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Sequential treatment with fluoxetine and relapse prevention CBT to improve outcomes in pediatric depression

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Introduction

Advances in the treatment of pediatric major depressive disorder have demonstrated effective acute phase treatments, including antidepressant medication (1, 2), psychotherapy (3, 4) and their combination (5, 6)). Despite these gains, 40%–70% of youth will experience a relapse/recurrence of depression (7–9). Most treatment studies focus on acute phase outcomes, and those studies which report long-term outcomes generally continue the acute phase treatments into long-term care. Few studies have included specific sequential continuation treatment strategies developed to improve long-term outcomes.

Acute treatment strategies are designed to achieve symptom response (significant reduction in depressive symptoms) and ultimately remission (minimal to no symptoms). Remission rates, however, have been low. Even with combination fluoxetine plus CBT in the Treatment for Adolescent Depression Study (TADS), only 37% remitted after 12 weeks of treatment (10). Residual symptoms after acute treatment are common and associated with poorer longer term outcomes in youth (10, 11).

Continuation treatment, on the other hand, follows acute treatment with the goals of targeting residual symptoms and preventing relapse. Over the past several years, sequential treatment models have been examined, typically beginning with pharmacotherapy for acute treatment, followed by another treatment modality to address residual symptoms once response is achieved (12, 13). A meta-analysis of psychotherapy delivered after

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pharmacotherapy suggests that sequencing these two treatment modalities may be an optimal strategy for preventing relapse (13).

Research on continuation treatment in youth with major depressive disorder is limited. Continuing antidepressants for 6–9 months reduces relapse rates; however, approximately 34%–40% of these youth will relapse even while continuing on medication (7, 14). Only 3 continuation studies of CBT in youth have been reported to date, with mixed results (15–17). In a pilot study of 46 adolescents conducted by the authors, a sequential treatment strategy using 12 weeks of fluoxetine to achieve response, followed by a specific Relapse Prevention Cognitive Behavioral Therapy (RP-CBT) delivered over 6 months, resulted in a lower risk of relapse in those receiving continuation medication and RP-CBT compared to those remaining on medication alone (17). This study led to a larger randomized controlled trial (reported here) to evaluate the efficacy of a continuation phase RP-CBT in reducing relapse rates. The current study aims were expanded to include not only relapse prevention, but also shorter time to remission.

Methods

We present on an NIMH-funded single-site, randomized continuation trial, which is the largest study examining continuation treatments for depressed youth. The study was approved by the University of Texas Southwestern Medical Center Institutional Review Board. All participants and their parents provided written consent and assent after the purpose, procedures, risks and benefits, and the rights of study subjects were explained, and all questions were answered.

Study Participants

Participants were outpatients (aged 8–17 years) in a general pediatric psychiatry outpatient clinic. Participants had a primary diagnosis of major depressive disorder for at least 4 weeks, a Children's Depression Rating Scale-Revised (CDRS-R) (18) score of ≥ 40 , and a Clinical Global Impression (CGI-S) (19) severity score of ≥ 4 . While MDD was the primary diagnosis, other concurrent disorders were allowed. Table 1 provides inclusion/exclusion criteria.

Diagnostic evaluation

Trained masters level independent evaluators interviewed participants and parents, using the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL) (20) to determine inclusion diagnostic criteria. Evaluators also obtained suicide and family history using the Columbia Suicide History form and the Family History Screen. The CDRS-R, CGI-S, and Suicide Severity Rating Scale - Short were also obtained.

Information regarding the course of illness and depression severity were obtained by a child psychiatrist one week later through a review of the K-SADS-PL, and interview of the participant and parents using the CDRS-R, the CGI-S, and the Suicide Severity Rating Scale-Short. Weekly meetings were held to review each participant for eligibility and appropriateness for the study.

Acute Treatment

Following assessment, eligible participants began 6 weeks of fluoxetine. The decision to limit the acute phase to 6 weeks was based on prior trial experiences, which suggested shortening time to remission leads to better long-term outcomes. Participants received an initial dose of 10mg/day of fluoxetine at the baseline visit, increasing to 20mg/day at week 1, unless side effects prevented titration. Dosage could be increased (based on clinical judgment) to 30–40mg after 4 weeks or reduced to 10mg/day if necessary.

