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Depression Change Profiles in Adolescents Treated for Comorbid Depression/Substance Abuse and Profile Membership Predictors

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Abstract

Objective: Using data from a randomized trial in which adolescents with depressive and substance use disorders (SUD) received treatments for both disorders in either a sequenced or coordinated manner, we (1) determine the number and nature of depression response profiles through 1-year post-treatment and (2) examine whether 8 previously identified factors predict profile membership.

Method: 170 adolescents (M age = 16.4 years; 22% female; 28% Hispanic, 61% Non-Hispanic White) with comorbid depressive disorder/SUD were randomized to one of three sequences of receiving the Adolescent Coping With Depression Course and Functional Family Therapy for SUD (depression treatment followed by SUD treatment; SUD treatment followed by depression treatment, coordinated treatment). Depression was assessed at seven points from baseline to 1-year follow-up.

Results: A 4-class solution fit the data best, with groups labeled Mildly Depressed Responders (57.1%), Depressed Responders (18.8%), Depressed Non-Responders (12.9%), and Depressed with Recurrence (11.2%). The four change profiles differed on indices of all but one predictor (age); most differences were driven by lower scores among Mildly Depressed Responders. Profile membership was most strongly predicted by depression severity, cognitive distortions, hopelessness, and global functioning. The strongest predictor of Nonresponse was low family cohesion, whereas Recurrence was associated with hopelessness, suicide attempts, and starting treatment near the end of the school year.

Conclusions: Most depressed adolescents experienced a positive response that was maintained. Understanding the most common profiles of depression change during and following treatment and the variables that predict change can help improve treatment outcomes and advance tailoring efforts.

Keywords

depression; adolescents; treatment; comorbidity; predictors

Randomized controlled trials (RCTs) evaluating treatments for adolescent depression have yielded consistent empirical support for the efficacy of cognitive-behavioral therapy (CBT) and other interventions (e.g., David-Ferdon & Kaslow, 2008; Wagner, 2005). However, depressive symptom reductions vary widely within any treatment intervention. Although the average response effect might be positive, substantial individual variability in patterns of change can be observed, including depressed subsets who fail to respond (e.g., Kennard et al., 2006) and those who experience relapse (i.e., return of depressive symptoms before a full remission has been achieved) or recurrence (i.e., onset of a new episode of depression following a full remission) (e.g., Curry et al., 2011). Furthermore, a high proportion of depressed adolescents have comorbid conditions (e.g., Rohde, Lewinsohn, & Seeley, 1991), including substance use disorders (SUD; Armstrong & Costello, 2002), which complicates the conceptualization and provision of treatment and is generally associated with higher rates of treatment drop-out, lower recovery, and poorer maintenance of gains (e.g., Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001). These diverse outcomes underscore the need for a greater understanding of the different patterns of treatment responding among depressed adolescents, especially those with more than one disorder. To the extent that we can identify individual change profiles shared by subgroups of depressed adolescents with comorbidity and predictors of such depression response profiles, our understanding of how to modify and best fit existing treatments to specific groups of depressed adolescents could be enhanced.

The first aim of the present study was to empirically ascertain the number and nature of depression response subgroups among adolescents being treated for depression and comorbid SUD. The responses of depressed adult and adolescent clients have generally been categorized as remission, recovery, relapse, and recurrence, based on the influential article by Frank et al. (1991), but these classifications have been conceptually driven rather than empirically based. An empirically derived classification might identify the optimal number of distinct profiles and the best methods for distributing depressed clients into their response profiles for understanding the change process.

Empirically based profiles of change were created using latent class growth analysis. In the area of adolescent depression, cluster analysis has been used to categorize patient (Carmanico et al., 1998) and nonpatient (Sears, 1997) samples on the basis of baseline depressive symptom profiles and to describe the course of depressive symptoms in nontreated samples (Repetto, Caldwell, & Zimmerman, 2004), but we were unable to find previous research using this approach to categorize the patterns of depression change in adolescent patient samples. In the area of adult depression treatment, studies have used cluster analysis to identify baseline depressive symptom profiles that predict treatment response (e.g., Hybels, Blazer, Pieper, Landerman, & Steffens, 2009; Schacht, Gorwood, Boyce, Schaffer, & Picard, 2014) but have not empirically determined profiles of depressive symptom change. We are aware of only one previous study that paralleled the present study design; Dew et al. (1997) used cluster analysis to identify four subgroups of older adult patients (M age = 67.1, N = 86) based on their 18-week response to combination treatment for recurrent depression, which they labeled (1) rapid sustained improvement (31%), (2) delayed but sustained improvement (22%), (3) partial or mixed response (23%), and (4) no response (24%).

Our second aim was to test whether variables that had been previously replicated in predicting nonresponse to depression treatment in adolescents with non-comorbid or primary depression also predicted depression nonresponse in adolescents with comorbid depression/SUD. The goal of these analyses was to determine whether we could identify at the beginning of treatment which depressed youth would benefit from the treatments (or a particular treatment sequence) and which youth may have poorer outcomes.

We identified eight variables that have repeatedly been found to predict nonresponse to depression treatment in adolescents. First, higher initial depression severity predicted failure to achieve clinical remission across three psychosocial treatments (Brent et al., 1998), lower recovery in group CBT (Clarke et al., 1992), and lower recovery across medication treatments with or without CBT (Asarnow et al., 2009). The second variable was suicidality. Baseline suicidal ideation predicted higher post-treatment depression levels across medication and CBT treatments (Curry et al., 2006) and lower recovery across medication treatments (with or without CBT; Asarnow et al., 2009); depressed adolescents with higher current and lifetime suicidality (a continuous measure including ideation and attempt) were more likely to be depressed at the end of three psychosocial treatments (Barbe et al., 2004). Third, higher levels of depressotypic cognitions predicted nonresponse (i.e., the presence of MDD after treatment) and failure to achieve remission across three psychosocial treatments (Brent et al., 1998) and higher levels of irrational thoughts predicted failure to recover in group CBT (Clarke et al., 1992). Fourth, higher levels of hopelessness predicted nonresponse and failure to achieve remission across psychosocial treatments (Brent et al., 1998), lower recovery rate across medication treatments (Asarnow et al., 2009), and higher post-treatment depressive symptoms scores across both medication and CBT treatments (Curry et al., 2006). The fifth variable was comorbid anxiety: the presence of anxiety disorders predicted nonresponse across psychosocial treatments (Brent et al., 1998) and higher post-treatment depression levels across treatments (Curry et al., 2006); higher state anxiety predicted failure to recover in group CBT (Clarke et al., 1992). Sixth, family conflict predicted lower response across medication treatments (Asarnow et al., 2009) and higher post-treatment depression levels across medication and CBT treatments (Feeny et al., 2009); parent-child conflict both at baseline and during follow-up predicted lack of recovery, chronicity, and recurrence across psychosocial treatments (Birmaher et al., 2000). Seventh, lower global functioning predicted higher depression levels post-treatment across treatments (Curry et al., 2006), lower response across medication treatments (Asarnow et al., 2009), and greater social impairment predicted CBT non-remission (Jayson, Wood, Kroll, Fraser, & Harrington, 1998). The eighth variable was the only demographic factor to consistently be associated with depression treatment response: older age among children and adolescents (ages 10–18 years) has been associated with non-remission in CBT (Jayson et al., 1998), higher depression levels post-treatment across treatments (Curry et al., 2006), and smaller reductions in depressive symptoms in group CBT (Clarke et al., 1992). We predicted these eight variables would continue to predict a poorer depression response among depressed adolescents with comorbid SUD.

