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Trajectories of Symptom Change in the Treatment for Adolescents With Depression Study

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Abstract

Objective: Depression is the most prominent mental health disorder among youth and has a profound impact with respect to morbidity and mortality if not addressed. The Treatment for Adolescent Depression Study (TADS) is one of the largest randomized controlled trials that compared the effectiveness of four treatments: cognitive-behavioral therapy (CBT); fluoxetine (FLX); combined cognitive-behavioral and fluoxetine treatment (COMB); and placebo (PBO). However, meaningful heterogeneous treatment courses are masked by these group mean comparisons of treatment impact. The present study sought to characterize the acute phase symptom trajectories of the depressed teens enrolled in TADS and to explore predictors of these trajectories, including TADS treatment condition.

Method: The TADS sample of 439 adolescent participants diagnosed with major depressive disorder was subjected to growth mixture modeling (GMM) to evaluate subgroups of adolescents with unique trajectories of depression symptom change.

Results: Growth mixture modeling revealed three unique classes of adolescents: (1) a high-severity class with early significant improvement; (2) a high-severity class with limited symptom change; and (3) a moderate severity class with late significant improvement. Baseline predictors of class membership included treatment condition, sex, age, stage of change, depression severity, number of comorbid disorders, hopelessness, melancholia, suicidality, and cognitive distortions.

Conclusion: Results of this study may have implications for the selection of which treatment to use for which depressed adolescent.

Keywords

depression; treatment; cognitive-behavioral therapy

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Clinical trial registration information: Treatment for Adolescents With Depression Study (TADS); <https://clinicaltrials.gov/NCT00006286>.

Depression is one of the most prominent mental health disorders affecting adolescents, with a 1-year prevalence of 4% to 5% worldwide.¹ Depression symptoms that emerge during adolescence are likely to recur across the lifetime if not properly addressed, and may lead to increased suicidality and academic and interpersonal concerns.^{2–4} Several clinical trials have produced evidence for psychotherapies in achieving clinically significant improvement in depression symptoms among adolescents. To date, the Treatment for Adolescent Depression Study (TADS) remains one of the largest randomized controlled trials to compare the effectiveness of cognitive-behavioral therapy (CBT), fluoxetine (FLX), combined CBT and FLX treatment (COMB), and placebo (PBO).⁵ Adolescents who met *DSM-IV* criteria for major depressive disorder (N 439) were randomized to one of the four conditions (CBT, FLX, COMB, or PBO) and received 12 weeks of treatment (acute treatment). TADS study results revealed that COMB treatment and FLX alone were the most effective for reducing symptoms of depression.⁵ The response rates (ie, percentage of adolescents characterized as very much or much improved) were 71% for the COMB condition, 60.6% for FLX, 43.2% for CBT, and 38.4% for PBO.⁵

Since the original TADS acute phase outcomes report, numerous publications have emerged that have explored which treatment worked best for whom. Secondary analyses revealed predictors (eg, client age, level of functioning, suicidal ideation, number of comorbid disorders)⁶; moderators (eg, family income, depression severity, trauma);^{6,7} and mediators (eg, readiness to change)⁸ that influenced acute phase treatment outcomes. In general, adolescents who were younger, who had better overall functioning, shorter depressive episodes, fewer comorbidities, minimal melancholic features, less suicidal ideation and hopelessness, and better expectancies for treatment outcome experienced greater reduction in symptoms. Adolescents with higher depression severity benefited equally from COMB or FLX.⁶ Adolescents with a history of sexual abuse benefitted most from COMB, FLX, or PBO.⁷ Finally, adolescents who demonstrated changes in their willingness to take action to address their problems earlier in treatment had better outcomes regardless of treatment received.⁸ Treatment condition also predicted improvements in other domains, including overall functioning, quality of life, and global health. COMB treatment outperformed CBT on all three measures, and FLX was better than both placebo and CBT in improving overall functioning.⁹

