Managing Depressive Symptoms in Substance Abuse Clients During Early Recovery: A Review of the Literature*

Update

Reviews Literature From July 1, 2011 Through December 31, 2011

Treatment Improvement Protocol (TIP) Series

48

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UPDATED FINDINGS FROM THE LITERATURE, JANUARY 2012

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Updated Findings From the Literature, January 2012

This Treatment Improvement Protocol (TIP) Literature Review update includes findings relevant to TIP 48, *Managing Depressive Symptoms in Substance Abuse Clients During Early Recovery*. These findings were published between July 1, 2011, and December 31, 2011.

Overview

Twelve research articles on depression and substance use disorders (SUDs) were identified for inclusion in this literature review update, which is organized around the following topics:

- Depression and SUD screening and assessment
- Efficacy of integrated treatment for alcohol use disorders (AUDs) and depression
- Efficacy of pharmacotherapy intervention
- Efficacy of psychotherapy or psychiatric treatment intervention

Depression and SUD Screening and Assessment

Given the prevalence of depression (or depressive symptoms) in individuals seeking SUD treatment and the negative impact depression can have on SUD treatment outcomes, selecting an effective depression screening tool for people with SUDs is a critical decision for mental health professionals.

Delgadillo et al. (2011) examined the reliability and validity of the Patient Health Questionnaire (PHQ-9) and its shorter version, PHQ-2, in a sample of individuals accessing substance use treatment in the United Kingdom. The PHQ-9 is a widely used nine-item questionnaire validated for depression screening. It yields scores ranging from 0 to 27, with scores of 5–9, 10–14, 15–19, and 20–27 representing mild, moderate, moderately severe, and severe depression, respectively.

The researchers compared the accuracy, reliability, and validity of PHQ-9 and PHQ-2 against the Revised Clinical Interview Schedule (CIS-R). The CIS-R elicits responses related to 14 symptom areas, based on diagnostic criteria of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (World Health Organization, 1992). The CIS-R can be used to assess six specific nonpsychotic disorders, including mixed anxiety and depressive disorder and depressive episode. It can also provide two (primary and secondary) diagnoses based on a symptom matching and scoring mechanism. A score of 12 or more indicates significant severity of symptoms.

The researchers recruited 103 patients from an outpatient drug treatment facility. The participant pool included individuals at various stages of treatment, and participation was not limited by substance use type (e.g., alcohol, heroin, stimulants). A subgroup of 60 patients participated in a retest 4 to 6 weeks after the initial assessment.

After participants completed the PHQ-9 and PHQ-2, trained clinical staff conducted a diagnostic interview using the CIS-R. The researchers analyzed the data from PHQ-9 and PHQ-2, assessed the performance of the measures relative to CIS-R and, via intra-class correlations, determined test-retest validity.

Almost half (49 percent) of the participants met diagnostic criteria for major depression. Based on their analyses, the researchers concluded that PHQ-9 was a valid and reliable depression screening tool with a high internal consistency and "fairly robust" test-retest reliability. They also found a significant positive correlation between PHQ-9 and CIS-R (r=.76, p<.001). The shorter PHQ-2 version had modest test-retest reliability.

Study limitations include possible recruitment bias (participants received supermarket vouchers as incentives), although the researchers indicated that demographics, clinical factors, and drug use patterns were comparable to those found in other studies. Second, the CIS-R does not account for the sequencing of symptoms. That is, the temporal relationship between substance use and mental disorders in this group of participants is unknown. Third, while the 4-week period between test-retest was sufficient for the purposes of this evaluation, it did not allow for the observation of longer-term patterns of symptom stability and change.

Despite these limitations, the study results support the use of PHQ-9 as an accurate depression screening tool with strong validity and high internal consistency. The shorter version had only modest reliability and was not recommended based on the study results.

Staiger, Thomas, Ricciardelli, and McCabe (2011) conducted diagnostic interviews in a sample of individuals who were seeking outpatient treatment for SUDs in Melbourne, Australia. Their purpose was to identify and measure the type and severity of high-prevalence mental disorders—such as depression and anxiety—and SUDs.