The present study examined the patterns of change in depressive symptoms during and following treatment for depressed adolescents with comorbid SUD, as well as predictors of those change processes. Data come from an RCT that evaluated various methods of treating

adolescents with co-occurring depressive disorders and SUD (Rohde, Waldron, Turner, Brody, & Jorgensen, 2014). In that trial, we evaluated three sequences of delivering two empirically supported interventions: (1) the Adolescent Coping With Depression course (CWD; Clarke, Lewinsohn, & Hops, 1990), a group CBT intervention for depression, previously shown to be efficacious for adolescent with primary depressive disorders (Clarke, Rohde, Lewinsohn, Hops, & Seeley, 1999) and depressed adolescents with comorbid conduct disorder (Rohde, Clarke, Mace, Jorgensen, & Seeley, 2004), and (2) Functional Family Therapy (FFT; Alexander, Waldron, Robbins, & Neeb, 2013), a family-based intervention for disruptive behaviors that has been adapted for SUD (Waldron & Brody, 2010). Our primary intention was to explore whether it was preferable to treat the depression first, the SUD first, or both concurrently. Contrary to hypothesis, we found no evidence of a differential depression response across sequences; instead all three treatment sequences exhibited a very strong depression remission effect that occurred early in treatment and was maintained through 1-year follow-up. In addition, across treatment sequences, a stronger depression response occurred for adolescents who entered treatment with major depressive disorder (MDD, 54% of sample) compared to those with less severe depression diagnoses (dysthymia, 18%; depression-not otherwise specified [D-NOS], 28%), indicating that the global analysis may have obscured relatively strong differential change among those with greater depression severity. In the present report, we continue our exploration of individual differences in depression change trajectories and identify potential predictors of change patterns.

In addition to the two primary aims of the present study, we explored whether any of the treatment sequences predicted change profile membership or whether alternative explanations might account for the number and nature of the change profiles. Because this type of study (i.e., provision of the same psychosocial treatments in three different sequences) has not been done previously, we did not have an a priori hypothesis regarding any of the three treatment sequences predicting specific change profile membership.

Regarding alternative explanations for the number or nature of the identified clusters, researchers have expressed concerns about the interpretation of cluster-analysis-derived trajectories of change in client's behavior during treatment (e.g., Sher, Jackson, & Steinley, 2011) because these trajectories may be an artifact of cyclic swings in disorders such as depression rather than meaningful differences in treatment response (e.g., some individuals are in the early phase of a depression cycle and are likely to display increasing severity regardless of treatment, whereas others are later in the depression cycle and should show reductions due to the natural course of disorder rather than treatment per se). We explored evidence concerning these alternative explanations for the change trajectories.

Methods

Participants and Procedures

Between 2007–2011, we recruited 170 participants from adolescents who had been referred for treatment at SUD research centers in two urban areas (Portland, OR and Albuquerque, NM) through a variety of sources (35% schools, 20% health clinics, 10% family service organizations, 25% juvenile justice agencies, 10% media). Parents provided written consent

and adolescents provided written assent. Inclusion criteria were: (1) current DSM-IV-TR (American Psychiatric Association, 2000) depressive disorder (major depressive disorder [MDD], dysthymia, adjustment disorder with depressed mood; depression not otherwise specified [D-NOS]); (2) current DSM-IV-TR non-nicotine SUD; (3) reported drug use in the last 90 days, (4) being 13–18 years of age, and (5) having at least one parent willing to participate. Exclusion criteria were: (1) acute suicidal ideation warranting immediate attention, (2) psychotic symptoms, (3) having a sibling in the study, and (4) recent (past 4 weeks) change in psychotropic prescription. Participants ranged in age from 13–18 years old ($M = 16.4$, $SD = 1.3$), 22% were female, 28% were Hispanic, 61% were Non-Hispanic White, 45% lived in a single-parent home, and 78% of parents had some college education. Most participants (54%) had MDD and cannabis abuse (21%) or dependence (73%); many also met criteria for alcohol abuse (34%) or dependence (31%). The Oregon Research Institute Institutional Review Board approved the study. Adolescents were recruited until a cohort (4–9 families) was formed, which was randomly assigned using a block design to one of three sequences: (a) FFT followed by CWD (FFT/CWD, $n = 61$), (b) CWD followed by FFT (CWD/FFT, $n = 56$), or (c) an intervention providing FFT and CWD simultaneously in a coordinated fashion (Coordinated Treatment; CT, $n = 53$). Therapists were assigned based on availability. Families were interviewed at baseline (Week 0), three points during treatment (Weeks 5, 10, and 15), the end of treatment (Week 20), and at 6- and 12-months post-treatment (Weeks 46 and 72, respectively). Adolescents and parents received financial compensation for completing assessments but not for attending treatments; treatment was provided at no cost to families. All families completed baseline measures and 88% provided at least one additional assessment (78% of all post-baseline assessments were completed); attrition was not associated with treatment sequence. Additional details regarding the study are available in Rohde et al., 2014.

Assessment of Depression and Predictor Measures

Depressive symptoms. Children's Depression Rating Scale-Revised (CDRS; Poznanski & Mokros, 1995) used information from adolescent and parent to assess 17 depression-related factors, resulting in a continuous measure of depression, which served to create the profiles of depressive symptom change during and following treatment (baseline inter-rater reliability Pearson $r = .88$). The reliability of the sum score for the CDRS was evaluated using Cronbach's $\alpha = .79$; and the Guttman split-half reliability coefficient $r = .71$ while the internal consistency was estimated from the ICC = .21. The Cronbach and Guttman criteria provide evidence of good reliability for the total score, but the ICC suggests only modest internal consistency at the item level. The CDRS includes items that assess different "locations" along a single continuum of depression, and they have very different rates of endorsement. Low depression items (e.g., anhedonia) are endorsed by nearly all of the respondents while high depression items (e.g., suicidality) are endorsed by fewer respondents. Scores of 40 or greater have been proposed as indicative of depressive symptomatology, with scores 28 or less indicative of depression remission (e.g., Mayes et al., 2010). Baseline total scores were used as the measure of initial depression severity.

Suicidality and hopelessness were assessed from symptom reports conducted at the baseline interview. Trained interviewers assessed adolescents and their parents on the mood disorder

module of the Schedule for Affective Disorders and Schizophrenia for School Age Children–Present and Life Version (K-SADS-PL; Kaufman, Birmaher, Brent, Rao, & Ryan, 1996). Interviews were videotaped and a randomly selected 20% were rated by the supervisor (fifth author) for reliability of current (but not past) symptom presentation (current symptom reliability Cronbach's $\alpha = .77$; single measure ICC = .08; Guttman split-half reliability $r = .60$). Suicidal ideation was rated on a 4-point scale (0 = No information; 1 = Not present; 2 = Occasional thoughts of suicide but has not thought of a specific method; 3 = Often thinks of suicide and has thought of a specific method); current (last month) suicidal ideation had an inter-rater agreement Pearson $r = .79$ (based on review of 27 ratings). Suicidal Actions were rated on a 4-point scale (0 = No information; 1 = No attempt or gesture with no intent to die (e.g., held pills in hand; 2 = Present but very ambivalent; 3 = Definite suicidal intent); current suicidal actions had an inter-rater agreement Pearson $r = .91$ (based on 29 ratings). Hopelessness was assessed in the K-SADS as a symptom of dysthymia and rated on a 4-point scale (0 = No information; 1 = Not at all discouraged about the future; 2 = Transient feelings of moderate to severe discouragement about the future; 3 = Often feels quite pessimistic about the future, prospects for the future appear dim); current hopelessness (past not assessed) had an inter-rater agreement Pearson $r = .80$ (based on 26 ratings).