Although each subsequent study of the TADS data made a significant contribution to answering the four-decade-old question: “*What* treatment, by *whom*, is most effective for *this* individual with *that* specific problem, and under which set of circumstances,”¹⁰ many of the secondary data analyses to date have used a variable-centered approach, which assumes no appreciable differences in adolescent baseline characteristics or trajectories of change within treatment groups.⁸ An innovative and complementary methodological approach is a person-centered analysis, which assumes that clients receiving treatment come from meaningfully different subpopulations that may be characterized by background variables, and that these subpopulations manifest in different treatment response trajectories.^{11–13}

Identifying subgroups of individuals through person centered approaches may bring new capacity for informing psychotherapeutic and pharmacological treatment in practice. Previous person-centered studies have identified suicidal ideation as an important

determinant of age of onset, duration, and short time to recurrence of major depressive episodes in adolescents. In addition, early age of onset of depression is associated with longer durations of depressive episodes.^{14,15} One secondary analysis of the TADS data did use a person-centered approach (latent profile analysis), identifying five subgroups of adolescents: a depressed only group; an anxious group; an oppositional behavior group; a non-anxious severely disruptive group; and an anxious, severely disruptive group.¹¹

Many of the most impactful randomized controlled trials and large-scale depression data sets have been reanalyzed using person-centered approaches.^{13,16–18} These re-analyses have consistently yielded different results from those obtained through variable-centered analyses. For example, reanalysis of the National Institute of Mental Health Treatment of Depression Collaborative Research Program (TDCRP) comparing CBT, Interpersonal Psychotherapy, Imipramine, and pill placebo¹⁹ identified three subgroups of adults with unique patterns of symptom change: moderate to severe depression with moderate early improvement, moderate to severe depression with rapid early improvement, and mild to moderate depression with moderate early improvement.¹³ Although treatment condition was not a significant predictor of subgroup in the TDCRP data, early symptom change predicted better outcomes later in treatment.¹³

A reanalysis of the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) study revealed three classes of response to SSRI treatment (venlafaxine; SSRI with CBT; or venlafaxine with CBT): rapid, slow, and no remission. Adolescents in the slow and no remission groups were more likely to have higher depression severity, longer depression symptom duration, poorer functioning, and manic symptoms.²⁰ More recently, reanalysis of the adolescent Blues Program study comparing cognitive-behavioral depression prevention treatment, cognitive-behavioral bibliotherapy, or brochure control revealed four trajectories: low and declining, high and declining, high and persistent, and resurging symptoms (declines then increases).¹⁸ Adolescents with high persistent symptoms were more likely to receive the brochure control, whereas adolescents with low declining symptoms were more likely to receive cognitive-behavioral prevention, suggesting that the intervention may have influenced treatment response. Male adolescents were more likely to be in the high persistent symptom group. Adolescents with negative cognitive styles were more likely to be in the high persistent or high declining groups. Motivation to reduce depression symptoms was more prevalent in the high persistent, high declining, and resurging groups of adolescents when compared to the low declining group.¹⁸

Outcomes from these re-analyses demonstrate the added value of a person-centered approach, including identification of subgroups of individuals with differing longitudinal symptom change patterns, and insight into the characteristics (ie, predictors) of individuals with a particular trajectory of symptom change. The TADS provides an unprecedented opportunity to use a person-centered approach to evaluate the impact of adolescent characteristics on trajectories of depression symptom change. The present study addressed the following aims: (1) to characterize the acute phase symptom trajectories of the depressed TADS teens; (2) to explore whether subgroups with unique trajectories could be classified according to treatment condition; and (3) to examine possible predictors of subgroup membership identified from the literature using variable-centered analytic approaches.