Ninety-five participants (56 men, 39 women) were recruited. Individuals either responded to advertisements at the SUD treatment facility or were referred by case managers. The goal was to target individuals who were likely to have a high-prevalence mental disorder.

The researchers used a range of screening instruments and measures, including the Composite International Diagnostic Interview (CIDI), Version 2.1; PTSD (Posttraumatic Stress Disorder) Checklist, Civilian Version; Beck Depression Inventory (BDI-II); State-Trait Anxiety Inventory (STAI), Trait Version, Form Y; and Addition Severity Index, 5th Edition.

The researchers found that more than 50 percent (n=48) of participants had used a drug by the age of 14. Approximately 63 percent (n=60) reported an AUD, the most common type of SUD among the participants. In regard to mental disorders, almost 76 percent (n=72) were diagnosed with a depressive disorder. In terms of the type and severity of high-prevalence mental disorders, 20 percent (n=19) were diagnosed with a single disorder, and 24 percent (n=23) were diagnosed with four or more high-prevalence mental disorders. In addition, those with a drug use disorder (which could include concurrent AUD) had significantly higher depression severity scores compared with the AUD-only group.

Due to the small sample size and the use of a nonrandom sampling technique, the researchers cautioned that the study results should not be generalized to the larger population.

Studies have also examined the standard definition and criteria of different types of depression. Dakwar et al. (2011) observed that the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association [APA], 2000) makes a distinction between depressive disorders that occur in association with substance use,

intoxication, or withdrawal (referred to as *substance-induced depression* [SID]) and depressive disorders that are not associated with substance use (i.e., a primary mood disorder, referred to as *independent depression* [ID]). These researchers compared SID and ID in a group of people dependent on cocaine, opioids, and/or cannabis. They hypothesized that:

- The severity of depressive symptoms would differ significantly between the two diagnostic categories of ID and SID.
- Regular drug use in the SID group would have started at a lower age.
- Patients with a history of SID would more likely be male and would be less likely to be contending with psychiatric comorbidities than those with a history of ID.

The researchers recruited 242 adults dependent on cocaine, opioids, and/or cannabis who had co-occurring depression. The subjects were seeking treatment at a university-based clinic. A modified structural clinical interview for DSM-IV-TR disorders (SCID) was administered during initial evaluation. The modification allowed researchers to distinguish between primary and secondary depression.

Of the subjects who met the eligibility criteria, 72.7 percent (*n*=176) had lifetime ID (dysthymic disorder [DD] or major depressive disorder [MDD]), and 27.3 percent (*n*=66) had lifetime SID. Further, 48.8 percent (*n*=118) had active ID, and 24.8 percent (*n*=60) had active SID.

The results indicated that men in the study sample were more likely than women to have SID, and women were more likely than men to have been diagnosed with ID. The researchers observed that men and women in the study had similar rates of DD, but female gender was a significant predictor of MDD. In addition, participants who were cocaine dependent had the highest prevalence of SID, while participants who were cannabis dependent had the highest prevalence of ID. The findings support other research that indicates that associations between primary and secondary depression vary among individuals affected by different substances of abuse.

The researchers acknowledged several study limitations. First, the design was cross-sectional, and the sample size was small. Second, several variables which may have been important to consider (e.g., the number of depressive episodes, drug use patterns) were not assessed. Third, even though uniform diagnostic procedures were followed, clinicians' subjective judgments may have contributed to the differences in measurements between ID and SID. Relative to this last limitation, interrater reliability was not assessed.

In a cross-sectional survey examining the prevalence of major depression in methamphetamine users, McKetin, Lubman, Lee, Ross, and Slade (2011) also made a distinction between major depression and substance-induced depression. They recruited 400 participants who were seeking treatment for methamphetamine use upon entry into 1 of 41 drug and alcohol treatment agencies located in Australia. Diagnostic measures included the CIDI (to assess major depression and methamphetamine dependence), the Short Form Health Survey (SF-12) (as a measure of physical and mental health), and the Opiate Treatment Index. Face-to-face interviews with each participant were conducted shortly after treatment entry.