Global functioning was assessed by the Children's Global Adjustment Scale (C-GAS; Shaffer et al., 1983), in which interviewers quantified the severity of functional impairment on a 100-point scale (e.g., scores between 50–41 indicate moderate functioning interference in most social areas or severe functional impairment in one area), which included behavioral examples as anchor points. Inter-rater agreement data were not collected but Rey, Starling, Wever, Dossetor, and Plapp (1995) reported that 75% of inter-rater reliability scores made by clinicians for child/adolescents patients were within 10 points.

Cognitive distortions were assessed by an abbreviated version of the Automatic Thoughts Questionnaire (ATQ, Hollon & Kendall, 1980). The ATQ assesses the frequency of automatic negative thoughts in the last week (1 = not at all; 2 = sometimes; 3 = moderately often; 4 = often; 5 = all the time). Two ATQ subscales (personal maladjustment/desire for change, negative self-concept/expectations; 12 items total) were selected because they correlated .90 with each other and correlated at least .96 with the total ATQ score in Rohde et al. (2004). Previous pilot testing ($n = 44$) indicated that a shortened form of the ATQ had excellent internal consistency ($\alpha = .92$) and 1-week test-retest reliability ($r = .74$). Cronbach's alpha in the present study was $\alpha = .95$.

Anxiety symptoms were assessed by the DSM-IV Anxiety Problems scale (Achenbach & Dumenci, 2001) of the Youth Self-Report (Achenbach, 1991), which contains 6 items in which adolescents describe themselves with the past 6 months (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true). Cronbach's alpha in the present study was $\alpha = .70$.

Problematic family interactions were assessed by adolescent report on the Conflict and Cohesion subscales of the Family Environment Scale (FES; Moos & Moos, 1986). The FES, one of the most widely used family assessment instruments, is comprised of ten subscales

measuring social-environmental characteristics of families. Moos and colleagues report internal consistency of subscales ranging from .61-.78, with test-retest reliabilities from .68-.86 at 2 months. The scale effectively distinguishes normal from disturbed families, including alcohol-abusing families (Finney, Moos, & Chan, 1981). The Conflict and Cohesion subscales were used to assess adolescent current perceptions of relationship functioning, measured with 9 statements about families for each, which were rated as true/mostly true or false/mostly false for their family. The two measures were significantly correlated; $r(168) = -.68, p < .001$. Cronbach's alphas in the present study were $\alpha = .75$ for the Conflict scale and $\alpha = .74$ for Cohesion.

Treatment Conditions

The Adolescent Coping with Depression Course (CWD) is a group intervention providing cognitive and behavioral strategies to address depression. The original intervention was modified from 16 to 12 sessions by removing communication and problem-solving skills (they were included in FFT), shortening sessions from 120 to 90 minutes, and adding a points system to reward participation.

Functional Family Therapy (FFT) is a systems-oriented, behaviorally based model of family therapy (Alexander et al., 2013; Waldron & Brody, 2010) that integrates intervention strategies for addictive behaviors to an ecological formulation of family disturbance; standard SUD delivery involves 10–18 sessions (standardized to 12 sessions in this trial) over 10 weeks with 5 treatment phases (engagement, motivation, relational assessment, behavior change, generalization).

Coordinated Treatment (CT) represented a synthesis of FFT and CWD, providing the same number of sessions with a more integrated content. Over the 20 weeks of treatment, 12 FFT sessions were offered between Weeks 1–18 and 12 sessions of CWD group were offered between Weeks 5–20. Overall, family sessions followed FFT, with additional attention to themes of family depression. Group treatment consisted of CWD augmented to provide cognitive-behavioral skills training aimed at reducing substance use (Waldron & Kaminer, 2004). Different therapists provided the FFT versus CWD interventions (unless unavoidable). Therapists had at least a master's degree in mental health, one year experience with adolescents and families, and were trained in two-day workshops. After FFT training, therapists conducted two pilot cases. Therapists were supervised weekly during treatment. Sessions were videotaped; a random 25% of CWD sessions were rated, as were 2 FFT sessions per family (15%) using established scales, which indicated that therapists adhered to the intervention with no differences across treatment sequences.

The planned design resulted in families being nested within cohorts which were also nested within therapists. To assess nesting dependency within groups, the intraclass correlation coefficient (ICC) was calculated; generally $ICC < .05$ suggest that dependency is negligible and each family can be treated as an independently sampled unit. Nesting effects of cohorts and therapists at Week 10 and 20 (controlling for baseline) indicated small ICCs (range = $-.05$ to $+.05$; e.g., average cohort ICC for the CDRS and for all drug use = $.020$ and $.023$, respectively). We also examined whether site moderated response and found that all Site X Sequence X Time interactions were nonsignificant.

Multiple imputation and missing data. Approximately 25% of scores were missing at any assessment after baseline. To estimate missing values, we used Markov Chain Monte Carlo multiple imputation (Schafer & Graham, 2002). SPSS19 imputed missing values to create nine data sets across assessments for the CDRS. Imputations were performed separately within treatment sequence; with age and gender being used to condition the estimates. We combined imputations into one analysis set and examined whether sets differed significantly; the sets did not differ on any imputed dependent variable or any interactions with independent variables (F 's < 1.0). Subsequent analyses used the nine imputed sets but statistics and alpha levels were corrected to reflect original sample size ($N = 170$).

Latent Growth Trajectory Modeling

To identify individual differences in patterns or profiles of change in depressive symptoms, we applied latent class growth analysis (LCGA) to the seven waves of CDRS scores using version 8.1 of MPlus (Muthen & Muthen, 2000). The analysis was performed on each of the nine replications of multiple imputed data sets. Results for the Vuong, Lo, Mendell, Rubin Log Likelihood Ratio (LR) Test (Muthen & Muthen, 2000) indicated that a 4-class solution was significantly better than a 3-class solution; difference between 3- and 4-class solutions $2* LR = 149.144, p = 0.0016$. We also conducted a bootstrap procedure in MPlus with 500 random draws to estimate the likelihood of a difference between 3- and 4-class solutions and the results were significant ($p < .0001$) suggesting that the 4-class solution was superior to the 3-class one.

Next, we performed a k-means cluster analysis in SPSS19 to corroborate our estimates of four change trajectories. We adopted the cluster procedure for cross validation because time intervals between assessments were much longer for the last two observations than the first five. While it is possible to model unequally spaced time periods in LGCA, the selection of values for estimating non-linear (e.g., quadratic, cubic) time parameters with widely varying spacing of assessments can seem arbitrary. We recognize that the varying time intervals can be modeled by piecewise change models. Since prior research has applied cluster analysis, we choose this option for cross validation of the clusters. This procedure also supported the presence of four change trajectories, which are presented in Figure 1. We conducted a sensitivity analysis to determine whether cluster membership was consistent across imputed data sets. Cluster membership was identical across imputation sets for 80% of the cases, and agreed at least 5/9 of the times on 98% of the cases.