METHOD

Design and Treatments

Complete descriptions of the TADS aims, rationale, and design have been published elsewhere.²¹ In brief, TADS was a 13-site comparative outcome study that included 439 participants, aged 12 to 17 years, diagnosed with major depressive disorder per the *DSM-IV*. Adolescent participants were randomly assigned to one of four treatment conditions for an acute phase of treatment (12 weeks): (1) CBT alone; (2) FLX alone; (3) COMB; or (4) PBO. The CBT involved 15 sessions of psychotherapy across the acute phase of treatment focused on depression psychoeducation, cognitive restructuring, and behavioral activation.²² The FLX and PBO treatments involved a pharmacotherapist providing medication psychoeducation and monitoring medication effects and dosages across six 20-to 30-minute medication management sessions.⁵ The COMB treatment included both 15 sessions of CBT and 6 FLX medication management sessions.

Participants

Participants (N = 439) for the current study consisted of those in the intent-to-treat sample of the established TADS dataset. Adolescents had an average age of 14.6 years (SD1.5 years), 45.6% were male, 73.8% were white, 12.5% African American, and 8.9% Hispanic. Adolescent depression was characterized as mild to severe at baseline (mean 60, SD = 10.4) as measured by the Child Depression Rating Scale–Revised (CDRS-R).²³

Measures

Age, Race, Sex, and Socioeconomic Status.—Age was measured in years. Race was categorized as white, African American, Hispanic, or other. Sex was categorized as male or female. Socioeconomic status was measured using two categories of gross family income: income less than \$75,000 or income greater than or equal to \$75,000.

Depression Severity.—The Children's Depression Rating Scale–Revised (CDRS-R)²³ was the primary outcome measure for TADS. It is a clinician rated, 17-item, semi-structured interview that evaluates symptom severity as reported by both the parent and adolescent. The CDRS-R evaluates functioning in school, mood, and interpersonal relationships, with scores ranging from 1 (normal/appropriate for age) to 7 (severe symptomatology). Total scores on the CDRS-R range from 0 to 113, and the measure demonstrated strong inter-rater reliability ($r = 0.86$) and construct validity in the initial validation sample.²⁴ The CDRS-R was administered by an independent evaluator at baseline, week 6, and week 12 of treatment.

Length of Depressive Episode.—The length of the current depressive episode was measured through an independent evaluator interview using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime (K-SADS-PL).²⁵ The TADS evaluators interviewed both adolescents and parents at baseline, and established onset and duration, in weeks, of the most recent major depressive episode.

Number of Comorbid Disorders.—The total number of comorbid disorders was computed at baseline by adding the total number of clinical disorders diagnosed by an independent evaluator on the K-SADS-PL.²⁵

Melancholic Features.—A baseline melancholic features scale was created using five items from the CDRS-R in line with previous TADS study moderator analyses.⁶ This scale consisted of pervasive anhedonia, appetite disturbance, insomnia, excessive guilt, and psychomotor retardation. The insomnia and appetite disturbance scales were measured on a Likert scale from 0 to 5, and were considered “positive” for melancholic features if the reported sleep disturbance was at least a 4 and affected sleep early in the morning and if the appetite disturbance was at least a 4 and was a decrease from typical eating habits. Pervasive anhedonia, excessive guilt, and psychomotor retardation were considered “positive” if the score was a 5. The total “positive” items were then summed to get a total melancholic features score ranging from 0 to 5.⁶

Hopelessness.—Baseline hopelessness was measured using the total score from the Beck Hopelessness Scale (BHS),²⁶ a 20-item measure with true/false questions. Scores on the BHS range from 0 to 20, with each item coded as 0 or 1. Higher scores indicated more severe symptoms of hopelessness. The BHS has strong internal consistency ($\alpha = 0.93$) and construct validity as established in the initial validation sample.

Suicidality.—Baseline suicide risk was assessed using the Suicidal Ideation Questionnaire Jr. High Version,²⁷ an adolescent specific version of the Suicidal Ideation Questionnaire (SIQ) using 15 items ranked on a scale of 0 to 6 based on frequency across the past month, with higher scores indicating greater severity. The SIQ also has strong internal consistency as established in the original measure validation sample ($\alpha = 0.94$).

