, 108, 109]. Pharmacotherapy was utilised in 60% of studies, however, this was used in combination with psychological therapy in all but one study [110]. Sertraline ($n = 1$) and fluoxetine ($n = 5$) were the medications used. Cognitive behavioural therapy was used in eight of the nine studies utilising a psychological component. One study failed to report explicitly what constituted the psychological component of therapy [109]. Contact was made with the corresponding author who stated that, “the therapy was not particularly CBT-based” (author communication, August, 2012). In addition to CBT, five studies also included a motivational enhancement component [108, 111-114] and one utilised a family and coping skills component [87]. One study included an additional mindfulness component to the intervention [108].

Table 1. Study characteristics.

Study	Intervention	Control	Sample, eligibility	Age range, yrs (% male)	Number of sessions (Follow-up period)	Age appropriate	Conclusions
Controlled trials							
Cornelius et al [112]	CBT/MET+ Fluoxetine	CBT/MET + Placebo	N = 50; outpatient, MDD, AUD	15-20 (44%)	12 (none)	Age specific CBT for MDD and AUD but separate manuals	Fluoxetine did not improve outcomes above that of placebo for either condition. The role of placebo effects, CBT/MET effects and natural disorder course are unclear.
Cornelius et al [111]	CBT/MET+ Fluoxetine	CBT/MET+ Placebo	N = 70; outpatient, MDD, CUD	14-24 (67%)	12 (none)	Age specific CBT for MDD & SUD but separate manuals	Fluoxetine did not demonstrate greater efficacy than placebo for treating either condition, the role of CBT/MET and placebo effects are unclear.
Cornelius et al [113]	CBT/MET	Naturalistic care	N = 118; outpatient, MDD, AUD	15-20 (49%)	12 (2-year)	Age specific CBT for MDD & AUD but separate manuals	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 [115]	CBT+Sertraline	CBT+Placebo	N = 10; outpatient, MDD, AUD	14-18 (80%)	12 (none)	Not reported	Sertraline did not improve outcomes above that of placebo, the role of CBT effects or placebo effects are unclear.
Findling et al [110]	Fluoxetine	Placebo	N = 34; outpatient, MDD, SUD	12-17 (85%)	8 (none)	Pharmacotherapy only	Fluoxetine did not improve outcomes above that of placebo.
Hides et al [114]	SC+CBT/MI	SC	N = 88; outpatient, MDD, SUD symptomatology	16-25 (44%)	12 (3-month)	Not reported	CBT/MI in combination with SC may accelerate short-term treatment gains.
Riggs et al [116]	CBT+ Fluoxetine	CBT+Placebo	N = 126; outpatient, MDD, SUD	13-19 (67%)	16 (none)	Age specific CBT for SUD	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 [93-96, 109]	Standard psychotherapy +Fluoxetine	UC	N = 13; outpatient, MDD, AUD	15-19 (23%)	12 (1,3,5 year)	Not reported	Preliminary evidence that the long-term therapeutic effects of fluoxetine and psychotherapy slowly decrease but did not disappear when fluoxetine is discontinued shortly after the acute phase trial.
Curry et al [87]	Family and coping skills CBT	UC	N = 13; outpatient, DD, SUD	14-18 (54%)	12 (none)	Age specific CBT for MDD & SUD	Preliminary evidence for the feasibility and effectiveness of the integrated CBT intervention.
Hides et al [108]	MI/CBT+ Mindfulness	UC	N = 60; outpatient, MDD, SUD	15-25 (57%)	20 (6-month)	Age specific CBT for MDD & SUD	Preliminary evidence for the effectiveness of the integrated CBT intervention.

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; UC = uncontrolled trial

Despite each intervention being aimed at an adolescent and young adult population, there was variation in how age-specific the interventions were. Five studies used a form of CBT developed for a young population [87, 108, 111-113]. One study reported using an age-appropriate CBT manual for SUD only [116]. The other three studies used a psychological therapy component that did not report on the age-appropriateness of the intervention [109, 114, 115].

Similarly, those that used an element of psychological therapy rarely used fully integrated approaches, preferring separate manuals for treating depression and substance use. In only two cases did the authors report use of a fully integrated treatment manual for comorbidity [87, 108].

The number of sessions ranged from 8 to 20, with 70% of studies using a 12-session model.

Sample characteristics and eligibility criteria

All studies used an outpatient population. The young people ranged in age across the ten studies from 12 [110] to 25 [108, 114] years of age. The percentage range of male participants was 23% [109] to 85% [110].

In all but one study a diagnosis of a depressive disorder was an eligibility requirement. In the final study [114] eligibility was based on high depressive symptomatology on the Kessler Psychological Distress Scale [K10; 117]. This study was retained due to a high rate of lifetime mood disorders and current distress across the sample. In eight of the other nine studies, depressive disorder eligibility criteria was a current diagnosis of major depressive disorder, while the remaining study included those with a current diagnosis of either major depression or dysthymia [87]. Depression was assessed using versions of the Structured Clinical Interview for DSM-IV [SCID; 118, 119] in two studies [108, 114] and the Child Schedule for Affective Disorders and Schizophrenia [K-SADS; 120, 121] in six studies [109-113, 115], the Diagnostic Interview Schedule for Children [122] in one study [116] and the Child and Adolescent Psychiatric Assessment [CAPA; 123] in one study [87].

The substance use disorder was specifically alcohol abuse/dependence in four studies [109, 112, 113, 115], cannabis abuse/dependence in one study [111]. In three of the remaining five studies, eligibility criteria specified a diagnosis of at least one current SUD. In the final two studies [108, 114], participants had a range of SUDs, but eligibility was based on either SUD diagnosis or high-risk substance use. SUDs were assessed using

the SCID [108, 109, 111-115], the CAPA [87], the Composite International Diagnostic Interview [CIDI; 116, 124] and the K-SADS [110].

Delivery

Sessions for psychological treatment components were delivered individually [108, 109, 111-114, 116], or in groups [87, 110, 115]. Family members were included to a minor degree in one study [116] and in concurrent family sessions in one study [87].

All interventions were delivered in university-affiliated clinics or research centres, except where no psychological component was administered [110]. In this case, medication was dispensed by parent at home. Eight of the 10 studies were conducted in the United States, the remaining two [108, 114] in Australia.

Data collection methods

Self-report and non-self-report measures. All 10 studies used a combination of self-report measures and corroborating interviews or observer reports. Four studies [87, 108, 110, 116] also used urine toxicology tests, however, reporting of these results was inconsistent.

Measurement instruments for substance use outcomes. In addition to diagnostic interviews and urine toxicology tests, other instruments used in the measurement of substance use outcomes included the Time-Line Follow-Back [TLFB; 125], used in eight studies [108, 109, 111-116]; and the Recent Recall Form [126] used in one study [87]. The Alcohol Use Disorders Identification Test [AUDIT; 127], and the Severity of Dependence Scale [SDS; 128] were both used in two studies [108, 114].