Results

The largest group ($n = 97$) was composed of youth generally without MDD (rate of current MDD = 29.9%) who entered treatment with mild-moderate depression scores that quickly dropped and remained low through follow-up (57.1%, labeled Mildly Depressed Responders). The other three groups generally experienced MDD at baseline (MDD rates = 93.8%, 72.7%, and 89.5% in clusters 2, 3, and 4, respectively) and had higher initial depression scores but displayed three different change patterns. The largest of these groups responded well to treatment and maintained improvements ($n = 33$, 18.8%, labeled Depressed Responders), followed by those who remained elevated on depression measures

($n = 22$, 12.9%, labeled Depressed Non-Responders) and those who initially responded to treatment but then experienced a large increase in depression levels by the 1-year follow-up ($n = 19$, 11.2%, labeled Depressed with Recurrence). Latent growth membership was not associated with participant gender, race (European American, Y/N), or ethnicity (Hispanic, Y/N).

We explored the frequency of occurrence of the four change profiles in each of the three treatment sequences. Results, shown in Table 1, indicated that membership in the four response profiles did not significantly differ by treatment sequence; $\chi^2(6) = 6.30$, $p < .39$.

Growth Trajectory Membership as a Function of Baseline Predictor Variables

We next examined whether previously identified predictors of depression treatment response in samples of generally non-comorbid depressed adolescents predicted change profile membership. Results are shown in Tables 2 (continuous measures) and 3 (dichotomous suicidality measures), with significant pairwise differences indicated by subscripts (pairwise contrasts based on Bonferroni adjusted confidence levels, $\alpha = .05/6$), including effect size estimates (eta-squared, generally interpreted as .01 = small, .06 = medium, .13 = large, Cohen, 1988). In the unadjusted analyses, the four change profiles significantly differed on indices of all but one of the eight examined baseline variables: age was nonsignificant. Most of these differences were driven by lower scores among the Mildly Depressed Responders but 3 variables had a significant pairwise difference (adjusted for number of contrasts) between the three profile groups that started with higher depression severity levels: (1) overall depression severity, (2) hopelessness, and (3) recent suicidal actions. Regarding depressive severity, the adolescents classified as Depressed Responders and Depressed with Recurrence had significantly higher initial depression levels than the Depressed Non-Responders. Regarding hopelessness and recent suicidal actions, the Depressed with Recurrence had significantly greater levels of hopelessness and recent suicidal actions compared to the Depressed Non-Responders (Depressed Responders were intermediate on both measures).

To ensure that associations were not driven by overall baseline depression severity level, analyses next controlled for depression severity (total CDRS score at intake); results appear in the last columns of Table 2 (not applicable for depressive severity and not computed for age because the unadjusted test was nonsignificant). Indices of two predictors remained significant controlling for overall depression level: hopelessness and family cohesion. Regarding the nature of profile differences for family cohesion, Depressed Non-Responders had significantly lower levels of family cohesion compared to Mildly Depressed Responders, with Depressed Responders and Depressed with Recurrence groups being intermediate. We could not adjust the overall chi-square analyses for the suicidality dichotomous measures but instead computed pairwise comparisons using multiple regression procedures with a dichotomous variable reflecting cluster condition with the CDRS covariate. Of the five suicide-related pairwise contrasts that had initially been significant, two remained significant controlling for depression severity: (1) past suicidal ideation in Mildly Depressed Responders vs. Depressed Non-Responders, $Beta = .346$, $t =$

3.474, $p = .001$, and (2) past suicidal acts in the Mildly Depressed Responders vs. Depressed with Recurrence, $Beta = .371$, $t = 3.252$, $p = .002$.

Alternative Explanations of Change Trajectories

Researchers (e.g., Sher et al., 2011) have proposed that change profile clusters may be artifacts resulting from natural fluctuations in problem behaviors rather than a truly differential response to treatment. This argument presumes that the change profiles emerge from the normal waxing and waning of emotional states. These oscillations could be caused by the cyclic nature of depression or by seasonal effects, distress at different phases of the academic school year, or other factors. If these effects were present, alternative clusters would be found because adolescents enter treatment at different phases of their cycle, although an important assumption of this model is that the duration of observations for each adolescent spans only a portion of the entire depression cycle for that individual. This four-group pattern has sometimes been referred to as the “cat’s cradle” (high-high; high-low; low-high; low-low). While we did not have the “low-high” cluster noted in the “cat’s cradle,” we did have clusters that corresponded to the high-high and high-low patterns, and somewhat corresponded to a low-low pattern. We conducted exploratory analyses examining factors that would be consistent with a cyclic model.

Some findings were consistent with the cyclic recurring premise, which recognizes that many participants have prior episodes of MDD, which we assessed in the K-SADS. The four clusters reported significantly different rates of past MDD [$\chi^2(3) = 15.85$, $p < .001$] with significantly lower rates in the Mildly Depressed Responders vs. Depression with Recurrence (11% vs. 47%); MDD rates in the Depressed Responder (28%) and Depressed Non-Responder (32%) clusters were intermediate.

Another assumption of the cyclic model is that detected clusters will differ in the duration of baseline depression symptoms since some adolescents enter treatment early while others enter later in their depression episode. The K-SADS assessed reported duration (in months) of current depressive episode and we examined episode duration median, mean, and standard deviation in each cluster (Mildly Depressed Responders median = 3.00, $M = 11.49$, $SD = 21.21$; Depressed Non-Responders median = 4.00, $M = 14.64$, $SD = 30.12$; Depressed Responders median = 10.00, $M = 20.28$, $SD = 23.37$; and Depressed with Recurrence median = 8.00, $M = 29.26$, $SD = 39.22$). Since the distribution was highly skewed, we conducted a one-way ANOVA on the square root transformed symptom duration and found a significant effect of baseline duration by cluster type; $F(3,166) = 4.67$, $p < .004$, $\eta^2 = .077$. Pairwise comparisons revealed that Mildly Depressed Responders had significantly shorter baseline duration compared to both Depressed Responders ($p < .007$) and Depressed with Recurrence ($p < .004$), and that the Depressed Non-Responders had significantly shorter baseline duration compared to Depressed with Recurrence ($p < .036$). These analyses are partially consistent with a cyclic premise (e.g., the longer duration of the recurrent group suggests that they have progressed further into their depressive cycle than the non-responders, who are earlier in their cycle).

To examine potential seasonal effects, we computed mean CDRS scores based upon the month in which adolescents entered treatment. We saw a generally flat/stable level of

depressive severity over the year with one notable increase around the months of April, May, and June. This period corresponds to the end of the school year, when many adolescents experience the consequences of poor academic functioning. A large proportion of adolescents in the Depressed with Recurrence group (47%) entered the study in April-June (versus 5% in January-March) and school pressures which ended or decreased in the summer may have contributed to their pattern, suggesting a pattern of depression linked to school performance. Seasonal fluctuations in the three other clusters did not vary substantially (all other groups were within 15%–35%, which is close the 25% for each season that would be expected by chance; statistical tests were not conducted given low sample sizes).

One potential problem with the “cat’s cradle” model is that the “high-high” and “low-low” clusters do not appear to represent a cyclic pattern. To address this issue, Sher et al. (2011) reasoned that either ceiling effects (high-high) or floor effects (low-low) due to a restriction of range of measurement led to the flat lines. Since an important assumption of the “cat’s cradle” model is restriction of range, we examined the distribution of CDRS scores at each assessment. Regarding floor effects, all adolescents who enrolled in the study had substantial levels of depression symptoms and none of them approached the CDRS floor. Regarding ceiling effects, only 1% of scores approached a maximum value on the CDRS suggesting that range restriction did not apply.

