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Comorbid Depression and Substance Use Disorder: Longitudinal Associations Between Symptoms in a Controlled Trial

Matthew J. Worley,

San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology

Ryan S. Trim,

VA San Diego Healthcare System and University of California, San Diego

Scott C. Roesch,

San Diego State University

Jennifer Mrnak-Meyer,

VA San Diego Healthcare System

Susan R. Tate, and

VA San Diego Healthcare System and University of California, San Diego

Sandra A. Brown

VA San Diego Healthcare System and University of California, San Diego

Abstract

The current study examined the longitudinal association between substance use and depressive symptoms, in veterans receiving outpatient treatment for comorbid substance use disorder and major depression. Veterans ($N = 237$, mean age = 48.2 years, 90% male, 70% Caucasian) received either six months of group Integrated Cognitive-Behavioral Therapy or Twelve-Step Facilitation. Hamilton Depression Rating Scale scores and Percent Days Using any substance were assessed every 3 months up to one year post-treatment. Greater substance use predicted time-varying elevations in depression above individual patterns of change in depression. Moreover, change in depressive symptoms was associated with change in both the likelihood of any substance use and the frequency of use during the treatment and follow-up periods. Changes in these symptoms appear to be linked, such that individuals with greater reductions in substance use have greater reductions in depressive symptoms (and vice versa).

Keywords

Comorbidity; latent growth curve; parallel process; depressive symptoms; substance use

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1. Introduction

Among individuals with a substance use disorder (SUD), comorbid major depressive disorder (MDD) is associated with a multitude of negative outcomes, including worse quality of life (Saatcioglu, Yapici, & Cakmak, 2008), greater rates of disability (Olfson et al., 1997), and greater risk of suicide (Glasner-Edwards et al., 2008). At the initiation of treatment for SUD, patients with comorbid MDD often have more severe impairments in multiple areas, including medical, legal, and social problems (Leventhal, Mooney, DeLaune, & Schmitz, 2006). In addition, MDD is the most common comorbid Axis I diagnosis for individuals with SUD. The 12-month prevalence of comorbid MDD in the community was estimated at 15.5% (Grant et al., 2004), and this prevalence is even greater among those receiving treatment for an alcohol use disorder (32.8%) or drug use disorder (44.3%). Although some interventions have shown efficacy, currently no psychological treatment meets the commonly accepted criteria for well-established and effective treatments (Hesse, 2009). Given the prevalence, severity, and costs of this comorbidity, it is important to understand factors contributing to ongoing symptoms and repeated treatment episodes to aid the development of improved therapies. One factor could be a strong and persistent longitudinal association between substance use and depressive symptoms, which would provide support for the refinement of integrated therapies. These symptoms are theoretically linked over time in comorbid patients, but no known studies have validated these effects empirically.

Many studies have shown that depression has a negative impact on SUD treatment outcome, whether it is considered as a comorbid diagnosis of MDD (Burns, Teesson, & O'Neill, 2000) or a continuous measure of depressive symptoms (Dodge, Sindelar, & Sihha, 2005). Alcohol-dependent patients with MDD were shown to have shorter times to first drink and greater likelihood of relapse after inpatient treatment (Greenfield et al., 1998). Similarly, greater depressive symptoms predicted greater odds of relapse after inpatient alcohol treatment (Curran, Flynn, Kirchner, & Booth, 2000) and poorer drinking outcomes in Project MATCH (Ilgen & Moos, 2005; Gamble et al., 2010). Even mild depressive symptoms increased the odds of relapse during follow-up of treatment for alcohol dependence and smoking cessation (Kodl et al., 2008). Similar results were found in studies of treatments for users of illicit substances. Cocaine-dependent patients with MDD had poorer outcomes from cognitive-behavioral therapy (Levin et al., 2008). Depressive symptoms at baseline predicted future methamphetamine use, and patients diagnosed with MDD at follow-up used methamphetamine more frequently and had lower odds of abstinence (Glasner-Edwards et al., 2008). These studies suggest MDD or greater baseline depressive symptoms negatively impacts substance dependence treatment. None of these studies examined reductions in depression and associated changes in substance use outcomes in comorbid patients, an important question as depression may reduce or increase over time.

The effect of substance use on depression outcome has received comparatively less empirical focus, with the majority of prior studies focusing on patients with SUDs in pharmacotherapy trials for depression. Patients with SUDs had lower rates of remission and longer time to remission during pharmacological treatment for depression (Davis et al., 2010; Howland et al., 2009). However, other studies found no differences in depression outcomes due to SUD status (Watkins, Paddock, Zhang, & Wells, 2006). It may be that depressive symptoms are only impacted when these patients are frequently using substances. In other pharmacotherapy trials, alcohol dependence predicted worse outcomes only for patients who were drinking heavily at baseline (Rae, Joyce, Luty, & Mulder, 2002), and greater alcohol consumption at baseline predicted poorer fluoxetine response (Worthington

et al., 1996). Continued use of substances during and after treatment could be associated with exacerbated depression, but prior studies have not examined these time-varying effects.

Prior studies of community and substance-dependent clinical samples support the longitudinal linkage between changes in depressive symptoms and substance use. Among community adolescents and adults assessed repeatedly over several years, depressive symptoms and alcohol use were associated over time (Marmorstein, 2009) and changes in depressive symptoms were correlated with changes in alcohol, marijuana, and tobacco use (Fleming, Mason, Mazza, Abbott, & Catalano, 2008). In two separate treatment samples greater reductions in methamphetamine use predicted greater reductions in depressive symptoms (Jaffe, Shoptaw, Stein, Reback, & Rotheram-Fuller, 2007), and transitions in negative affect and drinking were linked over time (Witkiewitz & Villarroel, 2009). The association between substance use and depressive symptoms could be particularly strong in comorbid patients, for whom episodes of substance use are more likely to be prompted by depressive symptoms (Tomlinson, Tate, Anderson, McCarthy, & Brown, 2006). In a meta-analysis of pharmacotherapy trials for depression and comorbid SUDs, studies with larger effects for depressive symptoms tended to have larger effects for substance use (Nunes & Levin, 2004), suggesting the rates of reduction in these dual symptoms could be associated. However, no known study has directly examined the association between changes in substance use and depressive symptoms during and following treatment for comorbid SUD-MDD.