Measurement instruments for depression outcomes. In addition to diagnostic interviews, the primary instruments used in the measurement of depression outcomes were most often either the Hamilton Depression scale [HAM-D; 129], used in seven studies [108, 109, 111-115], or the Beck Depression Inventory [BDI; 130], used in five studies [109-113]. Curry and colleagues [87] was the only study to use the Child and Adolescent Psychiatric Assessment [CAPA; 123] and the Children's Depression Inventory [CDI; 131]. While the Mood and Anxiety Symptom Questionnaire [MASQ; 132], and the Children's Depression Rating Scale [CDRS-R; 133] were used only in Hides and colleagues [108] and Findling and colleagues [110] respectively. Similarly, the Center for Epidemiologic Studies Depression Scale – Revised [CESD-R; 134] was used in only one study [114]

Other measures used. The Clinical Global Impressions (CGI) Scale [135] was used in four studies [108-110, 116]; while the Children's Global Assessment Scale [CGAS; 136] was used in two [110, 116]. Similarly, the Readiness to Change Questionnaire [RTCQ; 137]; the Automatic Thoughts Questionnaire [ATQ; 138]; the Drug Use Motives Measure [DUMM; 139]; the Coping Inventory for Stressful Situations [CISS; 140] and the Social and Occupational Functioning Assessment Scale [SOFAS; 141] were all used in two studies [108, 114]. Hides and colleagues [108] was the only study to use the Dysfunctional Attitudes Scale [DAS; 142], and the Hamilton Anxiety Scale [HAM-A; 143]. Similarly, Hides and colleagues [114] was the only study to use the K10 [144] and the Quality of Life Interview [QOLI; 145]. The Beck Hopelessness Scale [BHS; 146] was also only used in one study [110].

Methodological adequacy

Table 2 summarises the methodological adequacy of the 10 studies. Although no studies used a sample adequate to be deemed representative, the majority of studies minimised selection bias where possible and overall response rates were 80% or better (where reported). There was, however, a degree of self-selection in half the studies reviewed [87, 109, 111-113]. Fifty percent of the studies were randomised controlled trials [110-112, 115, 116], with randomisation described, thereby reducing the risk of allocation bias. A further 20% were controlled trials without randomisation [113, 114].

Four studies had baseline differences that were not controlled for post-intervention, and were generally related to diagnostic criteria [87, 109, 112, 113], and while one study had markedly differing group sizes [114]. Strong blinding procedures were conducted in two thirds of studies [110-112, 114-116]. Measures with established psychometric were used by all studies, with one exception, in which some non-validated measures were used to assess substance use [87]. Drop-out (loss to follow-up) was less than 20% (strong) in four studies [111, 112, 115, 116] and in the moderate/strong range for all other studies.

Sample size was small ($N \leq 34$) in four of ten studies [87, 109, 110, 115] and moderate in the remaining six (50 – 126 participants). Similarly, only four studies collected long-term follow-up data [108, 109, 113, 114], where follow-ups did occur, however, rates were over 60%.

In four studies an active control condition is likely to have been a factor in overall outcomes [111, 112, 115, 116], while two studies may have had unintended additional intervention, due to referrals offered to control groups [110, 113].

Table 2. Methodological adequacy.

Study	Selection bias	Design/allocation bias	Confounders	Blinding	Data collection methods	Withdrawals/dropout
Cornelius et al [93-96, 109]	Weak	Moderate	Moderate	Weak	Strong	Moderate
Cornelius et al [112]	Moderate	Strong	Moderate	Strong	Strong	Strong
Cornelius et al [111]	Moderate	Strong	Strong	Strong	Strong	Strong
Cornelius et al [113]	Moderate	Moderate	Moderate	Moderate	Strong	Moderate
Curry et al [87]	Moderate	Weak	Moderate	Weak	Moderate	Moderate
Deas et al [115]	Weak	Strong	Strong	Strong	Strong	Strong
Findling et al [110]	Moderate	Strong	Strong	Strong	Strong	Moderate
Hides et al [108]	Moderate	Weak	Strong	Moderate	Strong	Moderate
Hides et al [114]	Moderate	Moderate	Moderate	Strong	Strong	Moderate
Riggs et al [116]	Moderate	Strong	Strong	Strong	Strong	Strong

Notes: Measured by the Dictionary for the Effective Public Health Practice Project Quality Assessment tool for Quantitative Studies [99]. Information on Intervention Integrity (G) and Analysis (H) is contained in the text of the article.

Techniques to maintain intervention consistency were reported in four of the eight studies with a counselling component [109, 112, 113, 116]. In seven of the ten studies, participants completed over 80% of intervention [87, 109, 112, 113, 115, 116]. In the remaining three studies, participants completed over 70% of the intervention.

Overall analysis was generally appropriate with only three studies failing to conduct intention-to-treat analysis [87, 109, 114] and adequate statistical techniques were employed for the analysis of study outcomes, though referencing a source for their statistical approach was uncommon.

Effects

Table 3 shows the results of the data synthesis. In the majority of cases, primary depression and alcohol use outcomes included the BDI or HAM-D and the TLFB. As such, effect sizes were calculated for these outcomes for ease of comparison across studies. Where data was available, effect sizes were calculated for follow-up points, though this was rare.

Amongst the RCTs (all pharmacological trials), only one study reported a significant intervention effect size on a depression measure between groups (CDRS-R, $d = -0.78$; $p < 0.05$) [116]. This was in the medium to high range, but no significant change was found on the study's second depression measure. No RCT reported any significant effect between groups for alcohol outcomes. The two controlled trials (both psychological therapies) reported a significant intervention effect size on a depression measure between groups, but failed to find any significant effect on alcohol outcomes [113, 114]. When compared to a naturalistic control group at 2-year follow-up, Cornelius and colleagues [113] found those who had received a CBT/MET intervention had significantly ($p < 0.001$) improved HAM-D and BDI scores with large effect sizes ($d = -1.28$ and -1.14 , respectively). When compared to standard care at 3-month follow-up, Hides and colleagues [114] found those who had received a CBT/MI intervention had significantly ($p < 0.05$) improved CESD-R (but not BDI) scores ($d = -0.51$). No difference was found at 6-month follow-up. Although no differences were found on the TLFB for alcohol use, there was a significant reduction in cannabis use quantity ($d = -.57$; $p < 0.05$) and a reduction in rate of current SUD diagnoses at both 3 ($p < .02$) and 6 months post-baseline ($p < .02$) in the intervention group as compared with the standard care group.

Where no between-group effects were found between intervention and control groups, the study authors commonly reported overall improvement across both conditions. This was considered noteworthy as

psychological therapy was present in both groups in these studies. Cornelius and colleagues [112], for instance, reported significantly ($p < 0.001$) improved HAM-D and BDI scores with large effect sizes ($d = -1.56$ and -1.29 , respectively). Similarly, Cornelius and colleagues [111] reported significantly ($p < 0.001$) improved HAM-D and BDI scores with equally large effect sizes ($d = -1.64$ and -1.03). Deas and colleagues [115] reported significantly ($p < 0.001$) improved HAM-D scores with large effect sizes ($d = -1.56$) and medium to large effect sizes for improvements on the TLFB for drinking quantity ($d = -.83$; $p < .02$) and frequency ($d = -0.83$; $p < .02$).