Medication management visits were conducted weekly by a child psychiatrist during acute treatment (weeks 0–6), and included assessment of symptoms and adverse events. Standard clinical management was provided, which followed the medication management manual from TADS (21) and included supportive care, but no specific psychotherapy. Participants who were non-adherent to medication (<70% of pills on two consecutive visits based on pill count), and those who required additional treatment were discontinued.

Randomization

After 6 weeks of fluoxetine, independent evaluators reassessed participants for response. Non-responders were discontinued and given appropriate referrals. Responders (≥ 50% decrease in the CDRS-R total score) were eligible for randomization.^a Patients were stratified based on age (≤ 11 years; > 12 years) and remission status (CDRS-R ≤ 28; > 28), and randomized (1:1 ratio) to continue fluoxetine only (Medication Management) or fluoxetine plus Relapse Prevention CBT (Medication Management+CBT).

Continuation Treatment

Medication Management—All randomized patients (Medication Management and Medication Management+CBT) continued to receive fluoxetine for 6 months. Medication visit schedules for both groups were every other week for 3 months, and then monthly for the remainder of continuation (weeks 20, 24 and 30). Visits were 30–45 minutes, and consisted of assessment of symptoms and safety. Dosage was flexible during this phase and based on clinical need. Patients needing additional interventions were discontinued from study treatment, but continued with assessments.

RP-CBT—Patients randomized to Medication Management+CBT began CBT sessions at week 7. A total of 8 to 11 sessions of CBT were planned. CBT visits were weekly for the first month, every other week for 2 months, and 4 to 6 weeks for the last 3 months; however, number and frequency of sessions were individualized based on patient need. Sessions were typically 1 hour, with 1.5 hours for the first two sessions, which included a family component. Therapists were masters level and above with experience in manualized CBT.

^aNOTE: The study originally allowed youth with ≥ 30% reduction in CDRS-R to be randomized; however, the protocol was revised after approximately 1 year because patients with such minimal response were found to need additional interventions. A total of 9 patients were randomized with between 30%–50% reduction in CDRS-R. Separate Cox regression models for time-to-relapse and time-to-remission, similar to that used for the 30-week continuation treatment period, were replicated with these 9 partial responders excluded and revealed that our basic survival findings persisted (with no meaningful change). In other words, during the 30-week continuation treatment period with these 9 partial responders excluded, the hazard of relapse and the hazard of remission for those who received Medication Management+CBT treatment was 0.298 (95% CI=0.124 to 0.721; $\chi^2=7.15$, $p=.007$) and 1.241 (95% CI=0.851 to 1.812; $\chi^2=1.23$, $p=.264$) times that of those who received Medication Management treatment alone, respectively.

Therapy sessions were audiotaped, with a sample of sessions reviewed by the CBT supervisors (BDK, JMJ). Therapists also met weekly for supervision. Therapists and psychiatrists collaborated and communicated about the patient's care.

The goals of RP-CBT include: reducing residual symptoms, increasing periods of psychological well-being, and preventing relapse. RP-CBT was developed as a brief, individual treatment with a family component (average of three sessions with the adolescent and parent(s)) (17). The treatment format is modular and designed to be tailored to the specific needs of the child. Additionally, the treatment addresses risk factors for relapse (negative attributional style, family conflict and expressed emotion) and adds elements from well-being therapy (adapted from Ryff and Singer (22) found to be effective in reducing relapse (23) and promoting wellness. RP-CBT treatment components are available in Table 2.

Outcome Measures

Outcomes were based on blinded independent evaluator assessments at week 6 (randomization) and every 6 weeks during continuation treatment (6, 12, 18, 24, and 30), and included measures of symptoms and functioning (CDRS-R, Suicide Severity Rating Scale-Short, CGI) and course of illness using the Adolescent-Longitudinal Interval Follow-Up Evaluation (A-LIFE) (24). Patients continued with IE assessments even if they discontinued study treatments.

The primary outcomes for the study were time to remission and rate of relapse. Remission was defined as CDRS-R ≤ 18 , with timing of remission determined through clinical interview and A-LIFE. Relapse was defined as a CDRS-R ≥ 40 for at least 2 weeks or a CDRS-R ≥ 40 , but with significant clinical deterioration that would suggest full relapse if the patient's treatment was not altered (25). Only youth who had achieved remission (at any point in the study) were assessed for relapse (i.e. cannot relapse if not remitted). Time to relapse was also measured.