The current study used data from a trial of Integrated Cognitive Behavioral Therapy (ICBT) and Twelve-Step Facilitation (TSF) for veterans with comorbid SUD-MDD, with adjunct pharmacotherapy offered in both conditions. Latent growth curve models (LGCMs) were used to examine the relationship between substance use and depressive symptoms during the 6 month course of treatment and 12 months following treatment. Recognizing that treatment and follow-up are often characterized by differential patterns of symptom change (Donovan et al., 2008), these two time periods were estimated separately within a unified framework using piecewise growth models, with separate models to examine two primary research questions. First, we hypothesized that veterans would have elevations above their individual, typical pattern of depressive symptoms during periods of more frequent substance use. Second, we examined if change in depressive symptoms was separately associated with change in the likelihood of having any substance use, and with change in the frequency of use if any use had occurred. We expected that greater increase (or decrease) in depression would be associated with greater increase (or decrease) in both the likelihood of using and the frequency of use over time.

2. Materials and methods

2.1. Participants

Participants were 237 veterans who enrolled in a clinical trial of outpatient group psychotherapy for comorbid SUD-MDD (see Figure 1 for flow diagram of participant progress through the trial). To be eligible for the trial, participants had to meet (1) DSM-IV criteria for lifetime alcohol, cannabis, and/or stimulant dependence with recent substance use (past 90 days) and (2) DSM-IV criteria for major depressive disorder with at least one lifetime major depressive episode independent of alcohol/drug use. Exclusion criteria included (1) opiate dependence with intravenous administration, (2) DSM-IV diagnosis of bipolar disorder or psychotic disorder, (3) living more than 50 miles from the facility, or (4) severe memory impairment that would interfere with accurate recall during assessments. A total of 271 participants met the study eligibility criteria, provided informed consent, and initiated the intake assessment. We included the 237 participants who completed the intake

and were sequentially assigned to a treatment condition, with 111 participants in the TSF group and 126 in the ICBT group.

The participants averaged 48.2 years of age ($SD = 8.0$) and 13.4 years of education ($SD = 2.0$). The sample was predominantly male (90.3%) and Caucasian (70.3%). Very few of the participants (14%) were married, and most (80.9%) were not working at baseline. The sample averaged 3.7 previous inpatient treatment episodes for substance use ($SD = 5.4$) and 3.1 previous inpatient treatments ($SD = 7.0$) for depression. The majority of participants met DSM-IV criteria for lifetime alcohol dependence (80.9%), about half (50.7%) met criteria for lifetime stimulant dependence, and 27.4% met criteria for lifetime cannabis dependence. On average, participants had used substances on 28.4% of the 90 days prior to baseline ($SD = 24.9$). Over half (57.2%) of veterans received inpatient treatment during the pre-baseline phase, for an average of 28.7 days. The overall mean baseline Hamilton Depression Rating Scale (HAM-D) score was 28.5 ($SD = 10.8$), suggesting “severe depression”.

2.2. Procedures

The VA San Diego Healthcare System (VASDHS) and University of California, San Diego Institutional Review Boards approved the procedures for this study. The procedures have previously been described in detail (Lydecker et al., 2010) and are reviewed briefly here. Participants were recruited from referrals to the VA dual diagnosis clinic for veterans with comorbid SUD and other Axis I disorders. Clinic referrals were reviewed to determine eligibility and the study was explained in detail to eligible participants by research study staff. Participants consented to randomization to one of the two behavioral interventions, monthly psychotropic medication management appointments, random toxicology screens, and research assessments every 3 months (\$30 compensation for each assessment). With the exception of pharmacotherapy, participants agreed to cease formal treatment for SUD or depression during the 24 weeks of the study interventions. Following the baseline assessment, research assessments were conducted at 3-month intervals, hereafter referred to as “waves”: at mid-treatment (12 weeks), end of treatment (24 weeks), and every three months during one year of follow-up.

2.3. Treatment Conditions

2.3.1. Enrollment—After completing informed consent and intake assessments, participants were sequentially assigned to the treatment group with the next start date, as treatment was initiated via a rolling admission procedure with start dates every two weeks. Both interventions consisted of 12 weeks of group sessions meeting twice per week (Phase I), followed by 12 weeks of weekly group sessions (Phase II). Rates of attendance were similar across treatment groups. All participants attended initial medication consultation with a VA psychiatrist, who used standard VA protocol for prescription of medication for depression. Monthly medication management visits were scheduled for all participants who received pharmacotherapy. The percentage of patients prescribed an antidepressant were similar for both conditions during treatment (TSF = 99%, ICBT = 94%) and follow-up (TSF = 94%, ICBT = 90%).

2.3.2. Twelve-Step Facilitation (TSF)—The principal investigators modified the TSF intervention (Nowinski, Baker, & Carroll, 1994) provided in the Project MATCH study (Project MATCH Research Group, 1997) to allow for consideration of multiple substances and group delivery. Participants entered treatment at the onset of one of three modules. One module covered AA/NA Steps 1–3, a second module addressed Twelve-Step topics common to AA/NA meetings and Twelve-Step literature, and the third module focused on AA/NA Steps 4 and 5. In Phase I of treatment (the initial 12 weeks), each module was covered during a 4-week block. Phase II consisted of weekly sessions for an additional 12 weeks,

where content from Phase I was reviewed. All sessions included discussions of relevant readings (e.g., AA Big Book), new instructive material, and completion of recovery tasks, such as attending Twelve-Step meetings and participating in Twelve-Step activities, such as communicating with a sponsor. Depression was only discussed in the context of Twelve-Step themes or participants were encouraged to discuss these symptoms with their psychiatrist.

2.3.3. Integrated Cognitive-Behavioral Therapy (ICBT)—Integrated material addressing substance use and depression was adapted from two empirically validated treatments: group cognitive-behavioral treatment of depression (Munoz, Ying, Perez-Stable, & Miranda, 1993) and coping skills treatment from Project MATCH (Kadden et al., 1994). Similar to TSF, treatment was initiated at the start of one of three modules. The Thoughts module involved identifying and challenging negative cognitions related to depression and relapse situations. A second module (Activities) focused on increasing engagement in positive activities to improve mood and avoid relapse, and the third module (Interpersonal) involved communication and assertiveness training to increase positive social interaction and self-efficacy for refusing substance use and managing depression-provoking situations. As with TSF, these three modules were delivered in 4-week blocks during Phase I, with review of skills occurring during Phase II.

2.3.4. Therapists and Adherence—Both interventions were delivered by co-therapists: a senior clinician (clinical psychologist or postdoctoral therapist) and a doctoral-level psychology trainee. Therapists were trained in both interventions, typically rotated across conditions every 6–12 months, and changed every 1–2 years. Therapists were trained via a standard protocol, including manual and videotape review, video tape observation, direct observation, and supervised implementation. Therapists also received weekly supervision from study co-investigators with expertise in the specific interventions.

2.4. Measures

2.4.1. Demographics—Demographic characteristics were assessed with a baseline structured interview to measure age, gender, ethnicity, and other personal information (e.g., marital status, religion, level of education).