Cognitive Distortions.—Cognitive distortions were measured at baseline using the total score from the Children’s Negative Cognitive Errors Questionnaire (CNCEQ).²⁸ The CNCEQ is a 24-item measure that includes questions rated on a 1 (“not at all like I would think”) to 5 (“almost exactly like I would think”). Summed total scores ranged from 24 to 120, with higher scores indicating more severe cognitive distortions. The CNCEQ has strong internal consistency established in the original measure validation sample ($\alpha = 0.89$).

Stage of Change.—Baseline stages of change were measured using an 18-item version of the Stages of Change Questionnaire (SOCQ).²⁹ The SOCQ used in TADS assessed four stages of change and summed subscale items measured on a four-point Likert scale. The SOCQ has demonstrated adequate internal consistency across subscales ($\alpha = .75 = 0.87$).

Treatment Expectancy.—Adolescents and parents completed a treatment expectancy form before treatment. This treatment expectancy form included questions rated on a Likert scale (from 1 = very much improved, to 7 very much worse) that asked about adolescents’ and parents’ expectations of improvement in treatment (COMB, FLX, and CBT).

Statistical Methods

Models were developed in two stages: (1) a series of GMM for CDRS-R that differed only in the number of classes were fit to establish a model of CDRS-R trajectories; and (2) the three-step maximum likelihood (ML) approach was used to regress latent trajectory classes, established in the first stage, on independent variables.^{30,31} All models were fit using Mplus 7.3.³² The series of GMMs in the first stage were fit for CDRS-R scores at baseline, week 6, and week 12. The number of classes increased by one in each subsequent model until there was not improvement for a k class GMM over a $k-1$ class GMM. Growth curves were defined by a latent variable representing the intercept (ie, status at baseline), which was regressed on study site, and a time slope, the latter of which was represented by fixing the latent variable parameters for the slope to the natural log of days since baseline. To account for known differences in CDRS-R scores attributable to treatment, class membership was regressed on treatment condition, which was dummy coded using the PBO group as the reference group. The treatment of study site as a covariate and the transformation of time to a natural log of days since baseline is consistent with CDRS-R growth models in prior TADS publications.⁵ All GMMs were fit using ML estimation with robust standard errors, which makes use of all available data and is considered one of the optional techniques for fitting models in the presence of missing data³³ (see Supplement 1, Table S1, and Table S2, available online, for additional details).

In the second stage, class membership in the GMM was regressed on other constructs using the three-step ML approach. The first step of the three-step approach is a latent class model; in the applications presented herein, the first step was always the model developed in the first model-building stage described above. In the second step, the ML-corrected most likely class membership was estimated. In the third step, predictors were added in separate models. Multiple imputation was used in the third step to account for missing predictor data, as missing independent variables result in listwise deletion, unlike missing data for outcomes in the first step, in which all available data are included in ML estimates. Twenty data sets with plausible values for missing data that were imputed using Markov chain Monte Carlo implemented in Mplus 7.3 were generated.³⁴ For each predictor model, each of the twenty data sets was analyzed and parameter estimates and standard errors were aggregated and then used for inferential statistics.³⁵

RESULTS

Among the six models fit in stage 1, the three-class model exhibited the lowest BIC (9274.02). The three-class model exhibited significantly better fit than the two-class model (BLRT = -4563.14, $p < .001$), entropy was 0.77, and the minimal average class probabilities was 0.80. The best-fitting model according to the BIC criterion exhibited reasonable classification accuracy and was used in stage 2 to generate ML-corrected class memberships that were regressed on individual predictors in step 3. Growth curves for each class are presented in Figure 1. Table 1 presents the final estimated class counts and proportions for latent trajectory classes based on posterior probabilities, as well as counts and proportions based on most likely class membership. Class 1, high-severity adolescents with early symptom improvement ("high severity early improvement"), consisted of 9.2% of the

sample. Class 2, high-severity adolescents with limited symptom change (“limited improvement”), consisted of 15.5% of the sample. Finally, class 3, moderate-severity adolescents with significant improvement later in treatment (“later improvement”), represented 75.3% of the sample (Tables 1 and 2).