Amongst the uncontrolled trials, improvement from baseline effect sizes also tended to be large for depression outcomes. Cornelius and colleagues [109] for instance, reported significantly ($p < 0.001$) improved HAM-D and BDI scores with large effect sizes at 12 weeks post-baseline ($d = -2.81$ and -2.46 , respectively), along with improvements on the TLFB for drinking quantity ($d = -.76$; $p < .02$). Long-term follow-up data, though positive, failed to adequately report on these measures. Curry and colleagues [87] reported significantly ($p < 0.001$) improved CDI scores with a large effect size at 12 weeks post-baseline ($d = -1.3$). While no significant change was found on the use of alcohol, significant reductions were also found in the frequency of cannabis use ($d = -0.86$; $p < .02$). Finally, Hides and colleagues [108] reported significantly ($p < 0.001$) improved HAM-D and MASQ-depression scores with large effect sizes at 20 weeks post-baseline ($d = -1.78$ and -1.12 , respectively), and 44 weeks post-baseline ($d = -1.78$ and -1.09 , respectively). Again, no alcohol use outcomes were significant, however, both cannabis use quantity and other drug use frequency were found to reduce significantly ($p < .02$), with medium effect sizes at 20 weeks post-baseline ($d = -0.51$ and -0.31 , respectively). At 44 weeks post-baseline this reduction was still significant ($p < .02$ and $p < 0.001$, respectively), with medium sized effects ($d = -0.44$ and -0.62 , respectively).

Table 3. Study outcomes.

Study	Type of intervention	Time point	Between-groups		Within-groups	
			Depression outcomes	Substance use outcomes	Depression outcomes	Substance use outcomes
Controlled trials						
Cornelius et al [112]	RCT	Treatment end	HAM-D, $d = 0.27$ BDI, $d = 0.14$	TLFB-A-quantity, $d = 0.57$ TLFB-A-frequency, $d = 0.12$	HAM-D, $d = -1.56^{***}$ BDI, $d = -1.29^{***}$	TLFB-A-quantity, $d = -0.46$ TLFB-A-frequency, $d = -0.77$
Cornelius et al [111]	RCT	Treatment end	HAM-D, $d = -0.57$ BDI, $d = -0.1$	TLFB-A-quantity, $d = -0.02$ TLFB-A-frequency, $d = 0.11$ TLFB-C-use, $d = 0.25$	HAM-D, $d = -1.64^{***}$ BDI, $d = -1.03^{***}$	TLFB-A-quantity, $d = -0.36$ TLFB-A-frequency, $d = -0.06$ TLFB-C-use, $d = -0.48$
Cornelius et al [113]	CT	2-year follow-up	HAM-D, $d = -1.28^{***}$ BDI, $d = -1.14^{***}$	TLFB-A-quantity, $d = -0.34$ TLFB-A-frequency, $d = -0.38$		
Deas et al [115]	RCT	Treatment end	HAM-D, $d = 0.33$	TLFB-A-quantity, $d = -0.13$ TLFB-A-frequency, $d = 0.03$	HAM-D, $d = -1.56^{***}$	TLFB-A-quantity, $d = -0.83^{**}$ TLFB-A-frequency, $d = -0.73^{**}$
Findling et al [110]	RCT	Treatment end	BDI, $d = 0.35$ CDRS-R, $d = 0.42$	Urine toxicology, non significant ($F = 0.22$)		
Hides et al [114]	CT	Treatment end	BDI, $d = -0.17$ CESD-R, $d = -0.51^{*}$	TLFB-A-quantity, $d = 0.0$ TLFB-A-frequency, $d = 0.08$ TLFB-C-quantity, $d = -0.57^{*}$ TLFB-C-frequency, $d = -0.23$		
		6-month follow-up	BDI, $d = 0.28$ CESD-R, $d = -0.1$	TLFB-A-quantity, $d = -0.11$ TLFB-A-frequency, $d = -0.2$ TLFB-C-quantity, $d = -0.35$ TLFB-C-frequency, $d = 0.1$		
Riggs et al [116]	RCT	Treatment end	CDRS-R, $d = -0.78^{*}$ CGI-I, RR = 1.08	TLFB-S-frequency, $d = -0.07$		
Uncontrolled trials						
Cornelius et al [93-96, 109]	Uncontrolled	Treatment end			HAM-D, $d = -2.81^{***}$ BDI, $d = -2.46^{***}$	TLFB-A-quantity, $d = -0.76^{**}$ TLFB-A-frequency, $d = -0.69$
		Follow-up			Insufficient data reported CDI, $d = -1.3^{***}$	Insufficient data reported Alcohol frequency, $d = -0.05$ Cannabis frequency, $d = -0.86^{*}$
Curry et al [87]	Uncontrolled					
Hides et al [108]	Uncontrolled	Treatment end			HAM-D, $d = -1.78^{***}$ MASQ dep, $d = -1.12^{***}$	TLFB-A-quantity, $d = 0.04$ TLFB-A-frequency, $d = 0.03$ TLFB-C-quantity, $d = -0.51^{**}$ TLFB-C-frequency, $d = -0.31$ TLFB-O-frequency, $d = -0.31^{**}$
		44-week follow-up			HAM-D, $d = -1.78^{***}$ MASQ dep, $d = -1.09^{***}$	TLFB-A-quantity, $d = -0.09$ TLFB-A-frequency, $d = -0.06$ TLFB-C-quantity, $d = -0.44^{**}$ TLFB-C-frequency, $d = 0.33$ TLFB-O-frequency, $d = -0.62^{***}$

Significant difference between intervention (or post) and control (or baseline) $p < 0.001^{***}$, $p < 0.02^{**}$, $p < 0.05^*$. d = Cohen's d (effect size); RR = risk ratio; 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; CDI = Children's Depression Inventory; $MASQ\ dep$ = Mood and Anxiety Symptom Questionnaire-depression; $TLFB$ = Time-Line Follow-Back (A – alcohol, C – cannabis, O – other drugs).

Discussion

Overall, there is a lack of peer-reviewed trials of evidence-based treatments for young people with depression and substance use disorders. The vast majority of studies available were descriptive in nature. This review identified 10 intervention trials, six of which were feasibility trials of pharmacological treatments (with all but one including a psychological component). Of the nine studies that utilised some form of psychological therapy, CBT and MI were most often used. Overall, this review provides rigorous support for recent assertions that very few psychosocial interventions for young people with co-occurring disorders have been developed and evaluated, as not a single RCT of this kind existed [147].

Methodological adequacy

The methodological quality of the studies was variable. For example, although the majority of studies had strong data collection methods, selection bias was consistently rated as moderate or weak (due in most cases to self-selection, or limited recruitment range). Most studies did, however, control for confounders (including additional comorbidities, substance use, age, ethnicity, gender) when identified and 60% of studies had strong blinding methods. Data collection methods and data analysis was generally appropriate and 70% of studies performed an intention-to-treat analysis. Withdrawal and dropout was moderate to strong in all studies, however, follow-up data was collected in only 40% of studies. Sample size and inadequacy of control group (either no control or active control) was consistently problematic.

Limitations of available literature

All of the six RCTs (all pharmacological), found medications safe and well-tolerated, but generally no more effective than placebo. A reason consistently suggested for this finding was the presence of adjunct psychological therapy received by both intervention and control groups that may have lead to a global improvement across all study participants. Of the studies that tested psychological therapies specifically, methodological issues pertaining to sample size and inadequate control conditions make interpretation difficult. Collectively, the studies provide preliminary evidence for the feasibility and effectiveness of the integrated intervention, with motivational interviewing components. As such, there is great potential for further development and evaluation of psychological treatments in this population.

The psychological interventions conducted in these studies rarely utilised a fully integrated approach to treatment, preferring instead separate manuals for treatment of SUD symptoms and those of depression. This is likely to be the result of availability of such manuals at the time of study. In recent years, however, a number of

integrated, adult psychological treatments for comorbidity have emerged [47, 48, 148], ideally similar youth-based programmes will follow suit. Only two studies in this review reported use of an integrated, youth-specific intervention [87, 108]; both were uncontrolled trials.