2.4.2. Clinical Diagnosis—The Composite International Diagnostic Interview (CIDI; Robins et al., 1998), a computerized, structured clinical interview, was used to assess Axis I diagnoses. DSM-IV diagnoses for lifetime/current substance use disorder and lifetime/current major depressive disorder were obtained using the CIDI, which distinguishes between psychiatric symptoms that occur within vs. outside the context of substance use or withdrawal.

2.4.3. Recent Substance Use—Substance use during the previous 90 days was assessed with the Timeline Follow-Back (TLFB; Sobell & Sobell, 1992). The TLFB is a calendar-assisted interview, with documented reliability and validity (Maisto, Sobell, & Sobell, 1979). The TLFB was adapted to measure the frequency and type of drug use in addition to frequency and quantity of alcohol consumption, as demonstrated in previous research (Ehrman & Robbins, 1994). The primary outcome variable computed from the TLFB was percent days using (PDU) any substance during each wave (i.e., each three month period).

2.4.4. Depressive Symptoms—An assessment of depressive symptoms in the prior week was conducted with the Hamilton Depression Rating Scale (HAMD; Hamilton, 1960). The HAMD is a structured clinical interview with good sensitivity and specificity among SUD populations (Willenbring, 1986) and has been considered the “gold-standard” measure

of severity in depression treatment research (Williams, 2001). Across all waves, reliability of the HAMD ranged from .78 to .85. The outcome variable from the HAMD was the total score at each wave.

2.5. Data Analysis

To address the first hypothesis that depression would be elevated during periods of more frequent substance use, we estimated a latent growth curve model (LGCM) of HAMD with repeated measures of PDU included as time-varying covariates. LGCMs are a type of structural equation model where repeated measures are utilized as indicators of an underlying latent trajectory (Curran & Hussong, 2003). We modeled time as a piecewise process, by estimating means of the latent intercept (baseline level), one linear slope from baseline to Month 6 (duration of treatment), and a second linear slope from Month 6 to Month 18 (follow-up phase). Individual variability in latent growth factors was modeled and reflected by variance estimates for each factor, such that the model estimated the latent intake level, latent change during treatment, and latent change during follow-up separately for each individual. First, an unconditional (without covariates) LGCM was fit on the repeated measures of HAMD. Means, variances, and covariances of all latent factors were estimated, along with error terms for the repeated measures. After determining the fit of the unconditional piecewise model, we fit a conditional model that controlled for treatment group and demographic characteristics (i.e., age, gender, ethnicity, marital status, employment), retaining any significant predictors for subsequent models (using $p < .05$ as a cutoff). Finally, time-varying measures of PDU were added to predict remaining variance in observed measures of HAMD, to determine if depression was greater than expected during periods of more frequent use.

To examine the second hypothesis that change in depression is associated with change in the likelihood of use and the frequency of use, we first estimated a two-part LGCM for substance use, and then incorporated the LGCM of depression as a parallel process (see Figure 2). The two-part model (Olsen & Schafer, 2001) was ideal due to the preponderance of zeros for PDU at each wave (see Table 1) as well as our theoretical interest in exploring abstinence vs. frequency separately. The two-part model decomposed the original PDU measures into two variables that were modeled separately (e.g., Brown, Catalano, Fleming, Haggerty, & Abbott, 2005). For the first part (Any Use), binary variables were created to indicate either no use during the previous 3 months (coded 0) or any use (coded 1). These binary variables were modeled as a logistic trajectory model, with the log odds of use regressed on the growth factors. For the second part (Frequency of Use), we utilized continuous variables indicating the percentage of days that substances were used, if any use had occurred during that wave. As demonstrated in prior research with two-part models (Brown et al., 2005), non-use in any wave was coded as missing for the Frequency of Use variable. Frequency of use indicators were modeled in a piecewise LGCM as normally-distributed, continuous variables. Separate unconditional and conditional piecewise growth models for both parts were constructed in identical fashion as the LGCM for HAMD. That is, two models were used to separately estimate each individual's latent intake level, change during treatment, and change during follow-up for the likelihood of having any use and the frequency of use if use had occurred. After building the Any Use and Frequency of Use LGCMs separately, they were combined into a two-part model, and the LGCM for depression was added as a parallel process of both substance use parts. This overall model included correlations between all of the growth factors, to test associations between initial level, change during treatment, and change during follow-up for the three outcomes of interest.

All models were analyzed using Mplus 5.21 (Muthén & Muthén, 2007). The maximum likelihood estimator was used to incorporate all available data, and data was assumed

missing-at-random. When considering the two outcome measures across all time points, there were 84 participants (35% of sample) with complete data, and 153 with any missing data (65%). Participants completed an average of 5.07 TLFB and HAMD measures (max = 7). Analyses of variance and chi-square tests were used to determine any relation between missing data and demographic variables. No statistically significant differences were found for age, gender, ethnicity, marital status, or years of education as a function of missing data. Change in fit between nested models was examined with chi-square difference tests. We assessed overall model fit for the continuous variable models using the chi-square test, comparative fit index (CFI; Bentler, 1990), and root-mean-square error of approximation (RMSEA; Browne & Cudeck, 1993). Good model fit is indicated by a non-significant chi-square value (although this test is highly sensitive to sample size), and values above .95 for the CFI and below .06 for the RMSEA were used as benchmarks for good model fit (Hu & Bentler, 1999). These descriptive indices were not available for the Any Use models, which were evaluated by plotting predicted values against observed rates and inspecting for misfit, and by comparing nested models with chi-square difference tests.

3. Results

3.1. Depressive Symptoms and Frequency of Substance Use

Descriptive statistics for HAMD and PDU are displayed separately for the TSF and ICBT groups in Table 1, along with the proportions of participants with any use during each wave. As reported in our primary study of long-term outcomes (Lydecker et al., 2010), both groups showed a decline in depression from baseline levels (TSF $M = 27.81$, ICBT $M = 29.19$) to the end-of-treatment assessment at Month 6 (TSF $M = 19.00$, ICBT $M = 24.92$), with a relatively greater decline observed for the TSF group. During follow-up, the TSF group increased slightly in depression while the ICBT group continued to decline in depressive symptoms. By the Month 18 assessment, depression scores were similar for both groups (TSF $M = 20.48$, ICBT $M = 22.86$).

For frequency of substance use (defined as PDU), both groups declined substantially from baseline (TSF $M = .31$, ICBT $M = .26$) to the Month 6 post-treatment assessment (TSF $M = .11$, ICBT $M = .15$). During follow-up, both groups gradually increased in PDU over time, with relatively less increase over time observed for the ICBT group, as evidenced by relatively lower levels of PDU at Month 18 (TSF $M = .25$, ICBT $M = .17$). The proportion of participants with any use declined dramatically from baseline to Month 6 for both TSF (95.3% to 46.2%) and ICBT (92.5% to 50.9%). As evidenced at Month 18, both groups increased in the proportion of participants with any use during follow-up, with relatively greater increases observed for TSF (57.3%) than ICBT (52.5%).