"Time spent well in the study" was measured via the A-LIFE. The A-LIFE (adapted from the Longitudinal Interval Follow-up Evaluation (24)) is a psychiatric diagnostic interview for use in longitudinal studies. Generally, the A-LIFE is used at 6 month intervals to show status change of psychiatric disorders; however, the independent evaluators completed the ratings at each assessment. Time spent well was defined as each week that the youth was rated as a 1 or 2 (no or minimal disorder) on the A-LIFE, and was operationalized as the number of weeks of a rating of 1 or 2 divided by the total number of weeks in the study.

Safety

Adverse events were assessed by the psychiatrist at each visit. Adverse events were defined as any emergent or worsening untoward event requiring intervention. Serious adverse events were defined according to FDA criteria.

Statistical Analysis

Demographic and clinical characteristics were compared between the MM+CBT and MM treatment groups using an independent sample t-test (continuous outcomes) and a Chi-Square or Fisher's exact test (categorical outcomes).

A Cox Proportional Hazards Regression—with adjustment for CDRS-R total score, age (child vs. adolescent), and gender—was used to compare time-to-remission and, in a separate model, time-to-relapse between participants in the two treatment groups. Hazard ratios were also estimated and interpreted as the effect size estimator for our Cox Regression. As part of the survival analysis, right censoring was used and occurred when incomplete information was available about the survival time of a given participant; the information was incomplete because the participant did not have an event during study. Censoring (or a censored observation) meant a participant who dropped out or completed the study without remitting/relapsing. We also estimated the probability of remitting/relapsing as well as the rates of remission/relapse at each week across the 30-week continuation treatment trial.

A Poisson regression—with adjustment for CDRS-R total score, age (child vs. adolescent), and gender—was used to compare the log “time well” rates, or incidence of time spent well in the study, between the two groups. Maximum likelihood estimation and Type 3 tests of fixed effects were used with the Wald Chi-Square statistic. The Poisson model also accounted for overdispersion by adjusting the standard errors and test statistics appropriately using the Pearson scaling/dispersion parameter.

Statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Inc., Cary, NC) as well as MedCalc for Windows, version 12.7.5 (MedCalc Software, Ostend, Belgium). All analyses were intent-to-treat. The level of significance for all tests was set at $\alpha=.05$ (two-tailed) and to address multiple testing (multiplicity), where applicable, p -values were adjusted using the False Discovery Rate procedure. Hedges' g was also calculated to estimate effect sizes for between-group comparisons. The magnitude of Hedges' g can be interpreted using Cohen's (1988) convention as “small effect (0.20),” “medium effect (0.50),” and “large effect (0.80),” with the caveat that this conventional frame of reference (or *rules of thumb* regarding the size of the effect) is relative not only to each other but also to its substantive context, its operational definition, or even more particularly to the specific content and research method being employed in any given investigation (26).

Results

Participant Characteristics

A sample of 200 youth (54.5% female and 52% minorities) entered acute treatment (Figure 1). The mean age was 13.8 years ($SD=2.6$), with 79% being adolescent (≥ 12 years). Baseline CDRS-R score was 58.3 ($SD=7.7$).

Of the 200, 144 were responders and randomized to Medication Management ($n=69$) or Medication Management+CBT ($n=75$) for 6 months. There were no differences on baseline

demographic and clinical characteristics between those who were randomized (n=144) and those who were not (n=56).

The randomized sample characteristics are shown in Table 3. The two groups did not differ on baseline demographic and clinical characteristics.

Attrition

Of the 144 randomized youth, 114 (79.2%) remained in the study assessments for all 30 weeks, with similar rates for Medication Management+CBT and Medication Management only (82.7% vs. 75.4%). The overall rate of treatment completion (defined as remaining in the assigned treatment condition up to week 30) was 66% (95/144), with a slightly higher (but non-significant) treatment completion rate for the Medication Management+CBT group than for the Medication Management only group (70.7% vs. 60.9%; $p=.22$). The overall mean treatment exit week was similar between the two groups (26.3 ± 6.7 vs. 25.2 ± 7.1 ; $p=.36$).

Treatment dosage

Number of Medication Management visits ranged from 6–16, with similar visit frequency between Medication Management+CBT and Medication Management only (13.2 ± 2.6 vs. 13.3 ± 2.4 ; $p=.89$). Medication Management+CBT participants received an average of 9.8 ± 4.0 CBT sessions (range=0–20).