Discussion

This study empirically examined the patterns of depressive symptom change during and one year following treatment in a sample of depressed adolescents with comorbid SUD who received two forms of evidence-based treatment (one for each condition) delivered in one of three sequences. Our primary goals were to describe the number and type of distinct depression change trajectories (i.e., profiles) and examine whether previously identified predictors of poor depression treatment response were found in a comorbid sample. We also explored whether any of the three examined sequences predicted membership in a specific change profile and considered alternative explanations to the empirically based clustering.

A 4-cluster solution fit the data best. The largest cluster, which represented more than half of the sample, was composed primarily of youth without MDD who entered treatment with mild-to-moderate depression levels that dropped quickly and remained low through follow-up (57%, labeled Mildly Depressed Responders). That this depressive symptom pattern was most prevalent was perhaps to be expected, as the two centers were established as SUD clinics and most adolescents were referred for SUD treatment. We do not believe that the large size of this cluster indicates that adolescents in general are more likely to receive treatment for an SUD than for depression. Rather, the opposite may be the case, considering the 38% lifetime service utilization for adolescents with mood disorders versus 15% for those with SUD (Merikangas et al., 2011). Possibly, the primary pattern of depression among adolescents with comorbid SUD may include mild-moderate depressive symptoms not reaching the threshold for MDD diagnosis; these adolescents may not require depression-specific psychotherapy. Adolescents in the other three identified clusters generally were experiencing MDD and had clinically significant depression severity levels

(i.e., indicative of depressive disorder diagnosis) at baseline but each displayed a different change pattern across treatment and follow-up. The largest of these groups responded well to treatment and maintained their improvement; labeled “Depressed Responders,” they represented 19% of our sample and 44% of those who entered treatment with clinically significant depression scores. They can be considered to show a “high/low” response pattern. Combining this responders group with the Mildly Depressed Responders suggests that approximately 75% of adolescents entering with some degree of depression will experience a positive response and remain fairly symptom-free for one year following treatment.

The third and fourth clusters reflected poorer response profiles. The third cluster entered treatment with clinically significant depressive symptoms and failed to show much improvement during or after treatment. Labeled “Depressed Non-Responders,” they represented 13% of the sample (approximately 1 in 8) and were 30% of those who entered treatment with clinically significant depressive symptoms. They can be considered to show a “high/high” response pattern. The fourth cluster entered treatment quite depressed, initially responded well to treatments but then experienced a large increase in depressive symptom levels by 1-year post-treatment. Labeled “Depressed with Recurrence,” they represented 11% of the sample (approximately 1 in 10) and 26% of those who entered treatment with clinically significant depression. They can be considered to show a “high/low/high” response pattern. Membership in the four clusters was not associated with gender, race or ethnicity. Combining non-responders and those experiencing recurrence represented approximately 25% of the total sample, but more concerning, they represented more than half of the sample that entered treatment with clinically significant depression at the level indicative of an MDD diagnosis, which suggests that a group or family intervention may be insufficient depression treatment for the majority of adolescents with depression at the level of MDD with comorbid SUD. It is well-known that MDD is a highly recurrent disorder even when comorbidity is not present (e.g., Curry et al., 2011).

The study represents an extension of our previous work (Waldron, Slesnick, Brody, Turner, & Peterson, 2001) which used cluster analysis to classify substance use response in adolescents (generally nondepressed) being treated with various modalities for SUD. Four distinct response profiles of change were identified, with consistent findings across different substance use categories (rates for marijuana use shown in parentheses): rapid improvers with continuous low use (37%), rapid improvers followed by relapse (25%), continuous heavy users (25%), and gradual improvers (14%). It is noteworthy that we did not detect a “gradual improvers” cluster in the present report; it suggests that unlike problematic substance abuse, depression levels generally drop quickly from most forms of treatment, which has been noted previously (e.g., Renaud et al., 1998), perhaps due to nonspecific therapeutic factors (Ilardi & Craighead, 1994).

The empirical validation of adolescent change profiles is important because, to date, empirical support for adolescent depression treatments has been almost exclusively at the group level. Recent developments in analytic approaches, such as cluster analysis, have the potential to broaden our understanding of individual patterns of change across adolescents. Without the implementation of more advanced analytic strategies to examine differential patterns of treatment responding, important effects between individuals that might serve as a

guide for tailoring treatments to individual adolescents are likely to go undetected. Such effects could help address critical questions associated with treatment mechanisms, moderators, and long-term outcomes including patterns of relapse or recurrence.

Our second aim was to examine the degree to which constructs found to predict poor treatment response in replicated randomized controlled trials with generally non-comorbid depressed adolescents also predicted treatment nonresponse in depressed adolescents with comorbid SUD. Indices for seven of the eight examined predictor variables were significant in initial analyses. The largest effect associated with treatment response involved baseline depression severity. Depressed Responders and Depressed with Recurrence did not differ on depression severity but both groups entered treatment more depressed than the Depressed Non-Responders, who in turn were initially more depressed than the Mildly Depressed Responders. Other large magnitude ($\eta^2 = .13$) effects were found for cognitive distortions, hopelessness, and global functioning; the other significant variables reflected medium magnitude effects. Most of the measures with a significant overall effect appeared to be driven by better functioning in the Mildly Depressed Responders (i.e., there were no significant differences between the three initially highly depressed groups). Two variables were found that differentiated those who entered treatment highly depressed: hopelessness and recent suicidal actions. For both of these variables, scores were significantly worse among the Depressed with Recurrence compared to the Depressed Non-Responders. The effect for recent suicidal actions was striking (0% in the Depressed Non-Responders vs. 21% in the Depressed with Recurrence). The pattern of findings suggests that both hopelessness and recent suicidal actions may be indicators of adolescents who are prone to depression recurrence.

Given the strong effect of depression severity on cluster membership, we examined the impact of variables controlling for this factor. After adjusting for baseline depression severity, hopelessness, family cohesion, and some indices of suicidality remained significant markers of profile membership (e.g., the Depressed with Recurrence group reported greater hopelessness than both the Depressed Non-Responders and the Mildly Depressed Responders; rates of past suicidal ideation was elevated among the non-responders and rates of past suicidal actions were elevated among those with recurrence). What was most striking in these adjusted associations was the role of low family cohesion, which was poorest among the Depressed Non-Responders. This finding might provide some clue as to why this cluster failed to respond to a treatment protocol that consisted of group CBT and family-based treatment; high levels of depression in combination with low levels of shared affection, support, helpfulness, and caring among family members (all aspects of cohesion) appear to have interfered with the ability of either treatment to successfully treat depression. Functional Family Therapy may require a minimum level of cohesion when depression is present to effectively reduce depression levels among the children. Although past research found that family conflict rather than low cohesion increased the likelihood of treatment nonresponse among depressed adolescents, we examined both family conflict and cohesion, which were significantly correlated. We included both measures because our clinical perception was that, compared to the non-depressed families receiving FFT, families with a depressed son or daughter (and often a depressed parent or parents) are quieter, more withdrawn, more disconnected, as opposed to the intense, animated, conflicted interactions

often seen among nondepressed families receiving FFT. Thus, even though the scales are highly correlated, our perception was that low cohesion may be more important than high conflict in families with depressed/addicted adolescents. In summary, the Depressed Non-Responders started out less severely depressed than either Depressed Responders or the Depressed with Recurrence; they also entered treatment with less hopelessness and very little current suicidality. Their most marked baseline characteristic was a low degree of family cohesion. Adolescents with this pattern of baseline features appear to require treatments other than group cognitive-behavioral therapy and a standard FFT family-based treatment to achieve depressive symptom remission; alternative treatment options might include family therapy with a more in-depth focus on building cohesion or possibly antidepressant medications (Riggs et al., 2007).