3.2. Latent Growth Curve Model of Depressive Symptoms

3.2.1. Unconditional and conditional LGCM—The piecewise model was a significant improvement in fit over the linear-only model ($\Delta\chi^2(4, N=237) = 61.35, p < .001$), and fit the data well descriptively ($\chi^2(19, N=237) = 35.91, p < .05$, CFI = .96, RMSEA = .06). Table 2 displays the parameter estimates for the unconditional model (i.e., without predictors). The model-estimated mean trajectory of depression for the overall sample was characterized by an intercept of 28.5, with a significant decline during treatment of 2.92 ($p < .001$) points per wave, but no significant change during follow-up. As indicated by significant variance estimates, there was substantial individual heterogeneity in the latent intercept and slopes. In addition, the intercept and follow-up slope were negatively correlated, indicating participants with greater initial levels of depression tended to have greater decline during follow-up. We tested a conditional model with treatment group (TSF = 0, ICBT = 1) and demographics as covariates, and retained only treatment group as no demographic variables

were significant predictors. This model fit the data well $\chi^2(23, N=237) = 37.26, p < .05$, CFI = .97, RMSEA = .05. The effect of group on the treatment slope was significant ($\beta = .28, p < .01$), with TSF having greater reductions in depression. The group effect on the follow-up slope was non-significant ($\beta = -.18, p = .10$), and correlations between growth factors were similar to those in the unconditional model.

3.2.2. Time-varying effects of substance use—Time-varying measures of PDU were added to predict remaining variability in HAMD at each wave that wasn't accounted for by the growth factors. This model tested if time-varying deviations from an individual's typical trajectory of depression was predicted by frequency of current substance use. The model with time-varying effects of PDU was an excellent fit to the observed data, $\chi^2(65, N=237) = 78.04, p = .13$, CFI = .97, RMSEA = .03, with greater PDU predicting greater depression at all waves after baseline. The standardized coefficients ranged from 0.13 at wave 4 ($p < .05$) to 0.31 at wave 5 ($p < .001$), indicating small to medium effect sizes (Cohen, 1988). To illustrate the clinical significance, consider the average TSF patient at Wave 2 (end of treatment), with model-estimated HAMD of 19.62 and PDU of 11.3%. A TSF patient with PDU of one standard deviation above the TSF mean (22% days using) was predicted to have 2.7 points higher HAMD, which is a 14% increase above the Wave 2 HAMD for the average TSF patient.

3.3. Two-Part Latent Growth Curve Model for Substance Use

3.3.1. LGCM for Any Use—For Any Use, the piecewise model was a significant improvement in fit over a linear-only model, $\Delta LR \chi^2(5, N=237) = 149.50, p < .001$, and fit the data well both statistically ($\chi^2(118, N=237) = 127.23, p = .26$) and visually (overall fit indices are not available for logistic trajectory models). Table 2 provides parameter estimates for the unconditional model (the intercept was fixed at 1 to achieve model convergence). There was a significant decline in the likelihood of any substance use during treatment, but a significant increase in the likelihood of any use during follow-up. Significant variation in the treatment and follow-up slopes indicated substantial individual heterogeneity the trajectory of any use over time. The negative correlation between treatment and follow-up slopes indicated veterans with a greater decline in the probability of substance use during treatment had a greater increase in the probability of use during follow-up, likely reflecting difficulty in sustaining abstinence over time. In the conditional model, the effects of treatment group and demographics were non-significant and growth factor correlations were similar to those in the unconditional model.

3.3.2. LGCM for Frequency of Use—For Frequency of Use, the piecewise model was a significant improvement in fit over the linear slope model, $\Delta \chi^2(4, N=225) = 27.35, p < .001$, and was an adequate fit to the data based on descriptive indices, $\chi^2(18, N=225) = 31.74, p < .05$, CFI = .91, RMSEA = .06. As seen in Table 2, the model-implied trajectory of Frequency of Use was characterized by an intercept value of .24 ($p < .001$), with a significant decline during treatment of .03 ($p < .05$) points per wave, and a significant increase during follow-up of .02 ($p < .01$) points per wave. Significant individual variation was found in the intercept and both slopes. The intercept and treatment slope were negatively correlated, indicating that participants who used substances more frequently at intake had greater declines during treatment. A positive correlation between intercept and follow-up slope indicated participants with greater initial substance use frequency also tended to have greater increase in frequency of use during follow-up. Finally, a significant and negative covariation between treatment slope and follow-up slope indicated participants with greater declines during treatment also had greater increases during follow-up. The conditional model retained treatment group and ethnicity as predictors, and fit the data well $\chi^2(26, N=237) = 33.91, p = .14$, CFI = .95, RMSEA = .04. The group effect on slopes was

non-significant during treatment but significant during follow-up ($\beta = -.28, p < .05$), showing that participants in the ICBT group had less increase in substance use frequency during the 12-month post treatment follow-up period. In addition, white participants had greater decline in Frequency of Use during treatment ($\beta = -.25, p < .05$). Growth factor correlations were similar to those in the unconditional model.

3.3.1. Combined two-part model for substance use—When the LGCMs for Any Use and Frequency of Use were estimated together, there was significant positive covariance between the slopes during treatment ($r = .74, p < .001$) and follow-up ($r = .94, p < .001$), indicating participants with greater increase in the likelihood of any use also tended to have greater increase in the frequency of use once substance use occurred. All other covariance effects were identical to results from the univariate LGCM's (see Table 2).

3.4. Parallel Process Model for Substance Use and Depression

In order to consider the parallel association between changes in depression and both parts of substance use, a final model included the two-part, piecewise LGCM for substance use and the piecewise LGCM for HAMD. We modeled the correlations between all growth factors in the model, with our primary interest in the correlations between concurrent slopes. Table 3 displays results from the final model, after non-significant correlations ($p > .05$) were removed. The correlations between slopes for Any Use and HAMD were positive during treatment ($r = .41, 95\% \text{ CI } [0.22, 0.59], p < .001$) and follow-up ($r = .34, 95\% \text{ CI } [0.09, 0.60], p < .01$), indicating participants with greater increase/decrease in depressive symptoms over time also had greater increase/decrease in the odds of any use over time. In addition, the slopes for Frequency of Use and HAMD were positively correlated during treatment ($r = .57, 95\% \text{ CI } [0.30, 0.84], p < .001$) and follow-up ($r = .48, 95\% \text{ CI } [0.07, 0.90], p < .05$), indicating participants with greater increase/decrease in the frequency of use also had greater escalation/reduction in depressive symptoms.