Medication dosage at randomization was similar for Medication Management+CBT and Medication Management only (26.7 ± 7.9 vs. 28.5 ± 7.8 ; $t=-1.4$, $p=.25$). Fluoxetine dose following randomization was based on highest dose received. The mean maximum fluoxetine dose received across all randomized youth was $32.5\text{mg}\pm8.5$, with the Medication Management group receiving a significantly higher maximum dose ($34.2\text{mg}\pm8.3$) compared to the Medication Management+CBT group ($30.9\text{mg}\pm8.4$; $p=.02$).

Hazard of Remission

After adjustment for CDRS-R total score at baseline, age, and gender, the Cox Regression revealed that participants in the Medication Management+CBT group did not differ significantly on time-to-remission from those in the Medication Management only group during continuation treatment (hazard ratio=1.261, 95% CI=0.873 to 1.822; $\chi^2=1.51$, $p=.218$).

Mean time-to-remission for the Medication Management+CBT group was 11.33 weeks (SE=0.95) compared with 13.67 weeks (SE=1.17) for the Medication Management only group. A log rank test showed that the mean time-to-remission between the two treatment groups was not significant ($p=.133$), $g=0.251$. Figure 2 displays the survival curves, plotted at the mean of all covariates in the model. At weeks 12, 18, 24, and 30, the estimated probability of remitting with Medication Management+CBT was about 68%, 79%, 86%, and 90%, respectively, compared with about 59%, 71%, 80%, and 84% respectively with Medication Management. No significant treatment group effects emerged on remission rates at any individual week (raw p 's>0.343, False Discovery Rate-adjusted p 's>.461).

Hazard of Relapse

Relapse was assessed in participants who achieved remission at any time during the study (n=115). After adjustment for CDRS-R total score at randomization, age, and gender, the Cox Regression revealed that participants in the Medication Management+CBT group had a significantly lower risk of relapse than those in the Medication Management group during the 30-week continuation treatment (hazard ratio=0.313, 95% CI=0.130 to 0.753; $\chi^2=6.64$, $p=.010$). Thus, the hazard of relapse for those who received Medication Management+CBT was 0.313 times that of those who received Medication Management alone.

Figure 3 displays survival curves, plotted at the mean of all covariates in the model, and indicate that the survival probability of relapsing was greater at all time periods for Medication Management compared to Medication Management+CBT. At weeks 12, 18, 24, and 30, the estimated probability of relapse for the Medication Management+CBT group was about 1%, 3.5%, 7%, and 9%, respectively, compared with about 3%, 10%, 20.5%, and 26.5%, respectively, for the Medication Management group. Moreover, the two treatment groups differed significantly on relapse rates at week 24 (raw $p=.028$, False Discovery Rate-adjusted $p=.049$) and week 30 (raw $p=.011$, False Discovery Rate-adjusted $p=.043$), but not at week 12 (raw $p=.792$, False Discovery Rate-adjusted $p=.792$) and week 18 ($p=.217$, False Discovery Rate-adjusted $p=.291$).

During continuation treatment, the mean time-to-relapse for Medication Management+CBT was 28.77 weeks (SE=0.48) compared with 27.13 weeks (SE=0.68) for Medication Management only (log rank test: $p=.009$, $g=0.439$). While all analyses were not replicated to examine full relapse (CDRS-R 40) versus clinical deterioration, it is important to note that 9/17 (52.9%) of the Medication Management+CBT relapsers experienced full relapse, and 15/28 (53.6%) of the Medication Management only relapsers experienced full relapse.

Time Well

The incidence of time spent well was evaluated using a Poisson regression, with adjustment for CDRS-R total score at randomization, age, and gender. Analyses revealed that participants in the Medication Management+CBT group had a significantly higher estimated rate of “time spent well” than those in the Medication Management group (55.9% vs. 46.2%, $\chi^2=5.48$, $p=.02$, $g=0.395$). The Medication Management+CBT group spent 16.0 ± 9.1 weeks well versus 12.8 ± 9.5 weeks well with Medication Management ($p=.041$, $g=0.342$).

Safety outcomes

Adverse events leading to treatment discontinuation occurred equally between the two groups: 2.7% (2/75) in Medication Management+CBT vs. 4.3% (3/69) in Medication management only ($p=.58$). Adverse events relative to hypomania occurred only during acute treatment, with 2 patients discontinuing due to hypomania ($n = 1$) or agitation ($n= 1$). This rate (2%) is similar to the rate seen in the two RCT's of fluoxetine, in which 3.1% of fluoxetine patients had mania, hypomania, or agitation (1).