Regarding predictors of membership in the Recurrence group, it was noteworthy that none of the eight constructs significantly differentiated the Depressed Responders from the Depressed with Recurrence; both groups entered treatment highly depressed and each showed a strong positive response to all of treatment sequences but the second group failed to retain that effect. We explored alternate explanations for the four depression trajectories and the most striking difference appeared to be a seasonal effect for the Depressed with Recurrence group, more of whom entered the study in late spring. It is possible their sharp drop in depressive symptoms corresponded to the summer months, which has been noted as a potential confounding factor for adolescent depression scores in medication trials (Bostic, 2011), followed by return of symptoms approximately one year later. These exploratory results suggested that the pattern of symptoms found in the Depressed with Recurrence group may have been partially due to situational factors related to the end of the school year. Given our inability to predict which responders will maintain their depression gains, depressed/substance addicted adolescents may benefit from booster sessions, transitional care in which treatment is more gradually faded, or ongoing follow-up with periodic depression monitoring to provide additional treatment should recurrence occur.

We also explored whether the three methods of treatment delivery examined in this study (SUD-focused treatment first vs. depression-focused treatment first vs. coordinated treatments) were associated with differential response patterns. The four depression response profiles did not significantly differ in their distribution across sequences, suggesting that no one treatment format accounted for positive trajectories more than any other. A similar pattern of nonsignificant differences between treatments was found previously [Waldron et al., 2001], in which the four profiles of substance use change were generally distributed equally across the different treatment conditions (outpatient family and/or cognitive behavioral treatments for SUD), suggesting that no one treatment accounted for a positive substance use trajectory. However, post hoc, pairwise comparisons among the four clusters in that trial indicated that baseline depression was predictive of youth who experienced a positive substance use reduction in treatment but then relapsed, which suggested that treatments for adolescent SUD alone do not adequately address the needs of youth with co-occurring depression. This finding in combination with previous research evidence that depression monotherapy (i.e., depression group CBT; Rohde et al., 2004) and combination therapy (i.e., fluoxetine plus CBT vs. placebo plus CBT; Riggs et al., 2007) reduced depression but not SUD in adolescents with comorbid conditions suggests that both

treatments are required for change in comorbid conditions and that neither disorder routinely maintains the other.

One limitation of the present study is that we examined a relatively small number of potential predictor variables in relation to adolescent treatment response patterns. This was done due to the relatively small sample size per change trajectory. More research is needed to examine a broader range of variables in larger samples that may discriminate profiles of change, including other comorbid psychopathology, parental psychopathology, and other aspects of interpersonal functioning. Second, the study focused on changes in depressive symptoms in adolescents with comorbid depression/SUD and we did not attempt to model the trajectories of depressive symptoms and substance use simultaneously. Third, cluster analysis is a person-centered (rather than variable-centered) technique and is not a true multi-level analysis. Researchers must be mindful of several key limitations and caveats associated with this technique and appreciate that statistical guidelines and criteria for evaluating the accuracy and validity of cluster solutions are not well developed and do require some level of subjective judgment on the part of the researcher. Fourth, these results refer to depressed and substance-addicted adolescents who sought or were mandated to receive treatment and may not generalize to the broader population of youth with SUD, most of whom do not seek or receive intervention (Merikangas et al., 2011). As noted, treatment occurred in two centers known for SUD treatment and the results may be more representative of outcomes among depressed youth in which SUD is the factor driving treatment-seeking or where families are in need of no-cost treatment.

As a step toward an individually focused research agenda, this study provides support for the use of cluster analysis for studying profiles of individual depression level change in response to adolescent depression and substance abuse treatment. The differences in the depressive symptom profiles themselves, as well as factors related to cluster membership, hopefully provide some guidance with respect to tailoring treatments to the needs of different subgroups of adolescents (e.g., family cohesion should be assessed and may suggest the need for alternative treatments; past suicidality may be a marker for recurrence and the need for follow-up treatment; the impact of school functioning on course of depression). The present study highlights the need for a better understanding of pre-treatment predictors of different patterns of treatment responding, especially those associated with trajectories that reflect treatment failure, in order to inform the tailoring of treatments to particular profiles of change (Latimer, Winters, Stinchfield, & Traver, 2000; Wagner, Brown, Monti, Myers, & Waldron, 1999). Understanding the nature of change profiles and predictors of change through cluster analysis and other advanced procedures can help advance the science of adolescent depression and substance abuse treatment and facilitate efforts to transport such treatments into community treatment settings by better treatment matching.

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References

- Achenbach TM (1991). Manual for the Child Behavior Checklist/4–18 and 1991 Profile. Burlington, VT: University of Vermont Department of Psychiatry.
- Achenbach TM, & Dumenci L (2001). Advances in empirically based assessment: revised cross-informant syndromes and new DSM-oriented scales for the CBCL, YSR, and TRF: comment on Lengua, Sadowksi, Friedrich, and Fischer (2001). *Journal of Consulting and Clinical Psychology*, 69, 699–702. [PubMed: 11550735]
- Alexander JF, Waldron HB, Robbins MS, & Neeb A (2013). *Functional Family Therapy*. Washington, D.C.: American Psychological Association.
- American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders*, Fourth edition, Text revision. Washington, DC: American Psychiatric Association.
- Armstrong TD, & Costello EJ (2002). Community studies on adolescent substance use, abuse, or dependence and psychiatric comorbidity. *Journal of Clinical and Community Psychology*, 70, 1224–1239.
- Asarnow JR, Emslie G, Clarke G, Wagner KD, Spirito A, Vitiello B, ... Brent D (2009). Treatment of selective serotonin reuptake inhibitor-resistant depression in adolescents: Predictors and moderators of treatment response. *Journal of the American Academy of Child and Adolescent Psychiatry*, 48, 330–339. [PubMed: 19182688]
- Barbe RP, Bridge J, Birmaher B, Kolko D, & Brent DA (2004). Suicidality and its relationship to treatment outcome in depressed adolescents. *Suicide and Life-Threatening Behavior*, 34, 44–55. [PubMed: 15106887]
- Birmaher B, Brent DA, Kolko D, Baugher M, Bridge J, Holder D, Iyengar S, & Ulloa RE (2000). Clinical outcome after short-term psychotherapy for adolescents with major depressive disorder. *Archives of General Psychiatry*, 57, 29–36. [PubMed: 10632230]
- Bostic JQ (2011). Summer is the best time for treatment of resistant depression in adolescents (TORDIA): The importance of school in medication trials. *Journal of the American Academy of Child and Adolescent Psychiatry*, 50, 1095–1097. [PubMed: 22023997]
- Brent DA, Kolko DJ, Birmaher B, Baugher M, Bridge J, Roth C, & Holder D (1998). Predictors of treatment efficacy in a clinical trial of three psychosocial treatments for adolescent depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 37, 906–914. [PubMed: 9735610]
- Carmanico SJ, Erickson MT, Singh NN, Best AM, Sood AA, & Oswald DP (1998). Diagnostic subgroups of depression in adolescents with emotional and behavioral disorders. *Journal of Emotional and Behavioral Disorders*, 6, 222–232.
- Clarke G, Hops H, Lewinsohn PM, Andrews J, Seeley JR, & Williams J (1992). Cognitive-behavioral group treatment of adolescent depression: Prediction of outcome. *Behavior Therapy*, 23, 341–354.
- Clarke GN, Lewinsohn PM, & Hops H (1990). *Adolescent Coping With Depression Course*. Eugene, OR: Castalia Press.
- Clarke GN, Rohde P, Lewinsohn PM, Hops H, Seeley JR (1999). Cognitive-behavioral treatment of adolescent depression: Efficacy of acute group treatment and booster sessions. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, 272–279. [PubMed: 10087688]
- Cohen J (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.
- Curry J, Silva S, Rohde P, Ginsburg G, Kratochvil C, Simons A, Kirchner J, May D, Kennard B, Mayes T, Feeny N, Albano AM, Lavanier S, Reinecke M, Jacobs R, Becker-Weidman E, Weller E, Emslie G, Walkup J, Kastelic E, Burns B, Wells K, & March J (2011). Recovery and recurrence following treatment for adolescent major depression. *Archives of General Psychiatry*, 68, 263–269. [PubMed: 21041606]
- Curry J, Rohde P, Simons A, Silva S, Vitiello B, Kratochvil C, Reinecke M, Feeny N, Wells K, Pathak S, Weller E, Rosenberg D, Kennard B, Robins M, Ginsburg G, & March J (2006). Predictors and moderators of acute outcome in the treatment for adolescents with depression study (TADS). *Journal of the American Academy of Child & Adolescent Psychiatry*, 45, 1427–1439. [PubMed: 17135988]