In order to consider the clinical significance of these associations, we conducted secondary correlations within subgroups classified by level of response. Response was determined separately for depression (reduction in HAMD of $\geq 50\%$ of intake level) and substance use (abstinent for ≥ 1 90-day period). We examined correlations between the HAMD slopes and the substance use slopes within responders, using the individual latent factor scores for treatment and follow-up slopes predicted by the final LGCM (sample size did not permit re-estimating the full model within subgroups). Among depression responders (51% of sample), HAMD slopes were strongly correlated with Any Use slopes during treatment ($r = 0.62, p < .001$) and follow-up ($r = 0.47, p < .001$), and with Frequency of Use slopes during treatment ($r = 0.68, p < .001$) and follow-up ($r = 0.61, p < .001$). Similar relations were observed among substance use responders (79% of sample), whose HAMD slopes were strongly correlated with slopes for Any Use ($r = 0.52, p < .001$) and Frequency of Use ($r = 0.62, p < .001$) during treatment, and also during follow-up (Any Use $r = 0.51, p < .001$, Frequency of Use $r = 0.62, p < .001$). These results suggest that those with clinically-significant reductions in either depression or substance use experienced strong reductions in the other domain, and that these relations were consistent across the treatment and follow-up time periods.

4. Discussion

In the present study we examined the unfolding longitudinal relationship between depressive symptoms and substance use in veterans with comorbid substance dependence and independent major depressive disorder over the course of 6 months of treatment and 12 months of follow-up (18 months total). Prior studies examining these relations were not

conducted with comorbid samples, and have examined depression as a predictor of future SUD treatment outcome (Curran et al., 2000) or as a correlate of post-treatment substance use (Glasner-Edwards et al., 2008). More recent research indicates that substance use and negative affect are dynamically-linked over time (Witkiewitz & Villarroel, 2009). However, no prior study focused on associations between changes in depression and substance use within a comorbid sample. Patients with SUD and MDD change in substance use status and depressive symptoms over time and substance use may be linked to depressive symptoms more often in comorbid patients (Tomlinson et al., 2006). It is critically important to examine the strength of association between changes in these symptoms for comorbid patients, who may need specialized and more intensive interventions to reduce the severity of their depression and substance use.

When examining longitudinal patterns of change in depressive symptoms, greater frequency of substance use was associated with elevations in depressive symptoms at every time-point, supporting our first hypothesis. At the end of periods of more frequent substance use, individuals had greater levels of depressive symptoms than predicted by their underlying, individual pattern of change in depression. In prior studies, greater alcohol use at baseline predicted poorer depression treatment outcomes (Rae et al., 2002; Worthington et al., 1996), and cocaine use and depressive symptoms were positively correlated during a pharmacotherapy trial (Schmitz et al., 2001). Our study extends these findings, by showing that frequency of substance use predicts elevations in depressive symptoms over an extended time period, even after controlling for each individual's underlying pattern of depression symptoms. Although the mean trajectory of depressive symptoms showed a reduction during treatment and stability during follow-up, frequent substance use was associated with greater depressive symptoms at every assessment point. Therefore, even if comorbid patients are experiencing improvement in depressive symptoms over time, greater substance use is associated with disruptions in such improvement. Due to some overlap in the timing of measures, the current design and analysis prohibits concluding these associations as causal effects, but our study provides initial support that prospective effects of substance use on depression found in earlier studies (Rae et al., 2002; Worthington et al., 1996) may persist throughout treatment and post-treatment periods.

Our second major goal was to examine whether the degree of change in depressive symptoms was separately associated with changes in: (1) any substance use and (2) frequency of substance use if use occurred. Our two-part strategy modeled these aspects of substance use separately, based on previous findings that the predictors of abstinence vs. frequency of use may differ (Brown et al., 2005). The results supported our hypothesis; the magnitude of change in depressive symptoms was associated with change in both aspects of substance use during treatment and follow-up. Participants with the greatest change in depressive symptoms also had the greatest change in frequency of substance use across time, and this effect was large in magnitude. In prior studies, reductions in methamphetamine use predicted reductions in depressive symptoms (Jaffe et al., 2007), and changes in drinking states were associated with changes in negative affect states in patients with alcohol dependence (Witkiewitz & Villarroel, 2009). The results of our study extend these findings to a high-risk treatment sample with comorbid SUD-MDD. In fact, the large effect sizes we observed exceed those found in studies of non-comorbid clinical samples, and may indicate the trajectories of these dual symptoms are linked to a greater extent among patients with comorbid disorders. We also note that the strength of association between these symptoms was comparable during and after formal treatment. Patients with comorbid SUD-MDD may use substances for short-term, self-medication of negative mood states (Bolton, Robinson, & Sareen, 2009), but our study provides evidence that greater frequency of use over time is associated with long-term worsening of depressive symptoms. The opposite is also true; that patients with the greatest decreases in substance use frequency had the largest reductions in

depressive symptoms. Clinicians and comorbid patients may benefit from awareness of these short- and long-term effects.

Of note, increase in the likelihood of any use was associated with increases in depressive symptoms during both treatment and follow-up. This particular finding reinforces and empirically validates the emphasis on maintenance of complete abstinence for adults with protracted histories of comorbid SUD-MDD. In prior studies adults with elevated depressive symptoms at intake were more likely to relapse in the future (Curran et al., 1998; Dodge et al., 2005; Kodl et al., 2008). Our study suggests that increased likelihood of relapse may “travel together” with depressive symptoms. Of note, the moderate effect sizes observed for this relationship, compared to the large effects between depressive symptoms and frequency of use, suggest that limiting relapses to short-term “slips” may limit exacerbation of depressive. Alternatively, a greater emphasis on controlling depressive symptoms may reduce the risk of relapse. Treatments that simultaneously target depression and substance use, including limiting the duration of relapses, may produce better long-term outcomes than separate, parallel, or sequential treatments for co-occurring MDD and SUD.

There are many specific processes that could contribute to these associations between changes in depression, odds of substance use, and frequency of substance use over time. Depressive symptoms often dissipate with extended periods of abstinence (Brown & Shuckit, 1988), and some veterans in our study likely had great initial reductions in substance use that preceded dramatic reductions in depressive symptoms. Conversely, relapse and continued substance use may have led to increased depressive symptoms for some individuals, either due to the effects of substances and related withdrawal (Laine, Ahonen, Räsänen, & Tiihonen, 1999) or exacerbation of life problems (e.g., homelessness) that could increase depression (DeForge, Belcher, O’Rourke, & Lindsay, 2008). In comorbid patients depressive symptoms may be an especially potent trigger for relapse (Tomlinson et al., 2006), and some initially-abstinent veterans with continued depressive symptoms may have eventually used substances to alleviate negative mood states. Alternatively, reductions in depression attributable to pharmacotherapy or aspects of psychotherapy (e.g., behavioral activation, 12-step meetings) may have better enabled some veterans to reduce substance use. There may be important third variables (e.g., life stress) that independently increase the risk for both depressive symptoms and substance use (Brady & Sonne, 1999; Bulmash, Harkness, Stewart, & Bagby, 2009). Each of these processes likely operate within the population of comorbid patients, and specifically tailoring treatments to meet individual needs may be necessary for optimal implementation of interventions.