Sixteen participants experienced a total of 18 serious adverse events during continuation phase treatment. Seven events occurred in the Medication Management group (one

hospitalization for a suicide attempt, three for suicidal ideation, one for agitation, and two for medical conditions). Eleven events occurred in 9 patients in the Medication Management +CBT group (five hospitalizations for suicidal ideation, one suicidal behavior that did not result in hospitalization, and five hospitalizations for pre-existing medical conditions). These events were reported to the IRB and the Data Safety Monitoring Board (DSMB).

Discussion

This is the first randomized controlled trial of a sequential treatment strategy to prevent relapse in youth with major depressive disorder. This study demonstrates that, similar to the adult literature (13), sequencing treatments can reduce risk of relapse and lengthen time to relapse in depressed youth. Adding CBT as part of a sequential treatment strategy after response to antidepressant medication, as opposed to continuation treatment with pharmacotherapy alone, significantly reduced the hazard of relapse and lengthened time to relapse in this trial.

While the treatment was developed to prevent relapse, we did anticipate that it may also shorten time to remission, and therefore included this as a primary outcome. Our results did not support this hypothesis. Nonetheless, it is worth noting that those who received Medication Management+CBT reached remission about 2.5 weeks earlier than those who were on medication only. While not statistically significant, in the life of a child, two and a half weeks has potential clinical relevance.

An unexpected, but important finding is differences in fluoxetine dosing. Youth who received CBT had lower dosages of medication, and yet had better outcomes than those on higher doses in the Medication Management group. The difference in dosage, while statistically significant, may not be clinically significant; yet it suggests that differences in outcomes were not attributed to higher dosing in one group over the other.

The optimal timing of adding CBT is still not well understood. The NICE guidelines indicate that youth with depression should be treated with CBT as a first line treatment; however, acute phase CBT, at least in more severely depressed populations, does not compare as favorably to antidepressant medication or combination treatments (5, 27). In TADS, remission rates to CBT were not comparable to medication until 18 to 24 weeks into treatment (11). This study does not examine the effectiveness of antidepressant medication compared to CBT; rather it assesses whether adding CBT following initial improvement with an antidepressant will lead to greater improvement and prevent relapse. As such, this study demonstrates that CBT can be effective as a continuation strategy. While not tested in this study, it will be important in the future to determine the optimal timing of the onset of adding CBT in continuation treatment. Furthermore, whether a different treatment modality could be used for the acute phase is worthy of future examination.

We acknowledge that this study has some limitations. The time period for the study's primary outcomes was 30 weeks (reported here). Follow-up data were collected at weeks 52 and 78, and will be included in a subsequent report. Truncating the study outcomes at 30 weeks may have limited our ability to find significance on remission outcomes. The TADS

study demonstrated remission rates increase over time across groups (11). In addition, while relapse rates were statistically and clinically significant (a relapse rate of 9% in the Medication Management+CBT group vs. almost 27% in the Medication Management group), only an average of 1.6 weeks separated Medication Management+CBT and Medication Management on *time-to-relapse*.

Another limitation was that participants were not blinded to treatment assignment. There is a difference in clinical contact time between the two groups. We made every effort to limit additional clinic visits for the CBT condition, and in the treatment protocol we only scheduled two additional visits to the clinic for these patients to reduce subject burden; thus, all other CBT visits occurred in conjunction with Medication Management visits. As stated earlier, the number of medication visits was similar between the two groups. While we could have added a “sham” therapy to control for contact time, we wanted the current study to be ecologically valid and to mirror real-world practice. We also note here that results (not reported) from separate intercept-only frailty models (random effects survival models), with therapist included as a random effect, suggest that therapists do not introduce any significant concomitant variability concerning the interpretation of our basic findings.

Sequencing effective monotherapies improves outcomes in youth with depression, and may be a means of optimizing both medication and CBT treatment effects. This strategy is efficient, in that it reduces the traditional number of CBT sessions required for positive outcomes (12–16 sessions) (3), and thus reduces the burden of time and cost. Furthermore, we hypothesize, although not yet empirically validated, that a child who has had a positive response to medication is more fully able to participate in the CBT, and may be more likely to assimilate the skills and complete the practice between sessions. One might question whether the acute treatment must be medication treatment. Would results be similar if the acute treatment was CBT, followed by a continuation medication treatment? However, in adults with major depressive disorder, such sequencing (medication following acute cognitive therapy) did not result in decreased relapse rates compared to those who had continuation CBT only (28). In addition, the CBT in this trial emphasized reducing residual symptoms, preventing relapse, and promoting wellness. Similar to adult studies (29), continuation strategies focused on well-being may protect against relapse in depression.