Finally, eight of the 10 identified studies were conducted in the United States. Although outcomes of interventions evaluated in the US may be applicable to other high-income countries (with common socio-economic factors and infrastructure for young people), between-country differences in substance use patterns and prevalence might lead to different intervention effects in different countries. Rigorous evaluation trials, conducted in other countries, would be valuable additions to the evidence base.

Intervention effects

Although limited in number, the studies identified by this systematic review suggest pharmacotherapy rarely improves outcomes above that of placebo for depression or problematic alcohol use when both treatment and control groups also receive adjunct psychological therapy. This finding is consistent with the conclusions drawn from reviews of adult comorbid interventions [52, 59]. Despite these somewhat bleak findings regarding a pharmacological approach, results were more promising for the use of psychological treatment approaches within this population. Where within-group change was explored (and in uncontrolled trials) significant improvement in outcomes was consistently reported. Although, demand characteristics (or other extraneous variables) cannot be discounted in explaining this change, such findings hold promise.

Where psychological treatments were used in isolation, there was preliminary evidence for the effectiveness of such approaches. Often, however, intervention effects were limited to depression outcomes, indicating an increased need for improved approaches to reducing problematic alcohol use in this population. Nevertheless, evaluations using more rigorous methodologies are required before clear conclusions can be reached about the most effective interventions among youth with these forms of comorbidity.

Limitations of current review

Although a meticulous and thorough search strategy was used, there is a possibility that the review did not locate all relevant studies. Similarly, relevant intervention evaluations may have been misclassified during the search refinement process, although this is unlikely due to the high inter-rater agreement (92%). There is also the small possibility that relevant studies may have been published prior to the cut-off of 1993. Due to the historical tendency to treat conditions in isolation integrated approaches to comorbidity before this point [54,

55], any trials which may have been conducted prior to 1993 are likely to be outdated and may not reflect current practice.

A number of multidimensional family therapy-based [149-153] and multisystemic [154-156] interventions were excluded from the review as they were not specifically aimed at comorbid depressive disorders, but rather were aimed to treat problematic substance use in a more holistic way. Similarly, this included studies aimed at treating SUDs in samples with a range of co-occurring (often unspecified) internalising and externalising problems [10, 88-92]. Although beyond the scope of this review, it could be suggested that such treatments may be clinically appropriate for co-occurring depression specifically, and trials amongst this population may be warranted.

Finally, as evaluations with statistically significant findings are more likely to be published than those without, it is possible that the published evaluations reviewed overestimate the interventions' true effectiveness [157-159]. However, due to the low rates of between group differences this appears unlikely.

Future research

As mentioned prior, there has been recent interest in integrated treatment approaches for comorbidity in the general population [47, 48, 148], however, further work is required to develop and evaluate treatments that are specifically relevant to—and effective for—young people with depression and problematic substance use. This review suggests few trials and treatment manuals for this population exist. Due to the particular difficulties encountered in engaging young people in treatment [75, 160], this may require more innovative techniques in intervention design and implementation. This review indicates a gap exists regarding evidence-based approaches of this kind. Recent advances in Internet-, and mobile phone-based therapies and serious gaming, have lead to new delivery approaches to the treatment of individual disorders [161-166] and this may represent potential avenues by which to target those young people with co-occurring problems. These approaches have the potential to overcome many of the barriers to effectively treating this population, for instance, availability, cost, flexibility, privacy, anonymity, and avoidance of stigma associated with seeing a therapist [167-169]. Evidence exists to suggest that these approaches can be effectively applied to comorbid depression and substance use problems [47, 48, 148].

Conclusions

Overall, there is a scarcity of evidence-based intervention trials for treating co-occurring depression and problematic substance use in young people. More importantly, the studies that do exist are predominantly pharmacotherapy feasibility trials which do not adequately assess the role of psychotherapeutic treatment components. Interestingly, these trials consistently failed to find medication to be any more effective than placebo when both groups also receive psychological therapy. The few studies which do specifically examine psychological therapies rarely had adequate methodology. Further development and evaluation of integrated psychological interventions for co-occurring depression and problematic substance use in young people are required.

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References

1. Merikangas KR, He J-P, Burstein M, Swanson SA, Avenevoli S, Cui L, et al. Lifetime prevalence of mental disorders in U.S. adolescents: Results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry*. 2010;49(10):980-9.
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):593-602.
3. ABS. National Survey Mental Health and Wellbeing: Summary of Results, 2007. Canberra: Australian Bureau of Statistics, 2008 4326.0.
4. Grant BF, Hasin DS, Dawson DA. The relationship between DSM-IV alcohol use disorders and DSM-IV major depression: examination of the primary-secondary distinction in a general population sample. *J Affect Disord*. 1996;38(2-3):113-28.
5. Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004;61:807-16.
6. Compton WM, Conway KP, Stinson FS, Grant BF. Changes in the prevalence of major depression and comorbid substance use disorders in the United States between 1991-1992 and 2001-2002. *Am J Psychiatry*. 2006;163:2141-7.
7. Berkson J. Limitations of the application of 4-fold tables to hospital data. *Biom Bull*. 1946;2:47-53.
8. Kaminer Y, Bukstein O. Adolescent Substance Abuse: Psychiatric Comorbidity and High Risk Behaviors. New York: Haworth Press; 2007.
9. Chan Y-F, Dennis ML, Funk RR. Prevalence and comorbidity of major internalizing and externalizing problems among adolescents and adults presenting to substance abuse treatment. *J Subst Abuse Treat*. 2008;34(1):14-24.
10. Kaminer Y, Burleson JA, Goldberger R. Cognitive-behavioral coping skills and psychoeducation therapies for adolescent substance abuse. *J Nerv Ment Dis*. 2002;190(11):737-45.
11. Bukstein OG, Glancy L, Kaminer Y. Patterns of affective comorbidity in a clinical population of dually diagnosed adolescent substance abusers. *J Am Acad Child Adolesc Psychiatry*. 1992;31:1041 - 5.
12. Baker KD, Lubman DI, Cosgrave EM, Killackey EJ, Yuen HP, Hides L, et al. Impact of co-occurring substance use on 6 month outcomes for young people seeking mental health treatment. *Aust N Z J Psychiatry*. 2007;41:896-902.