Ninety-seven percent of participants met DSM-IV-TR criteria for methamphetamine dependence. Forty percent of the participants met the DSM-IV-TR criteria for a major depressive episode in the prior year. A further 44 percent of participants had what was deemed substance-induced depression. Symptom profiles between the two groups were similar, but the group diagnosed with major depression exhibited higher levels of suicidal ideation and included more participants reporting depressive episodes that lasted two or more weeks. Both major depression and substance-induced depression were associated with mental health disability, as measured by the SF-12.

Other results of note include the finding of a significant relationship between substance-induced depression and the initiation of methamphetamine use at a young age. Also, cannabis and benzodiazepines were found to be significantly associated with depression. This is similar to the 2011 study by Dakwar et al. (above) that found cannabis dependence to be a significant predictor of MDD. Consistent with earlier studies, major depression was more common among female participants than male participants.

The authors stressed the difficulty in distinguishing major depression from substance-induced depression. The difficulty partly lies with the need to identify a temporal relationship between the onset of the substance use and depressive symptoms. The researchers also noted the difficulty in diagnosing depression when patients were using methamphetamines, as the drugs' acute effects (e.g., insomnia) and withdrawal symptoms (e.g., depressed mood) overlap with the symptoms of depression. The researchers noted that further research is needed to determine whether methamphetamine use increases the risk of major depression.

Pilowsky, Wu, Burchett, Blazer, and Ling (2011) examined the relationship between depressive symptoms, substance use, and HIV-related sexual and injection risk behaviors among people who were opioid dependent and seeking treatment. The researchers recruited 343 participants (233 men and 110 women) from inpatient (n=113) and outpatient (n=230) sites participating in the National Drug Abuse Treatment Clinical Trials Network.

Data were gathered at baseline (i.e., prior to addiction treatment beginning). Depressive symptoms were evaluated using the Psychiatric Domain of the Addiction Severity Index (ASI). Individuals who responded affirmatively to a single question from the ASI about depression (i.e., sadness, hopelessness, lack of interest, and difficulty with daily function) were considered having current symptoms of depression. Anxiety symptoms and suicidal ideation and attempts were also assessed via the ASI (one question and two questions, respectively). The Short Form Health Survey (SF-36) was used to validate the "depressive symptoms" category (i.e., the variables measured in the SF-36 were expected to correlate with depressive symptoms). The 36-item, self-administered form measures health-related quality of life in physical and social functioning, such as role limitations due to physical health and emotional problems. Risky sexual and injection behaviors were measured via the HIV Risk Behavior scale. Substance use was measured via the ASI.

The results showed a significant association between depressive symptoms and increased likelihood of injection risk behaviors among people seeking treatment for opioid dependence. This association—even after adjustment for confounding demographic variables—was shown to be independent of other co-occurring substance use (i.e., amphetamine or cocaine use). No

positive association was identified between depressive or anxiety-related symptoms and an increased likelihood of risky sexual behaviors.

The researchers acknowledged several study limitations. First, the participant group included only those who were seeking treatment; the results may not be generalizable to other populations. Second, while the researchers sought to enhance validity via the SF-36, assessment of depressive symptoms consisted of a single question from the ASI. Third, as the study was cross-sectional in design, causality of results cannot necessarily be inferred.

Efficacy of Integrated Treatment for Alcohol Use Disorders and Depression

Farren, Snee, and McElroy (2011) studied the impact of integrated treatments for patients with a mood disorder (either bipolar disorder or depression) and co-occurring substance dependence. Previously, the researchers had studied short-term efficacy of an integrated psychotherapy and pharmacotherapy treatment program for affective disorders and AUDs. For the current study, which took place in Ireland, they developed a program that integrated psychotherapy and pharmacotherapy for co-occurring mental and substance use disorders and followed the treatment population for two years.