The current study provided novel and clinically-relevant findings, but limitations of our study should be noted. The study sample was composed of veterans who were mostly male and Caucasian, which negatively impacts the immediate generalizability of our findings. In addition, while we focused on the most common type of comorbidity for individuals with SUD in community and treatment settings (Grant et al., 2004), certain types of SUDs (e.g., intravenous opiate) and mood disorders (e.g., bipolar disorder) were excluded. In this initial evaluation of dual symptoms, we focused on the association between changes in symptoms over time, but our study did not explicitly examine causal relations. Thus, while we identified symptoms that tend to change together and provided evidence that the magnitude of changes in depression and substance use are linked over time, we cannot conclude that change in one symptom directly causes change in the other. There may be important clinical factors that moderate the strength of association between symptoms, such as the type of SUD diagnosis (e.g., alcohol, drug, polysubstance). Potential moderators of these effects were not examined here, but are an important area of inquiry for future research.

The current study provides strong empirical support for associated changes between depressive symptoms and substance use among participants receiving treatment for comorbid SUD-MDD. In a sample of comorbid veterans, we found evidence of a strong, positive association between the magnitude of change in frequency of substance use and depressive symptoms, as well as a positive association between the longitudinal change in odds of any substance use and greater depressive symptoms. Each of these effects persisted throughout 6 months of treatment and 12 months of post-treatment follow-up. These findings empirically validate that improvements or exacerbations in either type of symptom are associated with similar changes in the other, and reinforce the importance of focusing on both depression and substance use during treatment of patients with comorbid SUD-MDD.

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References

- Bakker A, van Dyck R, Spinhoven P, van Balkom AJLM. Paroxetine, clomipramine, and cognitive therapy in the treatment of panic disorder. *Journal of Clinical Psychiatry*. 1999; 60(12):831–838. [PubMed: 10665629]
- Bentler PM. Comparative fit indexes in structural models. *Psychological Bulletin*. 1990; 107(2):238–246. [PubMed: 2320703]
- Brady KT, Sonne SC. The role of stress in alcohol use alcoholism, treatment, and relapse. *Alcohol Research and Health*. 1999; 23:263–271. [PubMed: 10890823]
- Brown EC, Catalano RF, Fleming CB, Haggerty KP, Abbott RD. Adolescent substance use outcomes in the raising healthy children project: A two-part latent growth curve analysis. *Journal of Consulting and Clinical Psychology*. 2005; 73(4):699–710. [PubMed: 16173857]
- Brown RA, Evans DM, Miller IW, Burgess ES, Mueller TI. Cognitive-behavioral treatment for depression in alcoholism. *Journal of Consulting and Clinical Psychology*. 1997; 65:715–726. [PubMed: 9337490]
- Brown SA, Shuckit MA. Changes in depression among abstinent alcoholics. *Journal of Studies on Alcohol*. 1988; 49:412–417. [PubMed: 3216643]
- Browne, MW.; Cudeck, R. Alternative ways of assessing model fit. In: Bollen, KA.; Long, JS., editors. *Testing structural equation models*. Newbury Park, CA: Sage; 1993. p. 136-162.
- Bulmash E, Harkness KL, Stewart JG, Bagby RM. Personality stressful life events, and treatment response in major depression. *Journal of Consulting and Clinical Psychology*. 2009; 77:1067–1077. [PubMed: 19968383]
- Burns L, Teesson M, O'Neill K. The impact of comorbid anxiety and depression on alcohol treatment outcomes. *Addiction*. 2005; 101:787–796. [PubMed: 15918809]
- Chambless DL, Hollon SD. Defining empirically supported therapies. *Journal of Consulting and Clinical Psychology*. 1998; 66:7–18. [PubMed: 9489259]
- Curran GM, Flynn HA, Kirchner J, Booth BM. Depression after alcohol treatment as a risk factor for relapse among male veterans. *Journal of Substance Abuse Treatment*. 2000; 19(3):259–265. [PubMed: 11027896]
- Curran PJ, Hussong AM. The use of latent trajectory models in psychopathology research. *Journal of Abnormal Psychology*. 2003; 112(4):526–544. [PubMed: 14674867]
- Davis LL, Wisniewski SR, Howland RH, Trivedi MH, Husain MM, Fava M, et al. Does comorbid substance use disorder impair recovery from major depression with SSRI treatment? an analysis of the STAR*D level one treatment outcomes. *Drug and Alcohol Dependence*. 2010; 107(2–3):161–170. [PubMed: 19945804]