In the growth mixture portion of the model, each of the three classes exhibited significant decreases in CDRS-R scores across time. There was not variability in intercepts, however, there was variability in slopes, indicating that while the model fixed effects accounted for variability in starting CDRS-R scores, there was significant variability across time (Table 3). CBT adolescents were less likely than PBO adolescents to be in the high severity early improvement class compared to the other two classes. In fact, the extreme z value observed indicates that there are virtually no CBT cases in the high severity—early improvement class. The FLX adolescents were less likely than the PBO adolescents to be in the limited improvement class when compared to the later improvement class. The FLX adolescents were also more likely than the PBO adolescents to be in the high severity—early improvement class compared to the limited improvement class. There were no differences in likelihood of COMB cases across classes of adolescents.

There were no differences among classes for length of depressive episode, stages of change, CBT or COMB treatment expectancy, high SES, or race (Table 4). Adolescents in the high severity early improvement and the limited improvement classes had higher baseline depression severity when compared to the later improvement class ($z = 4.63, p < .001$; $z = 5.49, p < .001$, respectively) (Table 2). The high severity early improvement class also had high numbers of comorbid disorders and higher baseline melancholia when compared to the later improvement class ($z = 2.02, p = .044, z = 5.42, p < .001$, respectively). Baseline melancholia was also higher in the high severity early improvement class when compared to the limited improvement class ($z = 2.89, p = .004$) and higher in the limited improvement class than in the later improvement class ($z = 4.65, p < .001$).

Baseline hopelessness was higher in the high severity—early improvement compared to the later improvement class ($z = 2.10, p = .036$). Hopelessness was also higher in the limited improvement class compared to the later improvement class ($z = 2.93, p = .003$). Higher baseline suicidality was also associated with membership in the high severity early improvement adolescents had higher suicidality than the later improvement ($z = 4.18, p < .001$) and limited improvement adolescents ($z = 2.15, p = .031$). Limited improvement adolescents also had higher suicidality than those with later improvement ($z = 2.46, p = .014$). Limited improvement adolescents also had more severe baseline cognitive distortions compared to later improvement adolescents ($z = 2.11, p = .035$). Older adolescents were more likely to be in the limited improvement class when compared to the later improvement class ($z = 2.69, p = .007$). Finally, females were more likely to be in the high severity early improvement class than in the later improvement class ($z = 2.01, p = .044$).

DISCUSSION

A reanalysis of the TADS data using GMM revealed unique trajectories of depression symptom change. Similar to subgroups identified in TORDIA (rapid remission), the Blues

Program (high and declining group), and TDCRP GMM studies (moderate to severe with rapid early improvement),¹³ the TADS high severity early improvement class demonstrated the most dramatic early symptom change over the acute treatment phase. The high severity—early improvement class consists of a complicated and impaired group of adolescents, many of whom were female, who demonstrated early clinically significant improvement.

The limited improvement class of adolescents had lower baseline depression severity (although still severe) when compared to the high severity—early improvement group; they demonstrated very little symptom change. This group also aligned with a subgroup of adolescents in TORDIA (no remission) and the Blues Study (high severity and persistent)¹⁸; however, this subgroup did not emerge in the adult TDCRP reanalysis. It is possible that limited symptom change is more common among teenagers, perhaps related to capacity to engage in treatment (eg, to complete CBT homework), which was not explored in the present study. The limited improvement adolescents were older and had higher depression severity, melancholia, hopelessness, and suicidal ideation when compared to the late improvers. The older age of these adolescents may indicate a longer course of recurrent depressive episodes across their lifetimes,¹⁵ thereby leading to the development of cognitive distortions³⁶ that may require combined CBT and medication to maximize outcomes.