The program consisted of three stages:

- Detoxification and mood stabilization
- 4-week inpatient program
- After care on a weekly basis for the first 2 months, biweekly for the second 2 months, and monthly for the last 2 months

Participants underwent followup evaluation at four points—at discharge and 3 months, 6 months, and 2 years after treatment.

The researchers used the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV; APA, 1994) criteria for alcohol dependence and mania/hypomania or major depression, and assessment was based on the SCID (Research Version). The researchers found 189 individuals (ages 17 to 76) who met the study criteria (co-occurring mood and alcohol use disorders). The sample consisted of 51 percent women and 49 percent men.

After participants underwent alcohol detoxification and mood stabilization, a single psychologist assessed the participants using a range of screening instruments; urinary drug screening and blood tests were administered to assess substance use. Assessment tools included a Timeline Followback, Young Mania Rating Scale, Beck Depression Inventory, Beck Anxiety Inventory Scale, Alcohol Use Disorder Test, and Drug Abuse Screening Test. At each followup point, participants completed their assessments. At the 3-month and 6-month followups, they also provided information about their current medications, drug or alcohol use, aftercare attendance, employment, and any self-harming or parasuicide incidents that may have occurred.

The study had an overall retention rate of 75.1 percent at 2-year followup. Study results showed significant abstinence rates at 2-year followup, suggesting efficacy of the treatment program for patients with a mood disorder and co-occurring AUDs. They found that people with co-occurring

bipolar disorder or depression and alcohol dependence could be treated successfully in the "triple-integrated" treatment program. They also found significant gender differences in treatment outcomes. Female patients reported higher levels of abstinence (56.3 percent) at 2-year followup than men (29.3 percent). In addition, women with bipolar disorder reported higher levels of depression and anxiety at 2-year followup than men with bipolar disorder, although this was not the case in the depressed group or in the overall study.

The researchers noted the following study limitations. First, generalization of results is limited in that this was not a randomized controlled study. Second, the program relied on self-reports about substance use at the 2-year followup because collection of blood samples was not possible. Nevertheless, the preliminary findings from this study suggest that people with co-occurring bipolar disorder or depression and alcohol dependence can be treated successfully. It is important to note that although the authors specified that components of the study included psychotherapy and outpatient therapy, they did not include information about the nature of the psychotherapy or outpatient therapy that was included in the program except, perhaps, as it may have been part of "aftercare," which they described as patients meeting with a consultant or attending self-help groups.

In a meta-analysis of supplemental treatment for depressive and anxiety disorders in patients with alcohol dependence, Hobbs, Kushner, Lee, Reardon, and Maurer (2011) synthesized the effects from 15 randomized trials that examined supplementing AUD treatment with a psychiatric treatment for co-occurring anxiety and depressive disorders. To facilitate data analysis, the authors grouped anxiety and depressive disorders under what they termed "internalizing disorders," assuming that both anxiety and depression share the same underlying construct. Their goal was to examine the effect of psychiatric treatment on anxiety/depression outcomes in patients with AUDs and on the improvement of AUD treatment outcomes.

Building on and extending two previous quantitative reviews, one of which was a formal meta-analysis of current literature, the authors designed the current meta-analysis to examine clinical benefits of integrated treatment for both internalizing disorders and AUDs. The authors searched OVID Medline and PsycINFO databases. To supplement the search results, they conducted a bibliographic review of studies and identified additional resources from the current literature. The search identified 15 studies that met the inclusion criteria. Together, the studies had 1,310 subjects randomly assigned to treatment or control groups.

Of the 15 studies, 12 tested a pharmacological treatment and 3 tested a cognitive–behavioral therapy (CBT) intervention for a co-occurring internalizing disorder. Only two of the CBT studies reported usable outcomes in treating panic disorder or depression (both internalizing disorders). Six of the 15 studies treated a co-occurring anxiety disorder and 9 treated a co-occurring depressive disorder.