13. Kramer T, Robbins J, Phillips S, Miller T, Burns B. Detection and outcomes of substance use disorders in adolescents seeking mental health treatment. *J Am Acad Child Adolesc Psychiatry*. 2003;42:1318 - 26.
14. Rush AJ, Zimmerman M, Wisniewski SR, Fava M, Hollon SD, Warden D, et al. Comorbid psychiatric disorders in depressed outpatients: Demographic and clinical features. *J Affect Disord*. 2005;87(1):43-55.
15. Sher L. Risk and protective factors for suicide in patients with alcoholism. *TheScientificWorld J*. 2006;6:1405-11.
16. Esposito-Smythers C, Spirito A. Adolescent substance use and suicidal behavior: A review with implications for treatment research. *Alcohol Clin Exp Res*. 2004;28(5 SUPPL.):77S-88S.
17. Sher L, Zalsman G. Alcohol and adolescent suicide. *Int J Adolesc Med Health*. 2005;17(3):197-203.
18. Mann JJ. Neurobiology of suicidal behaviour. *Nat Rev Neurosci*. 2003;4(10):819-28.
19. Dumais A, Lesage AD, Alda M, Rouleau G, Dumont M, Chawky N, et al. Risk factors for suicide completion in major depression: A case-control study of impulsive and aggressive behaviors in men. *Am J Psychiatry*. 2005;162:2116-24.
20. Sher L, Oquendo M, Galfalvy H, Grunebaum M, Burke A, Zalsman G, et al. The relationship of aggression to suicidal behavior in depressed patients with a history of alcoholism. *Addict Behav*. 2005;30:1144-53.
21. Sher L, Oquendo MA, Richardson-Vejlgaard R, Makhija NM, Posner K, Mann JJ, et al. Effect of acute alcohol use on the lethality of suicide attempts in patients with mood disorders. *J Psychiatr Res*. 2009;43(10):901-5.
22. Davis LL, Uezato A, Newell JM, Frazier E. Major depression and comorbid substance use disorders. *Curr Opin Psychiatry*. 2008;21(1):14-8
23. Davis LL, Frazier E, Husain M, Warden D, Trivedi M, Fava M, et al. Substance use disorder comorbidity in major depressive disorder: A confirmatory analysis of the STAR*D cohort. *Am J Addict*. 2006;15(4):278-85.
24. Sullivan LE, Fiellin DA, O'Connor PG. The prevalence and impact of alcohol problems in major depression: A systematic review. *Am J Med*. 2005;118(4):330-41.
25. Lubman DI, Allen NB, Rogers N, Cementon E, Bonomo Y. The impact of co-occurring mood and anxiety disorders among substance-abusing youth. *J Affect Disord*. 2007;103(1-3):105-12.
26. Tomlinson KL, Brown SA, Abrantes A. Psychiatric comorbidity and substance use treatment outcomes of adolescents. *Psychol Addict Behav*. 2004;18(2):160-9.

27. Compton WM, Cottler LB, Jacobs JL, Ben-Abdallah A, Spitznagel EL. The role of psychiatric disorders in predicting drug dependence treatment outcomes. *Am J Psychiatry*. 2003;160:890-5.
28. Erfan S, Hashim AH, Shaheen M, Sabry N. Effect of comorbid depression on substance use disorders. *Subst Abus*. 2010;31(3):162-9.
29. Cornelius JR, Maisto SA, Martin CS, Bukstein OG, Salloum IM, Daley DC, et al. Major depression associated with earlier alcohol relapse in treated teens with AUD. *Addict Behav*. 2004;29(5):1035-8.
30. Dodge R, Sindelar J, Sinha R. The role of depression symptoms in predicting drug abstinence in outpatient substance abuse treatment. *J Subst Abuse Treat*. 2005;28:189-96.
31. Sayre SL, Schmitz JM, Stotts AL, Averill PM, Rhoades HM, Grabowski JJ. Determining predictors of attrition in an outpatient substance abuse program. *Am J Drug Alcohol Abuse*. 2002;28(1):55-72.
32. Gilbert M, Fine S, Haley G. Factors associated with dropout from group psychotherapy with depressed adolescents. *Can J Psychiatry*. 1994;39(6):358-9.
33. Agosti V, Nunes E, Stewart JW, Quitkin FM. Patient factors Related to early attrition from an outpatient cocaine research clinic: A preliminary report. *Int J Addict*. 1991;26(3):327-34.
34. Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harv Rev Psychiatry*. 1997;4(5):231-44.
35. Bolton JM, Robinson J, Sareen J. Self-medication of mood disorders with alcohol and drugs in the National Epidemiologic Survey on Alcohol and Related Conditions. *J Affect Disord*. 2009;115:367-75.
36. Mark TL. The costs of treating persons with depression and alcoholism compared with depression alone. *Psychiatr Serv*. 2003;54:1095-7.
37. Curran GM, Sullivan G, Williams K, Han X, Collins K, Keys J, et al. Emergency department use of persons with comorbid psychiatric and substance abuse disorders. *Ann Emerg Med*. 2003;41:659-67.
38. Curran GM, Sullivan G, Williams K, Han X, Allee E, Kotrla KJ. The association of psychiatric comorbidity and use of the emergency department among persons with substance use disorders: An observational cohort study. *BMC Emerg Med*. 2008;8:17.
39. O'Toole TP, Pollini R, Gray P, Jones T, Bigelow G, Ford DE. Factors identifying high-frequency and low-frequency health service utilization among substance-using adults. *J Subst Abuse Treat*. 2007;33:51-9.
40. Hoff RA, Rosenheck RA. Long-term patterns of service use and cost among patients with both psychiatric and substance abuse disorders. *Med Care*. 1998;36:835-43.
41. Hoff RA, Rosenheck RA. The cost of treating substance abuse patients with and without comorbid psychiatric disorders. *Psychiatr Serv*. 1999;50:1309-15.

42. Roberts AR, Corcoran K. Adolescents growing up in stressful environments, dual diagnosis, and sources of success. *Brief Treat Crisis Interv.* 2005;5:1-8.
43. Kay-Lambkin FJ, Baker A, Carr VJ. Depression and drug and alcohol problems. In: A.Baker, Velleman R, editors. *Clinical Handbook of co-existing mental health and drug and alcohol problems.* London: Routledge; 2007.
44. Kavanagh DJ. Psychological management of substance misuse in people with mental disorder. Kelvin Grove: Queensland University of Technology; 2008.
45. Kavanagh DJ, Mueser KT. Current evidence on integrated treatment for serious mental disorder and substance misuse. *Journal of the Norwegian Psychological Association.* 2007;44:618-37.
46. Watkins KE, Paddock SM, Zhang L, Wells KB. Improving care for depression in in-patients with comorbid substance misuse. *Am J Psychiatry.* 2006;163:125-32.
47. Baker A, Kavanagh DJ, Kay-Lambkin FJ, Hunt SA, Lewin TJ, Carr VJ, et al. Randomized controlled trial of cognitive-behavioural therapy for coexisting depression and alcohol problems: short-term outcome. *Addiction.* 2010;105(1):87-99.
48. Kay-Lambkin FJ, Baker AL, Lewin TJ, Carr VJ. Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy. *Addiction.* 2009;104(3):378-88.
49. Kelly TM, Daley DC, Douaihy AB. Treatment of substance abusing patients with comorbid psychiatric disorders. *Addict Behav.* 2012;37(1):11-24.
50. Mills KL, Teesson M, Back SE, Brady KT, Baker AL, Hopwood S, et al. Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: A randomized controlled trial. *JAMA.* 2012;308(7):690-9.
51. Lydecker KP, Tate SR, Cummins KM, McQuaid J, Granholm E, Brown SA. Clinical outcomes of an integrated treatment for depression and substance use disorders. *Psychol Addict Behav.* 2010;24(3):453-65.
52. Nunes EV, Levin FR. Treatment of depression in patients with alcohol or other drug dependence: a meta-analysis. *JAMA.* 2004;291(15):1887 - 96.
53. Horsfall J, Cleary M, Hunt GE, Walter G. Psychosocial treatments for people with co-occurring severe mental illnesses and substance use disorders (dual diagnosis): A review of empirical evidence. *Harv Rev Psychiatry.* 2009;17:24-34.
54. Riggs PD, Davies RD. A clinical approach to integrating treatment for adolescent depression and substance abuse. *J Am Acad Child Adolesc Psychiatry.* 2002;41(10):1253-5.
55. Libby AM, Riggs PD. Integrated substance use and mental health treatment for adolescents: Aligning organizational and financial incentives. *J Child Adolesc Psychopharmacol.* 2005;15(5):826-34.