Adolescents in the later improvement class, the largest class, demonstrated much slower symptom change than the high-severity adolescents. This class aligns with the TOR-DIA slow remission class, the Blues Study low severity and declining symptoms subgroup, and the mild to moderate depression with moderate early improvement TDCRP group, although there is not a direct match due to differences in remission versus improvement (TORDIA versus TADS), sample severity (TADS more severe than Blues Study), and stage of development (TADS adolescents versus TDCRP adults). The later improvement class comprised the largest percentage of adolescents receiving CBT. In contrast to the early improvement and limited improvement classes, these younger adolescents appear to have moderate depression symptoms that may have just emerged (ie, fewer lifetime depressive episodes), providing tentative support for the effectiveness of CBT in treating lower-severity depression.¹ CBT alone may also be effective for less severe, younger male adolescents who may not be as vulnerable to the heightened ruminative coping styles associated with increased depression risk in adolescent girls.^{1,34,37}

The findings presented herein enhance understanding of the trajectories of change that might be expected for adolescents. Interestingly, COMB did not predict trajectories of change, but it did predict rapid decline in suicidality, self-reported depression, and rates of remission in other analyses.^{38,39} One explanation for this finding is that self-reported depression and suicidality are both self-reports; therefore, COMB adolescents who were aware of their treatment condition may have had higher treatment expectancies (an acute-phase outcomes predictor).⁶ It is also striking that COMB did not predict change in severity among the full constellation of depression, but did predict time to remit in prior studies. Although COMB might be expected to predict membership in the high severity early improvement group, this group made clinically significant changes but remained clinically depressed at week 6, whereas the late improvement group came closer to remittance at week 6. Given that these markers (remittance versus severity change) are clinically distinct, we have evidence that

COMB can increase the remission rate of depression, but it may not be the preferred treatment to help those who are severely depressed to achieve a steep decline in symptom severity. FLX may be important to offer in these cases. In addition, a moderate severity—early improvement class did not emerge, perhaps due to challenges in forming therapeutic alliances and/or lower treatment motivation due to less acute symptoms.^{18,40}

In sum, using a person-centered GMM approach complements traditional analytic methods and may do the following: (1) enable early depression prognosis prediction; (2) inform appropriate treatment based on adolescent characteristics; and (3) allow ongoing assessment of progress to inform treatment changes. Findings suggest that CBT may be the most appropriate treatment selection for younger male adolescents. In addition, high-severity depressed adolescents may demonstrate rapid improvement in symptoms and benefit most from fluoxetine early in treatment, potentially followed by adjunct treatment (eg, CBT).

This study has several limitations. First, the GMM approach used TADS acute phase data; therefore, findings do not allow evaluation of long-term trajectories of change. Future research should explore trajectories of change across the full 36 weeks of active treatment to determine whether the trajectories identified are maintained across time.²¹ Second, the analyses collapsed all treatment conditions because of limited sample size, thereby preventing identification of trajectories of change within each treatment condition (eg, COMB treatment alone). Third, the current study focused solely on baseline predictors. Additional research is needed to identify time-varying symptom-change predictors. Fourth, the predictors of symptom trajectories explored in this study were not exhaustive; therefore, more work is needed to explore additional predictors of which treatment approaches work best for which adolescents. Fifth, the approach taken to explore predictors in this study does not allow conclusions regarding the incremental predictive utility of the variables explored. Additional work is needed to use the three-step approach to explore multiple predictors in each model to identify variables that emerge as most predictive of symptom trajectories within each class. Sixth, we did not adjust *p* values for multiple comparisons, although we did report the impact of adjustments in Table 4. We acknowledge that 5% of hypothesis tests with a 95% CI will reflect Type 1 errors; by accepting this error rate, it is not necessary to correct for multiple tests.⁴¹

Finally, the model presented here enhances understanding of depression trajectories but should not be construed as a true finite mixture in the population. Because the data were collected in a treatment setting, the trajectories may have different characteristics in an unperturbed setting. Further-more, latent groups are subject to modeling decisions based on multiple criteria that are not always in agreement; in fact, a similar analysis of the TADS data resulted in a four-class model. As such, the model herein should be viewed as a heuristic that characterizes common underlying adolescent depression trajectories.