To assess anxiety outcome measures, the authors used the Hamilton Rating Scale for Anxiety (HAM-A), Social Phobia Inventory, Symptom Checklist-90, and Anxiety Discomfort Scale. For depression outcome measures, they used the Hamilton Rating Scale for Depression (HAM-D), the Beck Depression Inventory, the Profile of Mood States, and the Montgomery and Asberg Depression Rating Scale.

For the study, the authors developed measures of alcohol-related outcomes in four domains—abstinence (absence of alcohol consumption during followup), frequency (number of drinking days and percent days drinking), intensity (number of heavy drinking days per week), and quantity (number of drinks per drinking day). They also defined an overall alcohol outcome composite measure by averaging the entire alcohol outcome effect sizes. The researchers tested the effects of treatment type, disorder type, and magnitude of the internalizing treatment on the alcohol outcome.

Synthesized effects from the meta-analysis indicate that psychiatric treatments for co-occurring internalizing disorders are moderately effective in populations with AUD and add clinically significant value to AUD treatment even though the overall effects may be small.

The researchers identified typical methodological issues as limitations of the study. Chief among these issues are the stringent inclusion criteria, which excluded many studies that could otherwise be potentially relevant to the study topic. The generalizability of the study results is also limited to those undergoing AUD treatment and thus cannot be applied to those under drug treatment. In addition, the lack of consistency in how different studies reported study outcomes presented a challenge in summarizing and presenting the effect size.

Efficacy of Pharmacotherapy Intervention

Oliveto et al. (2011) looked into the efficacy of sertraline in delaying relapse in individuals with depressive symptoms who were cocaine dependent and recently abstinent. They selected sertraline as they wanted to examine the effects of an antidepressant that would inhibit the reuptake of both serotonin and dopamine (both of which are involved in depression and substance dependence). The study was a rigorous, double-blind, randomized controlled clinical trial.

Individuals were screened for cocaine dependence per DSM-IV criteria via the SCID. Depression was measured via the Hamilton Depression Scale (all participants had a score >15). In addition, the ASI and the Cocaine Selective Severity Assessment were completed at intake. Participants could earn up to $250 for attending required treatment sessions and returning urine collection specimens.

Eighty-six individuals (53 males and 33 females, ages 18 to 52) who were seeking treatment for cocaine dependence met the study inclusion criteria and were randomly assigned to either the sertraline or placebo group.

The 12-week clinical trial was divided into four phases: enrollment, residential stay, outpatient, and analysis. The treatment program consisted of a 2-week residential stay followed by 10 weeks of outpatient participation. During weeks 1–3, participants attended a Department of Veterans Affairs Substance Abuse Day Treatment Program. During weeks 4–12, participants attended a weekly 1-hour, individual CBT session. During weeks 3–12, participants were onsite at the outpatient treatment research program at least 3 days per week. Of the 86 participants enrolled in this study who met inclusion criteria, 27 dropped out prior to week 2. Data from the 59 participants who remained beyond the 2-week residential portion were analyzed. Thirty-four participants completed the 12-week clinical trial.

Results showed that participants in the placebo group relapsed significantly sooner than the sertraline group. Sertraline use did not appear to be related to the decline in depression symptoms, as the decline was observed in both groups. These findings indicate that sertraline may have efficacy for cocaine dependence and may delay time to relapse, particularly in patients who are recently abstinent from cocaine use.

A meta-analysis study conducted by Pedrelli et al. (2011) investigated the efficacy of antidepressants in the treatment of MDD and DD in patients receiving methadone maintenance treatment (MMT). After searching Medline/PubMed databases, the authors found four studies for inclusion. The studies were randomized, double-blind, placebo-controlled clinical trials published between January 1, 1980, and June 30, 2010. The studies represented 317 patients, with 164 randomized to receive antidepressant treatment and 153 to receive placebo.

The authors analyzed the clinical response rates of the pooled studies. They found no statistically significant difference in response rates between antidepressant therapy and placebo treatment for patients receiving MMT.