- David-Ferdon C, & Kaslow NJ (2008). Evidence-based psychosocial treatments for child and adolescent depression. *Journal of Clinical Child & Adolescent Psychology*, 37, 62–104. [PubMed: 18444054]
- Dew MA, Reynolds CF, Houck PR, Hall M, Buysse DJ, Frank E, & Kupfer DJ (1997). Temporal profiles of the course of depression during treatment: Predictors of pathways toward recovery in the elderly. *Archives of General Psychiatry*, 54, 1016–1024. [PubMed: 9366658]
- Feeny N, Silva S, Reinecke M, McNulty S, Findling R, Rohde P, Curry J, Ginsburg G, Kratochvil C, Pathak S, May D, Kennard B, Simons A, Wells K, Robins M, Rosenberg D, & March J (2009). An exploratory analysis of the impact of family functioning on treatment for depression in adolescents. *Journal of Clinical Child & Adolescent Psychology*, 38, 814–825. [PubMed: 20183665]
- Finney JW, Moos RH, & Chan DA (1981). Length of stay and program component effects in the treatment of alcoholism: A comparison of two techniques for process analyses. *Journal of Consulting and Clinical Psychology*, 49, 120–131. [PubMed: 7217465]
- Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, & Weissman MM (1991). Conceptualization and rationale for consensus definitions of terms in major depressive disorder: Remission, recovery, relapse, and recurrence. *Archives of General Psychiatry*, 48, 851–855. [PubMed: 1929776]
- Hollon SD, & Kendall PC (1980). Cognitive self-statements in depression: Development of an Automatic Thoughts Questionnaire. *Cognitive Therapy and Research*, 4, 383–395.
- Hybels CF, Blazer DG, Pieper CF, Landerman LR, & Steffens DC (2009). Profiles of depressive symptoms in older adults diagnosed with major depression: Latent cluster analysis. *The American Journal of Geriatric Psychiatry*, 17, 387–396. [PubMed: 19390296]
- Ilardi SS, & Craighead WE (1994). The role of nonspecific factors in cognitive-behavior therapy for depression. *Clinical Psychology: Science and Practice*, 1, 138–155.
- Jayson D, Wood A, Kroll L, Fraser J, & Harrington R (1998). Which depressed patients respond to cognitive-behavioral treatment? *Journal of the American Academy of Child and Adolescent Psychiatry*, 37, 35–39. [PubMed: 9444897]
- Kaufman J, Birmaher B, Brent D, Rao U, & Ryan N (1996). Diagnostic Interview - Kiddie-SADS-Present and Lifetime Version (K-SADS-PL). Pittsburgh, PA: Western Psychiatric Institute and Clinic.
- Kennard B, Silva S, Vitiello B, Curry J, Kratochvil C, Simons A, Hughes J, Feeny N, Weller E, Sweeney M, Reinecke M, Pathak S, Ginsburg G, Emslie G, March J, and The TADS Team (2006). Remission and residual symptoms after short-term treatment in the Treatment of Adolescents with Depression Study (TADS). *Journal of the American Academy of Child and Adolescent Psychiatry*, 45, 1404–1411. [PubMed: 17135985]
- Latimer WW, Winters KC, Stinchfield R, & Traver RE (2000). Demographic, individual, and interpersonal predictors of adolescent alcohol and marijuana use following treatment. *Psychology of Addictive Behaviors*, 14, 162–173. [PubMed: 10860115]
- Mayes TL, Bernstein IH, Haley CL, Kennard BD, & Emslie GJ (2010). Psychometric properties of the Children's Depression Rating Scale-Revised in adolescents. *Journal of Child and Adolescent Psychopharmacology*, 20, 513–516. [PubMed: 21186970]
- Merikangas KR, He J-P, Burstein M, Swendsen J, Avenevoli S, Case B, Georgiades K, Heaton L, Swanson S, & Olfson M (2011). Service utilization for lifetime mental disorders in U.S. adolescents: Results of the National Comorbidity Survey-Adolescent Supplement (NCS-A). *Journal of the American Academy of Child & Adolescent Psychiatry*, 50, 32–45. [PubMed: 21156268]
- Moos RH, & Moos BS (1986). Family Environment Scale manual. Palo Alto, CA: Consulting Psychologists Press.
- Muthén L, & Muthén B (2000). Mplus user's guide. Los Angeles, CA: Muthén & Muthén.
- Poznanski E, & Mokros H (1995). Children's Depression Rating Scale – Revised (CDRS-R). Los Angeles: Western Psychological Services.