This study revealed three different trajectories of symptom change among depressed adolescents enrolled in TADS, each with unique profiles. The study findings serve as a preliminary exploration of which interventions work best for whom and when in treatment to begin applying them. Given the high prevalence of depression in adolescent populations and the potential for recurrence of symptoms across the lifetime, identification of optimal

treatments and prediction of treatment response may have a powerful impact on prevention and intervention for high-risk adolescents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The research presented herein was deemed exempt by the Indiana University Institutional Review Board (protocol #1401404427) due to being research involving existing data from a de-identified, publicly available National Institutes of Health (NIH) Database.

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FIGURE 1. Fitted Child Depression Rating Scale–Revised (CDRS-R) Values for Each Growth Mixture Modeling (GMM) Class

Note: HE = high severity–early improvement class; LATE = later symptom improvement class; LIM = limited symptom improvement class.

TABLE 1

Class Counts and Proportions Based on Posterior Probability and Most Likely Membership

Latent Trajectory Class	Posterior Probability Membership		Most Likely Membership	
	Count	Proportion	Count	Proportion
1. HE	40.42	0.098	40	0.091
2. LIM	68.01	0.155	57	0.130
3. LATE	330.56	0.753	342	0.780

Note: HE = high severity early improvement class; LATE later symptom improvement class; LIM limited symptom improvement class.

TABLE 2

Descriptive Statistics for Baseline, Week 6, and Week 12 Child Depression Rating Scale–Revised (CDRS-R) Scores by Class

Latent Trajectory Class	Baseline CDRS-R		Week 6 CDRS-R		Week 12 CDRS-R	
	Mean (SD)		Mean (SD)		Mean (SD)	
1. HE	79.60 (7.39)		44.46 (12.75)		35.24 (12.53)	
2. LIM	70.98 (5.67)		58.42 (9.89)		56.59 (11.25)	
3. LATE	56.01 (6.77)		39.07 (10.20)		35.52 (11.33)	

Note: HE = high severity early improvement class; LATE = later symptom improvement class; LIM = limited symptom improvement class.

TABLE 3

Parameter Estimates for the Latent Trajectory Class Model

Growth Mixture Model							
Fixed effects							
	Latent Class	Parameter	Coefficient	SE	z	p	
	1. HE	Intercept	80.03	4.29	18.64	<.001	
		Time	-9.46	0.76	-12.45	<.001	
	2. LIM	Intercept	70.76	2.47	28.65	<.001	
		Time	-3.53	0.61	-5.81	<.001	
	3. LATE	Intercept	58.17	2.16	26.94	<.001	
		Time	-4.67	0.30	-15.44	<.001	
Random effects							
Latent Trajectory Classes as Multinomial Outcome							
	Class Contrast	Parameter	Coefficient	SE	z	p	
	HE vs. LATE	Intercept	-2.21	0.51	-4.35	<.001	
		CBT	-19.27	0.00	-3864.79	<.001	
		COMB	0.71	0.62	1.14	.254	
	LIM vs. LATE	FLX	0.29	0.65	0.44	.657	
		Intercept	-0.97	0.54	-1.78	.075	
		CBT	-0.02	0.48	-0.05	.958	
	HE vs. LIM	COMB	-2.29	1.48	-1.55	.122	
		FLX	-1.70	0.72	-2.37	.018	
		Intercept	-1.24	0.73	-1.70	.089	
		CBT	-19.22	0.48	-39.78	<.001	
		COMB	3.003	1.68	1.79	.073	
		FLX	1.985	1.00	1.99	.047	

Note: CBT = cognitive-behavioral therapy; COMB = combined cognitive-behavioral therapy and fluoxetine treatment; FLX = fluoxetine; HE = high severity-early improvement class; LATE = later symptom improvement class; LIM = limited symptom improvement class; SE = standard error.