- DeForge BR, Belcher JR, O'Rourke M, Lindsay MA. Personal resources and homelessness in early life: Predictors of depression in consumers of homeless multiservice centers. *Journal of Loss and Trauma*. 2008; 13:222–242.
- Dodge R, Sindelar J, Sinha R. The role of depression symptoms in predicting drug abstinence in outpatient substance abuse treatment. *Journal of Substance Abuse Treatment*. 2005; 28(2):189–196. [PubMed: 15780549]
- Donovan DM, Anton RF, Miller WR, Longabaugh R, Hosking JD, Youngblood M, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence (the COMBINE study): Examination of posttreatment drinking outcomes. *Journal of Studies on Alcohol and Drugs*. 2008; 69(1):5–13. [PubMed: 18080059]
- Ehrman RN, Robbins SJ. Reliability and validity of 6-month timeline reports of cocaine and heroin use in a methadone population. *Journal of Consulting and Clinical Psychology*. 1994; 62(4):843–850. [PubMed: 7962889]
- Fleming CB, Mason WA, Mazza JJ, Abbott RD, Catalano RF. Latent growth modeling of the relationship between depressive symptoms and substance use during adolescence. *Psychology of Addictive Behaviors*. 2008; 22(2):186–197. [PubMed: 18540716]
- Gamble SA, Conner KR, Talbot NL, Yu Q, Tu XM, Connors GJ. Effects of pretreatment and posttreatment depressive symptoms on alcohol consumption following treatment in Project MATCH. *Journal of Studies on Alcohol and Drugs*. 2010; 71:71–77. [PubMed: 20105416]
- Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, Ang A, Mooney LJ, Rawson R. Depression among methamphetamine users: Association with outcomes from the Methamphetamine Treatment Project at 3-year follow-up. *Journal of Nervous and Mental Disease*. 2009; 197:225–231. [PubMed: 19363377]
- Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, Hillhouse M, Ang A, Rawson R, et al. Risk factors for suicide attempts in methamphetamine-dependent patients. *The American Journal on Addictions*. 2008; 17(1):24–27. [PubMed: 18214719]
- Grant BF, Stinson FS, Dawson DA, Chou P, 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. *Archives of General Psychiatry*. 2004; 61(8):807–816. [PubMed: 15289279]
- Greenfield SF, Weiss RD, Muenz LR, Vagge LM, Kelly JF, Bello LR, et al. The effect of depression on return to drinking: A prospective study. *Archives of General Psychiatry*. 1998; 55(3):259–265. [PubMed: 9510220]
- Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry*. 1960; 23:56–61.
- 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; 9:1–8. [PubMed: 19133132]
- Howland RH, Rush AJ, Wisniewski SR, Trivedi MH, Warden D, Fava M, et al. Concurrent anxiety and substance use disorders among outpatients with major depression: Clinical features and effect on treatment outcome. *Drug and Alcohol Dependence*. 2009; 99(1–3):248–260. [PubMed: 18986774]
- Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling*. 1999; 6(1):1–55.
- Ilgen M, Moos R. Deterioration following alcohol-use disorder treatment in project MATCH. *Journal of Studies on Alcohol*. 2005; 66(4):517–525. [PubMed: 16240559]
- Jaffe A, Shoptaw S, Stein JA, Reback CJ, Rotheram-Fuller E. Depression ratings, reported sexual risk behaviors, and methamphetamine use: Latent growth curve models of positive change among gay and bisexual men in an outpatient treatment program. *Experimental and Clinical Psychopharmacology*. 2007; 15(3):301–307. [PubMed: 17563217]
- Kadden, K.; Carroll, K.; Donovan, D.; Cooney, N.; Monti, P.; Abrams, D., et al. Cognitive-Behavioral Coping Skills Therapy Manual. Project Match, NIAAA, NIH, 94-3724. 1994.

- Kodl MM, Fu SS, Willenbring ML, Gravely A, Nelson DB, Joseph AM. The impact of depressive symptoms on alcohol and cigarette consumption following treatment for alcohol and nicotine dependence. *Alcoholism: Clinical and Experimental Research*. 2008; 32(1):92–99.
- Laine TP, Ahonen A, Räsänen P, Tiihonen J. Dopamine transporter availability and depressive symptoms during alcohol withdrawal. *Psychiatry Research*. 1999; 90:153–157. [PubMed: 10466734]
- Leventhal AM, Mooney ME, DeLaune KA, Schmitz JM. Using addiction severity profiles to differentiate cocaine-dependent patients with and without comorbid major depression. *The American Journal on Addictions*. 2006; 15(5):362–369. [PubMed: 16966192]
- Levin FR, Bisaga A, Raby W, Aharonovich E, Rubin E, Mariani J, et al. Effects of major depressive disorder and attention-deficit/hyperactivity disorder on the outcome of treatment for cocaine dependence. *Journal of Substance Abuse Treatment*. 2008; 34(1):80–89. [PubMed: 17574796]
- Lydecker KP, Tate SR, Cummins KM, McQuaid J, Granholm E, Brown SA. Clinical outcomes of an integrated treatment for depression and substance use disorders. *Psychology of Addictive Behaviors*. 2010; 24:453–465. [PubMed: 20853931]
- Maisto SA, Sobell LC, Sobell MB. Comparison of alcoholics' self-reports of drinking behavior with reports of collateral informants. *Journal of Consulting and Clinical Psychology*. 1979; 47(1):106–112. [PubMed: 429642]
- Marmorstein NR. Longitudinal associations between alcohol problems and depressive symptoms: Early adolescence through early adulthood. *Alcoholism: Clinical and Experimental Research*. 2009; 33(1):49–59.
- Marmorstein NR, Iacono WG, Malone SM. Longitudinal associations between depression and substance dependence from adolescence through early adulthood. *Drug and Alcohol Dependence*. 2010; 107(2–3):154–160. [PubMed: 19926409]
- Marrone S, Mitchell JE, Crosby R, Wonderlich S, Jollie-Trottier T. Predictors of response to cognitive behavioral treatment for bulimia nervosa delivered via telemedicine versus face-to-face. *International Journal of Eating Disorders*. 2009; 42(3):222–227. [PubMed: 18951452]
- Munoz, RF.; Ying, Y.; Perez-Stable, EJ.; Miranda, J. The prevention of depression: Research and practice. Baltimore, MD: John Hopkins University Press; 1993.
- Muthén, LK.; Muthén, BO. Mplus User's Guide. Fifth Edition. Los Angeles, CA: Muthén & Muthén; 1998–2007.
- Nowinski, J.; Baker, S.; Carroll, K. Twelve-Step Facilitation Therapy Manual: A Clinical Research Guide for Therapists Treating Individuals With Alcohol Abuse and Dependence, National Institute on Alcohol Abuse and Alcoholism, Project MATCH Monograph series, Vol. 1. NIH Publication No. 94 - 3722. Washington, DC: Supt. of Docs., U.S. Govt. Print Off; 1994.
- Nunes EV, Levin FR. Treatment of depression in patients with alcohol or other drug dependence: A meta-analysis. *JAMA: Journal of the American Medical Association*. 2004; 291(15):1887–1896.
- Olfson M, Fireman B, Weissman M, Leon AC, Sheehan DV, Kathol RG, et al. Mental disorders and disability among patients in a primary care group practice. *The American Journal of Psychiatry*. 1997; 154(12):1734–1740. [PubMed: 9396954]
- Olsen MK, Schafer JL. A two-part random-effects model for semicontinuous longitudinal data. *Journal of the American Statistical Association*. 2001; 96:730–745.
- Project Match Research Group, US. Matching alcoholism treatments to client heterogeneity: Project MATCH posttreatment drinking outcomes. *Journal of Studies on Alcohol*. 1997; 58(1):7–29. [PubMed: 8979210]
- Rae AM, Joyce PR, Luty SE, Mulder RT. The effect of a history of alcohol dependence in adult major depression. *Journal of Affective Disorders*. 2002; 70(3):281–290. [PubMed: 12128240]
- Robins LN, Wing J, Wittchen HU, Helzer JE, Babor TF, Burke J, et al. The Composite International Diagnostic Interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Archives of General Psychiatry*. 1988; 45:1069–1077. [PubMed: 2848472]
- Saatcioglu O, Yapici A, Cakmak D. Quality of life, depression and anxiety in alcohol dependence. *Drug and Alcohol Review*. 2008; 27(1):83–90. [PubMed: 18034385]