- Renaud J, Brent DA, Baugher M, Birmaher B, Kolko DJ, & Bridges J (1998). Rapid response to psychosocial treatment for adolescent depression: A two-year follow-up. *Journal of the American Academy of Child & Adolescent Psychiatry*, 37, 1184–1190. [PubMed: 9808930]
- Repetto PB, Caldwell CH, & Zimmerman MA (2004). Trajectories of depressive symptoms among high risk African-American adolescents. *Journal of Adolescent Health*, 35, 468–477. [PubMed: 15581526]
- Rey JM, Starling J, Wever C, Dossetor DR, & Plapp JM (1995). Inter-rater reliability of Global Assessment of Functioning in a clinical setting. *Journal of Child Psychology & Psychiatry & Allied Disciplines*, 36, 787–792.
- Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, & Stover SK (2007). A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Archives of Pediatric and Adolescent Medicine*, 161, 1026–1034.
- Rohde P, Clarke GN, Lewinsohn PM, Seeley JR, & Kaufman NK (2001). Impact of comorbidity on a cognitive-behavioral group treatment for adolescent depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 40, 795–802. [PubMed: 11437018]
- Rohde P, Clarke GN, Mace DE, Jorgensen JS, & Seeley JR (2004). An efficacy/effectiveness study of cognitive-behavioral treatment for adolescents with comorbid major depression and conduct disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43, 660–668. [PubMed: 15167082]
- Rohde P, Lewinsohn PM, & Seeley JR (1991). Comorbidity of unipolar depression: II. Comorbidity with other mental disorders in adolescents and adults. *Journal of Abnormal Psychology*, 100, 214–222. [PubMed: 2040773]
- Rohde P, Waldron HB, Turner CW, Brody J, & Jorgensen J (2014). Sequenced versus coordinated treatment for adolescents with comorbid depressive and substance use disorders. *Journal of Consulting and Clinical Psychology*, 82, 342–348. [PubMed: 24491069]
- Schacht A, Gorwood P, Boyce P, Schaffer A, & Picard H (2014). Depression symptom clusters and their predictive value for treatment outcomes: Results from an individual patient data meta-analysis of duloxetine trials. *Journal of Psychiatric Research*, 53, 54–61. [PubMed: 24572681]
- Schafer JL, & Graham JW (2002). Missing data: Our view of the state of the art. *Psychological Methods*, 7, 147–177. [PubMed: 12090408]
- Sears HA (1997). Manifestations of depressive symptoms in adolescents: Identifying subtypes and their distinguishing features. *Dissertation Abstracts International: Section B: The Sciences and Engineering*, 57(10-B), 6593.
- Shaffer D, Gould M, Brasic J, Ambrosini P, Fisher P, Bird H, & Aluwahlai S (1983). A children's global adjustment scale. *Archives of General Psychiatry*, 40, 1222–1231.
- Sher KJ, Jackson KM, & Steinley D (2011). Alcohol use trajectories and the ubiquitous cat's cradle: cause for concern? *Journal of Abnormal Psychology*, 120, 322–335. [PubMed: 21319874]
- Wagner EF, Brown SA, Monti PM, Myers MG, & Waldron HB (1999). Innovations in Adolescent Substance Abuse Intervention. *Alcoholism: Clinical and Experimental Research*, 23, 236–249.
- Wagner KD, (2005). Pharmacotherapy for major depression in children and adolescents. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 29, 819–826. [PubMed: 15908090]
- Waldron HB, & Brody J (2010). Functional Family Therapy for adolescent substance use disorders In Weisz J & Kazdin A (Eds), *Evidence-based psychotherapies for children and adolescents* (2nd Ed.), pp. 401–415. New York: Guilford Press.
- Waldron HB, & Kaminer Y (2004). On the learning curve: The emerging evidence supporting cognitive-behavioral therapies for adolescent substance abuse. *Addiction*, 99 Suppl. 2, 93–105.
- Waldron HB, Slesnick N, Brody JL, Turner CW, & Peterson TR (2001). Treatment outcomes for adolescent substance abuse at 4- and 7-month assessments. *Journal of Consulting and Clinical Psychology*, 69, 802–813. [PubMed: 11680557]

Figure 1.
Depressive symptom change trajectories from baseline (Week 0) through one-year post-treatment (Week 72)

Table 1

Membership in Latent Growth Trajectory Group as a Function of Treatment Sequence

Treatment Sequence	Mildly Depressed Responders (<i>n</i> = 97)	Depressed Responders (<i>n</i> = 32)	Depressed Non-Responders (<i>n</i> = 22)	Depressed with Recurrence (<i>n</i> = 19)
FFT/CWD (<i>n</i> = 61)	32 (33% / 53%)	10 (31% / 16%)	8 (36% / 13%)	11 (58% / 18%)
CWD/FFT (<i>n</i> = 56)	32 (33% / 57%)	10 (31% / 18%)	9 (41% / 16%)	5 (26% / 9%)
Coordinated Tx (<i>n</i> = 53)	33 (34% / 62%)	12 (38% / 23%)	5 (23% / 9%)	3 (16% / 6%)

Note. First percentage reflects rates within latent growth group; second percentage reflects rate within treatment sequence.

Table 2
Comparison of Means and Standard Deviations for Predictor Variables (Continuous) by the Depression Change Clusters

Dependent Measures	Means and SD within each Depression Change Cluster						Unadjusted Statistics		Controlling for CDRS	
	Mildly Depressed Responders		Depressed Non-Responders		Depressed Responders		Depressed with Recurrence		$F(p)$	
									η^2	
Depressive severity (CDRS)	38.92 (8.09) _a		50.05 (8.02) _b		63.09 (8.97) _c		58.05 (10.62) _c		78.09 (.000)	
Automatic Thoughts Questionnaire	1.69 (0.67) _a		2.19 (1.06) _{ab}		2.67 (1.29) _b		2.80 (1.09) _b		13.96 (.000)	
Hopelessness	1.42 (0.68) _a		1.68 (0.78) _{ab}		1.88 (0.79) _{bc}		2.32 (0.82) _c		9.58 (.000)	
Anxiety problems	2.26 (1.98) _a		4.05 (2.77) _b		4.00 (2.95) _b		3.42 (2.99) _{ab}		6.40 (.000)	
Global functioning	56.54 (7.56) _a		50.91 (6.12) _b		48.75 (6.82) _b		50.21 (7.12) _b		12.61 (.000)	
Family conflict	3.82 (2.51) _a		5.76 (2.02) _b		5.03 (2.38) _b		5.11 (2.00) _b		5.47 (.001)	
Family cohesion	5.49 (2.42) _a		3.50 (2.59) _b		4.83 (2.27) _{ab}		4.11 (2.69) _{ab}		4.62 (.004)	
Age	16.46 (1.42)		16.18 (1.74)		16.31 (1.31)		16.32 (1.29)		0.29 (.84)	
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Note. *F*-test degrees of freedom varied from (3, 155) to (3, 166). Cell entries are means (*M*) and standard deviations (*SD*) for the scale values for participants in each cluster. Cells which share a subscript in common are not significantly different based on Bonferroni adjusted confidence levels ($\alpha = .05/6$). Comparisons are to be made only within a row representing a single dependent measure.

Table 3
Comparison of Percentages for Suicidality Variables (Dichotomous) by the Depression Change Clusters

Suicide Related Dependent Measure	Depression Change Cluster				Statistics χ^2 (3)	p
	Mildly Depressed Responders	Depressed Non- Responders	Depressed Responders	Depressed with Recurrence		
Current Ideation	17% ^a	18% ^a	41% ^a	42% ^a	10.64	.014
Past Ideation	26% ^a	65% ^b	39% ^{ab}	63% ^b	16.87	.001
Current Suicidal Actions	0% ^a	0% ^{ab}	9% ^{ab}	21% ^b	21.15	.000
Past Suicidal Actions	6% ^a	25% ^{ab}	16% ^{ab}	37% ^b	15.10	.002

Note. Cell entries are the percent of each cluster that was classified as having either a subthreshold (2) or threshold (3) value on each of the current or past suicide dimensions. The measures are the summary judgements which combine parent and child reports. Cells which share a subscript in common are not significantly different based on Bonferroni adjusted confidence levels. Comparisons are to be made only within a row representing single dependent measure.