TABLE 4

Predictors of Growth Mixture Model Class Membership in Three-Step Models

Predictors	Class Contrast	Coefficient	SE	z	p
Length of depressive episode	HE vs. LATE	0.001	0.002	0.52	.602
	LIM vs. LATE	0.002	0.002	1.06	.291
Depression severity	HE vs. LIM	-0.001	0.003	-0.34	.733
	HE vs. LATE	3.873	0.837	4.63	<.001
	LIM vs. LATE	2.852	0.520	5.49	<.001
Number of comorbid disorders	HE vs. LIM	1.021	0.630	1.62	.105
	HE vs. LATE	0.379	0.188	2.02	.044
	LIM vs. LATE	0.190	0.148	1.28	.201
Melancholia	HE vs. LIM	0.189	0.218	0.87	.385
	HE vs. LATE	2.475	0.456	5.42	<.001
	LIM vs. LATE	1.384	0.298	4.65	<.001
Stages of change	HE vs. LIM	1.092	0.378	2.89	.004
	HE vs. LATE	-0.014	0.059	-0.23	.818
	LIM vs. LATE	0.000	0.052	0.00	.998
Hopelessness	HE vs. LIM	-0.014	0.082	-0.16	.869
	HE vs. LATE	0.083	0.039	2.10	.036
	LIM vs. LATE	0.148	0.051	2.93	.003
Suicidality	HE vs. LIM	-0.065	0.063	-1.04	.300
	HE vs. LATE	0.049	0.012	4.18	<.001
	LIM vs. LATE	0.021	0.008	2.46	.014
CBT treatment expectancy	HE vs. LIM	0.028	0.013	2.15	.031
	HE vs. LATE	0.124	0.212	0.58	.56
	LIM vs. LATE	0.074	0.212	0.35	.725
COMB treatment expectancy	HE vs. LIM	0.049	0.282	0.17	.862
	HE vs. LATE	-0.068	0.198	-0.34	.731
	LIM vs. LATE	0.132	0.171	0.77	.442
Cognitive distortions	HE vs. LIM	-0.200	0.242	-0.83	.408
	HE vs. LATE	0.017	0.012	1.38	.167

Predictors	Class Contrast	Coefficient	SE	z	p
High socioeconomic status	LIM vs. LATE	0.024	0.011	2.11	.035
	HE vs. LIM	-0.007	0.017	-0.40	.688
	HE vs. LATE	0.297	0.462	0.64	.519
	LIM vs. LATE	-1.074	0.682	-1.57	.115
Age	HE vs. LIM	1.371	0.814	1.69	.092
	HE vs. LATE	0.089	0.157	0.57	.570
	LIM vs. LATE	0.431	0.160	2.69	.007
	HE vs. LIM	-0.342	0.224	-1.53	.127
Sex					
Female	HE vs. LATE	0.995	0.494	2.01	.044
	LIM vs. LATE	0.397	0.390	1.02	.308
	HE vs. LIM	0.598	0.621	0.96	.335
Race					
African American	HE vs. LATE	-0.408	0.731	-0.56	.577
	LIM vs. LATE	-0.256	0.642	-0.40	.690
	HE vs. LIM	-0.152	0.965	-0.16	.875
Hispanic	HE vs. LATE	-0.309	0.836	-0.37	.712
	LIM vs. LATE	-0.001	0.679	0.00	.998
	HE vs. LIM	-0.307	1.059	-0.29	.772
Other	HE vs. LATE	0.161	1.054	0.15	.878
	LIM vs. LATE	1.016	0.707	1.44	.151
	HE vs. LIM	-0.855	1.181	-0.72	.469

Note: Boldface p values reflect statistically significant predictors of latent class membership ($p < .05$). We evaluated the familywise error rate among depression severity, melancholia, hopelessness, and suicidality using a Benjamini and Yekutieli correction within each contrast (eg, high severity_early improvement class [HE] vs. later symptom improvement class [LATE]). All reported p values remained significant except for the HE vs. LATE contrast for hopelessness ($p = .075$) and the HE vs. limited symptom improvement class [LIM] contrast for suicidality ($p = .129$). CBT = cognitive-behavioral therapy; COMB = combined cognitive-behavioral therapy and fluoxetine treatment; FLX = fluoxetine; SE = standard error.