- Schmitz JM, Averill PM, Rothfleisch J. Fluoxetine treatment of cocaine-dependent patients with major depressive disorder. *Drug and Alcohol Dependence*. 2001; 63:207–214. [PubMed: 11418225]
- Sobell, LC.; Sobell, MB. Timeline follow-back: A technique for assessing self-reported alcohol consumption. In: Litten, RZ.; Allen, JP., editors. *Measuring alcohol consumption: Psychosocial and biochemical methods*. Totowa, NJ, US: Humana Press; 1992. p. 41-72.
- Tomlinson KL, Tate SR, Anderson KG, McCarthy DM, Brown SA. An examination of self-medication and rebound effects: Psychiatric symptomatology before and after alcohol or drug relapse. *Addictive Behaviors*. 2006; 31:461–474. [PubMed: 15972246]
- Watkins KE, Hunter SB, Hepner KA, Paddock SM, de la Cruz E, Zhou AJ, Gilmore J. An effectiveness trial of group cognitive behavioral therapy for patients with persistent depressive symptoms in substance abuse treatment. *Archives of General Psychiatry*. 2011; 68:577–584. [PubMed: 21646576]
- Watkins KE, Paddock SM, Zhang L, Wells KB. Improving care for depression in patients with comorbid substance misuse. *The American Journal of Psychiatry*. 2006; 163(1):125–132. [PubMed: 16390899]
- Willenbring ML. Measurement of depression in alcoholics. *Journal of Studies on Alcohol*. 1986; 47(5):367–372. [PubMed: 3762159]
- Williams JBW. Standardizing the hamilton depression rating scale: Past, present, and future. *European Archives of Psychiatry and Clinical Neuroscience*. 2001; 251(8):II6–II12. [PubMed: 11824839]
- Witkiewitz K, Villarroel NA. Dynamic association between negative affect and alcohol lapses following alcohol treatment. *Journal of Consulting and Clinical Psychology*. 2009; 77(4):633–644. [PubMed: 19634957]
- Worthington J, Fava M, Agustin C, Alpert J. Consumption of alcohol, nicotine, and caffeine among depressed outpatients: Relationship with response to treatment. *Psychosomatics: Journal of Consultation Liaison Psychiatry*. 1996; 37(6):518–522.

Figure 1.
Flow diagram of participant progress through the randomized trial.

Figure 2.

Path diagram for piecewise, two-part latent growth curve model (LGCM) of any substance use (Any Use) and frequency of substance use if using (PDU) with parallel, piecewise LGCM of Hamilton depression scores (HAMD). All non-concurrent correlations (i.e., between intercepts and slopes, between treatment (TX) slopes and follow-up (FUP) slopes) are omitted for clarity.

Descriptive Statistics of Depressive Symptoms, Frequency of Substance Use, and Proportion of Patients with Any Substance Use Across Time, by Treatment Group (N=237)

	Intake	Month												
		3		6		9		12		15		18		
		TSF	ICBT	TSF	ICBT	TSF	ICBT	TSF	ICBT	TSF	ICBT	TSF	ICBT	
HAMD														
<i>M</i>	27.81	29.19	23.99	26.04	19	24.92	19.41	24.03	19.65	22.65	22.01	23.20	20.48	22.86
<i>SD</i>	11.55	10.08	12.81	12.57	10.90	13.52	12.55	14.43	11.97	12.28	11.98	13.32	12.80	12.54
PDU														
<i>M</i>	.31	.26	.09	.11	.11	.15	.14	.15	.17	.15	.19	.13	.25	.17
<i>SD</i>	.26	.24	.19	.19	.22	.26	.26	.25	.27	.27	.31	.24	.34	.30
Any Use														
(%)	95.3	92.5	41.2	51.4	46.2	50.9	44.2	47.5	48.8	49.5	56.8	49.5	57.3	52.5

Note. HAM-D = Hamilton Depression Scale. PDU = Percent Days Using.

TSFT = Twelve-Step Facilitation Therapy. ICBT = Integrated Cognitive-Behavioral Therapy

Table 2

Parameter estimates for unconditional latent growth curve models (N = 237).

Variable	Parameters							
	Mean of intercept	Variance of intercept	Mean of TX slope	Variance of TX slope	Mean of FollowUp slope	Variance of FollowUp slope	Covariance of TX slope and intercept	Covariance of FollowUp slope and intercept
HAMD								
Coefficient	28.50 ***	69.87 ***	-2.92 ***	15.58 **	-0.11	5.05 ***	-0.07	-0.40 **
SE	0.69	15.31	0.44	5.34	0.25	1.42	0.22	0.15
Any Use								
Coefficient	.a	0.03	-1.41 ***	3.17 ***	0.37 **	0.92 **	0.32	0.64
SE	.a	0.03	0.19	0.84	0.11	0.30	0.58	0.47
Frequency of Use								
Coefficient	0.240 ***	0.018 **	-0.026 *	0.010 ***	0.018 **	0.002 **	-0.61 ***	0.39 *
SE	0.012	0.005	0.011	0.003	0.007	0.001	0.11	0.16
								0.11

Note. TX = Treatment phase (Months 0–6). FollowUp= Follow-up phase (Months 7–18). HAMD = Hamilton Depression Scale Score. PDU = Percent Days Using.

* p < .05,

** p < .01,

*** p < .001.

^aIntercept was fixed at 1 to achieve model convergence.

Significant correlations between growth factors in the final piecewise latent growth curve models for depression, any substance use, and frequency of substance use if use occurred ($N = 237$).

Table 3

	HAMD Intercept	HAMD TX slope	HAMD FUP slope	Any Use Intercept	Any Use TX Slope	Any Use FUP Slope	PDU Intercept	PDU TX Slope
HAMD TX slope	<i>ns</i>							
HAMD FUP slope	-.52***	<i>ns</i>						
Any Use Intercept	<i>ns</i>	<i>ns</i>	<i>ns</i>					
Any Use TX slope	<i>ns</i>	.45***	<i>ns</i>	<i>ns</i>				
Any Use FUP slope	<i>ns</i>	<i>ns</i>	.33***	<i>ns</i>	-.53***			
PDU Intercept	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>		
PDU TX slope	<i>ns</i>	.56***	<i>ns</i>	<i>ns</i>	.50***	<i>ns</i>	-.62***	
PDU FUP slope	<i>ns</i>	<i>ns</i>	.48*	<i>ns</i>	<i>ns</i>	<i>ns</i>	.37*	-.50***

Note. HAMD = Hamilton Depression Scale Score. PDU = Percent Days Using it Use Occurred. TX = Treatment phase (Months 0–6). FUP= Follow-up phase (Months 7–18).

“*ns*”denotes correlation was non-significant and removed from the final model.

*
p < .05,

**
p < .01,

***
p < .001.