The meta-analysis has several limitations. Only four studies met the selection criteria, and the studies differed from one another in several important aspects, including variability in the amount and type of psychosocial treatment patients received and the different classes of antidepressants used. The small numbers of patients enrolled in the studies (e.g., fewer than 50 in two of the studies) and the potential possibility of drug interactions between antidepressants and methadone (e.g., changes in methadone serum levels could affect antidepressant levels) further limited the findings of this meta-analysis. The authors suggested the need for further study to identify effective classes of antidepressants and psychosocial intervention for patients with co-occurring opioid dependence and depressive symptoms in MMT.

Efficacy of Psychotherapy or Psychiatric Treatment Intervention

Granholm et al. (2011) examined whether neuropsychological functioning was related to the treatment efficacy of two psychotherapy interventions for co-occurring depression and SUDs in a sample of veterans receiving outpatient treatment. The study was a secondary analysis of data from a previous randomized clinical trial performed by the researchers.

The researchers compared the outcomes of Integrated Cognitive Behavioral Therapy (ICBT) and the Twelve-Step Facilitation Therapy (TSF). Based on Cognitive–Behavioral Depression Treatment and Cognitive–Behavioral Coping Skills Training of Addiction (the latter integrated into the former), ICBT consisted of three modules:

- The cognitions module emphasized identifying maladaptive thoughts, creating alternative thoughts, and rehearsing these thought-challenging techniques to help prevent relapse to substance use or increased depressive symptoms.
- The activities module included identifying, scheduling, and assessing the effectiveness of new activities to increase positive affect and help manage pressure to relapse.
- The social module consisted of assertiveness and communication training to help increase positive social interactions and resist social pressure to use.

TSF is a therapist-guided group intervention based on the Alcoholics Anonymous 12-Step principles. As a common form of treatment intervention in different settings, TSF was used as the control condition in this study. The version used was modified from the manual that was developed and tested in the Matching Alcoholism Treatment to Client Heterogeneity (MATCH) study.

A total of 164 veterans with MDD and co-occurring alcohol, cannabis, and/or stimulant use disorders participated in the study. Participants were randomly assigned to either the ICBT or the TSF group. Both groups received two consecutive 12-week treatments provided in two phases. In Phase I, participants attended an hour-long group session twice weekly for 12 weeks and monthly individual medication management visits. In Phase II, the hour-long group sessions were reduced to once a week for 12 weeks. Assessments took place during intake (baseline), the end of Phase I (12 weeks), the end of Phase II (24 weeks), and thereafter quarterly for an additional 12 months. Participants underwent a diagnostic assessment using the CIDI. Additional assessment instruments included the Timeline Followback for assessing alcohol and drug involvement and the 21-item HAM-D for structured assessments of depression and substance use. Random toxicology screens were conducted to confirm the self-reported data.

The researchers used a variety of measures to test neuropsychological functioning in the following domains:

- Attention and speed of processing
- Verbal IQ
- Verbal learning and memory
- Visuospatial construction and memory

Contrary to the authors' hypotheses:

- Participants with poorer neuropsychological functioning in the ICBT group had better substance use outcomes than participants with poorer neuropsychological functioning in the TSF group.
- The ICBT participants with poorer neuropsychological functioning also showed a greater reduction in depressive symptoms compared with ICBT participants who had better neuropsychological functioning.
- Participants in the TSF group who had poorer neuropsychological functioning showed less of a reduction in depressive symptoms compared with TSF participants with better neuropsychological functioning.

Results suggest that participants with poorer neuropsychological functioning may benefit more from ICBT than TSF in the treatment of substance use and depression.

The study has some limitations. The participants were primarily male and exclusively veterans, and most had histories of multiple treatments for co-occurring depression and SUDs; the results may not be generalizable to other populations. Although all participants were taking prescribed medication, the researchers did not monitor medication compliance or other variables related to pharmacological treatment, so the effects of medication compliance and noncompliance on study

results are unknown. Also, research staff members were not blinded to the group treatment assignment, which could have resulted in bias.

Methodology

The same methodology used in developing the literature review for TIP 48 was used for this update.

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