56. Kavanagh DJ, Baker A, Teesson M. Co-morbidity of mental disorders and substance misuse: introduction. *Drug Alcohol Rev.* 2004;23(405 - 406).
57. Dumaine ML. Meta-analysis of interventions with co-occurring disorders of severe mental illness and substance abuse: Implications for social work practice. *Res Social Work Prac.* 2003;13:142-65.
58. Cleary M, Hunt GE, Matheson S, Walter G. Psychosocial treatments for people with co-occurring severe mental illness and substance misuse: systematic review. *J Adv Nurs.* 2009;65(2):238-58.
59. Hesse M. Integrated psychological treatment for substance use and co-morbid anxiety or depression vs. treatment for substance use alone. A systematic review of the published literature. *BMC Psychiatry.* 2009;9:e6.
60. Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics.* 2003;111(6 Pt 1):e699-705.
61. McGorry P. Should youth mental health become a specialty in its own right? Yes. *Br Med J.* 2009;339:b3373.
62. Burgess PM, Pirkis JE, Slade TN, Johnston AK, Meadows GN, Gunn JM. Service use for mental health problems: findings from the 2007 National Survey of Mental Health and Wellbeing. *Aust N Z J Psychiatry.* 2009;43(7):615-23.
63. Reavley NJ, Cvetkovski S, Jorm AF, Lubman DI. Help-seeking for substance use, anxiety and affective disorders among young people: results from the 2007 Australian National Survey of Mental Health and Wellbeing. *Aust N Z J Psychiatry.* 2010;44(8):729-35.
64. Keyes KM, Hatzenbuehler ML, McLaughlin KA, Link B, Olfson M, Grant BF, et al. Stigma and treatment for alcohol disorders in the United States. *Am J Epidemiol.* 2010. Epub November 2, 2010.
65. Teesson M, Hall W, Slade T, Mills K, Grove R, Mewton L, et al. Prevalence and correlates of DSM-IV alcohol abuse and dependence in Australia: Findings of the 2007 National Survey of Mental Health and Wellbeing. *Addiction.* 2010;105(12):2085-94.
66. Coyle JT, Pine DS, Charney DS, Lewis L, Nemeroff CB, Carlson GA, et al. Depression and Bipolar Support Alliance Consensus statement on the unmet needs in diagnosis and treatment of mood disorders in children and adolescents. *J Am Acad Child Adolesc Psychiatry.* 2003;42(12):1494-503.
67. Link BG, Struening EL, Rahav M, Phelan JC, Nuttbrock L. On Stigma and its consequences: Evidence from a longitudinal study of men with dual diagnoses of mental illness and substance abuse. *J Health Soc Behav.* 1997;38(2):177-90.
68. Wagner EF, Brown SA, Monti PM, Myers MG, Waldron HB. Innovations in adolescent substance abuse intervention. *Alcohol Clin Exp Res.* 1999;23(2):236-49.

69. Griffin KW, Botvin GJ, Epstein JA, Doyle MM, Diaz T. Psychosocial and behavioral factors in early adolescence as predictors of heavy drinking among high school seniors. *Journal of Studies on Alcohol and Drugs*. 2000;61:603-6.
70. Beal AC, Ausiello J, Perrin JM. Social influences on health-risk behaviors among minority middle school students. *J Adolesc Health*. 2001;28(6):474-80.
71. Singh SP. Transition of care from child to adult mental health services: the great divide. *Curr Opin Psychiatry*. 2009;22:386-90.
72. Parry-Jones W. The future of adolescent psychiatry. *Br J Psychiatry*. 1995;166:299-305.
73. Pottick K, Bilder S, Vander Stoep A, Warner L, Alvarez M. US patterns of mental health service utilization for transition-age youth and young adults. *Journal of Behavioral Health Services and Research*. 2008;35(4):373-89.
74. Tonin V. Young people seeking mental health care. *Lancet*. 2007;369:1239-40.
75. Rickwood DJ, Deane FP, Wilson CJ. When and how do young people seek professional help for mental health problems? *Med J Aust*. 2007;187(7 suppl):S35-9.
76. Schwartz SJ, Cote JE, Arnett JJ. Identity and agency in emerging adulthood: Two developmental routes in the individualization process. *Youth Soc*. 2005;37(2):201-29.
77. McDermott B, Baigent M, Chanen A, Fraser L, Graetz B, Hayman N, et al. Clinical practice guidelines: Depression in adolescents and young adults. Melbourne: beyondblue: the national depression initiative, 2010.
78. Winters KC. Treating Adolescents with Substance Use Disorders: An Overview of Practice Issues and Treatment Outcome. *Subst Abus*. 1999;20(4):203-25.
79. Masten AS, Burt KB, Roisman GI, Obradović J, Long JD, Tellegen A. Resources and resilience in the transition to adulthood: continuity and change. *Dev Psychopathol*. 2004;16(4):1071-94.
80. Deas D, Riggs P, Langenbucher J, Goldman M, Brown S. Adolescents are not adults: Developmental considerations in alcohol users. *Alcohol Clin Exp Res*. 2000;24(2):232-7.
81. Sawyer MG, Arney FM, Baghurst PA, Clark JJ, Graetz BW, Kosky RJ, et al. The mental health of young people in Australia: Key findings from the child and adolescent component of the National Survey of Mental Health and Well-Being. *Aust N Z J Psychiatry*. 2001;35(6):806-14.
82. Bender K, Springer DW, Kim JS. Treatment effectiveness with dually diagnosed adolescents: A systematic review. *Brief Treat Crisis Interv*. 2006;6(3):177-205.
83. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington DC: American Psychiatric Association; 1994.
84. Riosa PB, McArthur BA, Preyde M. Effectiveness of psychosocial intervention for children and adolescents with comorbid problems: A systematic review. *J Child Adolesc Ment Health*. 2011;16(4):177-85.

85. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions: The Cochrane Collaboration; 2011. Available from: www.cochrane-handbook.org.
86. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Med*. 2009;6(7):e1000100.
87. Curry JF, Wells KC, Lochman JE, Craighead WE, Nagy PD. Cognitive-behavioral intervention for depressed, substance-abusing adolescents: Development and pilot testing. *J Am Acad Child Adolesc Psychiatry*. 2003;42(6):656-65.
88. Kaminer Y, Burleson JA, Blitz C, Sussman J, Rounsaville BJ. Psychotherapies for adolescent substance abusers: A pilot study. *J Nerv Ment Dis*. 1998;186(11):684-90.
89. Kaminer Y, Burleson JA. Psychotherapies for adolescent substance abusers: 15-month follow-up of a pilot study. *Am J Addict*. 1999;8(2):114-9.
90. Pressman M, Brook DW, Maidman P, Orlowski B. Clinical improvement in adolescents comorbid for substance abuse and psychiatric diagnoses through multiple group psychotherapy. *Group*. 2001;25(4):321-32.
91. Cleminshaw HK, Shepler R, Newman I. The Integrated Co-Occurring Treatment (ICT) Model: A promising practice for youth with mental health and substance abuse disorders. *J Dual Diagn*. 2005;1(3):85-94.
92. Jenson JM, Potter CC. The effects of cross-system collaboration on mental health and substance abuse problems of detained youth. *Res Social Work Prac*. 2003;13(5):588-607.
93. Cornelius JR, Bukstein OG, Salloum IM, Kelly TM, Wood DS, Clark DB. Fluoxetine in Depressed AUD Adolescents: A 1-Year Follow-up Evaluation. *J Child Adolesc Psychopharmacol*. 2004;14(1):33-8.
94. Cornelius JR, Clark DB, Bukstein OG, Birmaher B, Kelly TM, Salloum IM, et al. Fluoxetine in adolescents with comorbid major depression and an alcohol use disorder a five-year follow-up study. *J Dual Diagn*. 2006;2(1):11-25.
95. Cornelius JR, Clark DB, Bukstein OG, Birmaher B, Salloum IM, Brown SA. Acute phase and five-year follow-up study of fluoxetine in adolescents with major depression and a comorbid substance use disorder: A review. *Addict Behav*. 2005;30(9):1824-33.
96. Cornelius JR, Clark DB, Bukstein OG, Kelly TM, Salloum IM, Wood DS. Fluoxetine in adolescents with comorbid major depression and an alcohol use disorder: A 3-year follow-up study. *Addict Behav*. 2005;30(4):807-14.
97. Curry JF, Wells KC, Lochman JE, Craighead WE, Nagy PD. Group and family cognitive behavior therapy for adolescent depression and substance abuse: A case study. *Cogn Behav Pract*. 2001;8(4):367-76.
98. Riggs PD, Mikulich SK, Coffman LM, Crowley TJ. Fluoxetine in drug-dependent delinquents with major depression: An open trial. *J Child Adolesc Psychopharmacol*. 1997;7(2):87-95.

99. Hamilton Effective Public Health Practice Project Team. Dictionary for the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies. Hamilton: Effective Public Health Practice Project, 2003.
100. Thomas BH, Ciliska D, Dobbins M, Micucci S. A process for systematically reviewing the literature: Providing the research evidence for public health nursing interventions. *Worldviews Evid Based Nurs*. 2004;1(3):176-84.
101. Armijo-Olivo S, Stiles CR, Hagen NA, Biondo PD, Cummings GG. Assessment of study quality for systematic reviews: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment tool: methodological research. *J Eval Clin Pract*. 2012;18(1):12-8.
102. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
103. Walter SD, Yao X. Effect sizes can be calculated for studies reporting ranges for outcome variables in systematic reviews. *J Clin Epidemiol*. 2007;60(8):849-52.
104. Morris SB. Estimating effect sizes from pretest-posttest-control group designs. *Org Res Methods*. 2008;11(2):364-86.
105. Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. *Psychol Methods*. 2002;7(1):105-25.
106. Becker BJ. Synthesizing standardized mean-change measures. *Br J Math Stat Psychol*. 1988;41:257-78.
107. Morris SB. Distribution of the standardized mean change effect size for meta-analysis on repeated measures. *Br J Math Stat Psychol*. 2000;53:17-29.
108. Hides LM, Carroll S, Catania L, Cotton SM, Baker A, Scaffidi A, et al. Outcomes of an integrated cognitive behaviour therapy (CBT) treatment program for co-occurring depression and substance misuse in young people. *J Affect Disord*. 2010;121(1-2):169-74.
109. Cornelius JR, Bukstein OG, Birmaher B, Salloum IM, Lynch K, Pollock NK, et al. Fluoxetine in adolescents with major depression and an alcohol use disorder: an open-label trial. *Addict Behav*. 2001;26(5):735-9.
110. Findling RL, Pagano ME, McNamara NK, Stansbrey RJ, Faber JE, Lingler J, et al. The short-term safety and efficacy of fluoxetine in depressed adolescents with alcohol and cannabis use disorders: A pilot randomized placebo-controlled trial. *Child Adolesc Psychiatry Ment*. 2009;3:e11.
111. Cornelius JR, Bukstein OG, Douaihy AB, Clark DB, Chung TA, Daley DC, et al. Double-blind fluoxetine trial in comorbid MDD-CUD youth and young adults. *Drug Alcohol Depend*. 2010;112(1-2):39-45.
112. Cornelius JR, Bukstein OG, Wood DS, Kirisci L, Douaihy A, Clark DB. Double-blind placebo-controlled trial of fluoxetine in adolescents with comorbid major depression and an alcohol use disorder. *Addict Behav*. 2009;34(10):905-9.

113. Cornelius JR, Douaihy A, Bukstein OG, Daley DC, Wood SD, Kelly TM, et al. Evaluation of cognitive behavioral therapy/motivational enhancement therapy (CBT/MET) in a treatment trial of comorbid MDD/AUD adolescents. *Addict Behav.* 2011;36(8):843-8.
114. Hides LM, Elkins KS, Scaffidi A, Cotton SM, Carroll S, Lubman DI. Does the addition of integrated cognitive behaviour therapy and motivational interviewing improve the outcomes of standard care for young people with comorbid depression and substance misuse? *Med J Aust.* 2011;195(3 SUPPL.):S31-S7.
115. Deas D, Randall CL, Roberts JS, Anton RF. A double-blind, placebo-controlled trial of sertraline in depressed adolescent alcoholics: A pilot study. *Hum Psychopharmacol.* 2000;15(6):461-9.
116. Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, Stover SK. A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Arch Pediatr Adolesc Med.* 2007;161(11):1026-34.
117. Kessler RC, Barker PR, Colpe LJ, Epstein JF, Groerer JC, Hiripi E, et al. Screening for serious mental illness in the general population. *Arch Gen Psychiatry.* 2003;60(2):184-9.
118. First M, Spitzer R, Gibbon M, Williams J. Structured Clinical Interview for DSM-IV-TR axis I disorders, research version, patient edition. New York: Biometrics Research, New York State Psychiatric Institute; 2001.
119. Spitzer R, Williams J, Gibbon M, First M. Structured Clinical Interview for DSM-III-R. Washington, DC: American Psychiatric Press; 1990.
120. Chambers W, Puig-Antich J, Hirsch M, Paez P, Ambrosini P, Tabrizi M, et al. The assessment of affective disorders in children and adolescents by semistructured interview. Test-retest reliability of the schedule for affective disorders and schizophrenia for school-age children, present episode version. *Arch Gen Psychiatry.* 1985;42(7):696-702.
121. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry.* 1997;36:980-8.
122. Shaffer D. NIMH Diagnostic Interview Schedule for Children-Version IV. New York: New York State Psychiatric Institute; 1997.
123. Angold A, Costello EJ. The Child and Adolescent Psychiatric Assessment (CAPA). *J Am Acad Child Adolesc Psychiatry.* 2000;39(1):39-48.
124. Cottler L, Robins L, Helzer J. The reliability of the CIDI-SAM: a comprehensive substance abuse interview. *Br J Addict.* 1989;84(7):801-14.
125. Sobell LC, Sobell MB, Leo GI, Cancilla A. Reliability of a timeline method: assessing normal drinkers' reports of recent drinking and a comparative evaluation across several populations. *Br J Addict.* 1988;83:393-402.

126. Curry JF, Wells K. Recent Recall Form. Durham, NC: Duke University; 1997.
127. Saunders JB, Aasland OG, Babor TF, Fuente JRdl, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption - II. *Addiction*. 1993;88:791-804.
128. Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, et al. The severity of dependence scale (sds):psychometric properties of the sds in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction*. 1995;90:607-14.
129. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.
130. Beck A, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561-71.
131. Kovacs M. Children's Depression Inventory Manual. North Tonawanda, NY: Multi-Health Systems; 1992.
132. Watson D, Weber K, Assenheimer J, Clark L, Strauss M, McCormick R. Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. *J Abnorm Psychol*. 1995;104(1):3-14.
133. Poznanski E, Freeman L, Mokros H. Children's depression rating scale - revised. *Psychopharmacol Bull*. 1985;21:979-89.
134. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol*. 1977;1:385-401.
135. NIMH. Clinical Global Impressions Scale. *Psychopharmacol Bull*. 1985;21:839-43.
136. Shaffer D, Gould M, Brasic J, Ambrosini P, Fisher P, Bird H, et al. A children's global assessment scale (CGAS). *Arch Gen Psychiatry*. 1983;40:1228-31.
137. Heather N, Rollnick S. Readiness to Change Questionnaire: User's Manual. Centre for Alcohol & Drug Studies: Newcastle, UK; 2000.
138. Hollan S, Kendall P. Cognitive self-statements in depression: development of an Automatic Thoughts Questionnaire. *Cogn Ther Res*. 1980;4:383-95.
139. Mueser KT, Pallavi N, Tracy JI, DeGirolamo J, Molinaro M. Expectations and motives for substance use in schizophrenia. *Schizophr Bull*. 1995;21:367-78.
140. Endler NS, Parker JD. Assessment of multidimensional coping: task, emotion, and avoidance strategies. *Psychol Assess*. 1994;6:50-60.
141. Morosini PL, Magliano L, Brambilla L, Ugolini S, Pioli R. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr Scand*. 2000;101(4):323-9.

142. Weisman AN, Beck AT. Development and Validation of the Dysfunctional Attitudes Scale: a Preliminary Investigation. Toronto, Canada: The American Education Research Association; 1978.
143. Clark DB, Donovan JE. Reliability and validity of the Hamilton Anxiety Rating Scale in an adolescent sample. *J Am Acad Child Adolesc Psychiatry*. 1994;33:354-60.
144. Kessler RC. Kessler's 10 Psychological Distress Scale. Boston, MA: Harvard Medical School, 1996.
145. Lehman A. A quality of life interview for the chronically mentally ill. *Eval Program Plann*. 1988;11:51-62.
146. Beck A, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol*. 1974;42:861-5.
147. Bukstein OG, Horner MS. Management of the Adolescent with Substance Use Disorders and Comorbid Psychopathology. *Child Adolesc Psychiatr Clin N Am*. 2010;19(3):609-23.
148. Kay-Lambkin FJ, Baker AL, Kelly B, Lewin TJ. Clinician-assisted computerised versus therapist-delivered treatment for depressive and addictive disorders: A randomised controlled trial. *Med J Aust*. 2011;195(3 SUPPL.):S44-S50.
149. Henderson CE, Dakof GA, Greenbaum PE, Liddle HA. Effectiveness of Multidimensional Family Therapy with higher severity substance-abusing adolescents: Report from two randomized controlled trials. *J Consult Clin Psychol*. 2010;78(6):885-97.
150. Liddle HA, Rowe CL, Dakof GA, Henderson CE, Greenbaum PE. Multidimensional family therapy for young adolescent substance abuse: twelve-month outcomes of a randomized controlled trial. *J Consult Clin Psychol*. 2009;77:12-25.
151. Liddle HA, Dakof GA, Parker K, Diamond GS, Barrett K, Tejeda M. Multidimensional family therapy for adolescent substance abuse: Results of a randomized clinical trial. *Am J Drug Alcohol Abuse*. 2001; 27:651-8.
152. Liddle HA, Rowe CL, Dakof GA, Ungaro RA, Henderson CE. Early intervention for adolescent substance abuse: Pretreatment to posttreatment outcomes of a randomized controlled trial comparing multidimensional family therapy and peer group treatment. *J Psychoactive Drugs*. 2004;36(1):2-37.
153. Liddle HA, Dakof GA, Turner RM, Henderson CE, Greenbaum PE. Treating adolescent drug abuse: a randomized trial comparing multidimensional family therapy and cognitive behavior therapy. *Addiction*. 2008;103(10):1660-70.
154. Henggeler SW, Clingempeel WG, Brondino MJ, Pickrel SG. Four-year follow-up of multisystemic therapy with substance-abusing and substance-dependent juvenile offenders. *J Am Acad Child Adolesc Psychiatry*. 2002;41(7):868-74.
155. Henggeler SW, Pickrel S, Brondino M. Multisystemic treatment of substance abusing and dependent delinquents: outcomes, treatment fidelity, and transportability. *Ment Health Serv Res*. 1999;1:171-84.

156. Timmons-Mitchell J, Bender MB, Kishna MA, Mitchell CC. An independent effectiveness trial of Multisystemic Therapy with juvenile justice youth. *J Clin Child Adolesc Psychol.* 2006;35(2):227-36.
157. Dickersin K, Chan S, Chalmers T, Sacks H, Smith HJ. Publication bias and clinical trials. *Control Clin Trials.* 1987;8(4):343-53.
158. Easterbrook P, Berlin J, Gopalan R, Matthews D. Publication bias in clinical research. *Lancet.* 1991;337(8746):867-72.
159. Dwan K, Altman D, Arnaiz J, Bloom J, Chan A, Cronin E, et al. Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS One.* 2008;3(8):e3081.
160. Barker G, Olukoya A, Aggleton P. Young people, social support and help-seeking. *Int J Adolesc Med Health.* 2005;17:315-35.
161. Preziosa A, Grassi A, Gaggioli A, Riva G. Therapeutic applications of the mobile phone. *Brit J Guid Couns.* 2009;37:313-25.
162. Deady M, Kay-Lambkin F, Thornton L, Baker A, Teesson M. Social Influence, Addictions and the Internet: The potential of Web 2.0 technologies in enhancing treatment for alcohol/other drug use problems. *J Addict Res Ther.* 2012;S8.
163. Griffiths KM, Christensen H. Review of randomised controlled trials of Internet interventions for mental disorders and related conditions. *Clin Psychol.* 2006;10(1):16 - 29.
164. Ybarra ML, Eaton WW. Internet-based mental health interventions. *Ment Health Serv Res.* 2005;7(2):75-87.
165. Merry SN, Stasiak K, Shepherd M, Frampton C, Fleming T, Lucassen MFG. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *Br Med J.* 2012;344.
166. Shandley K, Austin D, Klein B, Kyrios M. An evaluation of 'Reach Out Central': an online gaming program for supporting the mental health of young people. *Health Educ Res.* 2010;25(4):563-74.
167. Burns J, Rapee RM. Adolescent mental health literacy: young people's knowledge of depression and help seeking. *J Adolesc.* 2006;29:225-39.
168. Nicholas J, Oliver K, Lee K, O'Brien M. Help-seeking behavior on the Internet: An investigation among Australian adolescents. *AeJAMH.* 2004;3:1-8.
169. Burns J, Durkin LA, Nicholas J. Mental health of young people in the United States: What role can the internet play in reducing stigma and promoting help seeking? *J Adolesc Health.* 2009;45(1):95-7.