Continuation phase strategies designed to reduce the high rates of relapse in depressed youth have important public health impact. In youth with depression, recurrence of depression is more likely when multiple episodes are present (9, 27). It is important that we move beyond the acute goal of getting children well to the enduring goal for this population of promoting and maintaining wellness.

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Figure 1.

Consort diagram

NOTE: Reason for discontinuing study assessments and reason for discontinuing treatment may have been different for an individual patient due to timing (i.e. one could discontinue treatment early in the study due to needing additional treatment, but later discontinue assessments due to withdrawing consent).

Figure 2.
Remission Survival Curve at Week 30
Note. Survival Probability on y-axis= Probability of not Remitting

Figure 3.

Relapse Survival Curve at Week 30

Note. Survival Probability on y-axis= Probability of not Relapsing

Table 1

Inclusion and Exclusion Criteria.

INCLUSION	EXCLUSION
Outpatients 7–18 years of age.	Lifetime psychotic disorder (including psychotic depression), bipolar I or II, anorexia nervosa or bulimia.
Primary diagnosis of non-psychotic Major Depressive Disorder for at least 4 weeks (CDRS-R 40 and CGI-Severity 4 at baseline).	Alcohol or substance abuse or dependence within the past 6 months.
Good general medical health.	Concurrent medical condition that will interfere with the conduct of the study or endanger the patient.
Of normal intelligence. ¹	Pregnant or lactating females, sexually active females not using adequate contraception. ³
English speaking (both subject and parent). ²	Concurrent medications with psychotropic effects. ⁴
	1 st degree relatives with bipolar I disorder
	Severe suicidal ideation requiring more intensive treatment (i.e. inpatient hospitalization).
	Previous failure of an adequate trial (4 weeks of at least 40mg) or intolerance to fluoxetine.

Table 2

Description of RP-CBT Treatment

Treatment Stage	Stage Objectives	Session	Session Content
Stage 1 (4 wkly sessions)	<ul style="list-style-type: none"> Reduce residual symptoms through core skills Assess and identify core beliefs Identify and increase areas of strength and wellness 	1	<ul style="list-style-type: none"> Psychoeducation (child and family) Begin timeline (case conceptualization) Mood monitoring
		2	<ul style="list-style-type: none"> Psychoeducation Behavioral coping skills (behavioral activation) Family module on negative emotion
		3	<ul style="list-style-type: none"> Cognitive restructuring Core beliefs and positive self-schema
		4	<ul style="list-style-type: none"> Problem solving Begin wellness assessment Family communication skills
Stage 2 (4 sessions over 8 wks)	<ul style="list-style-type: none"> Consolidation and further practice of core skills and wellness skills to manage mood Relapse prevention 	5–7	<ul style="list-style-type: none"> Introduce concept of wellness^{**} Practice and application of core and wellness skills for relapse prevention Family wellness session
		8	<ul style="list-style-type: none"> Relapse Prevention and Wellness Plan
Stage 3 (3 monthly sessions)	<ul style="list-style-type: none"> Consolidation of treatment gains Evaluate and revise the relapse prevention and wellness plans as needed 	9–11	<ul style="list-style-type: none"> Content varies depending on patient's needs

^{**} Six general areas of wellness: self-acceptance, social, success, self-goals, spiritual, and soothing. Using a wellness log designed for RP-CBT, the therapist assessed for existing strengths and areas of improvement. The wellness aspect of the treatment resulted in the development of an individualized wellness plan for a given patient

Table 3

Randomized Sample Demographic and Clinical Characteristics

Variables	All Randomized (N=144)				Treatment Group			
Categorical	N	%	N	%	Medication Management + CBT (N=75)	%	Medication Management Only (N=69)	%
Age								
11 years	31	21.5	19	25.3	12	17.4		
12 years	113	78.5	56	74.7	57	82.6		
Female	77	53.5	38	50.7	39	56.5		
Ethnicity								
Hispanic	43	29.9	23	30.7	20	29.0		
Non-Hispanic	101	70.1	52	69.3	49	71.0		
Race								
Caucasian	118	81.9	64	85.3	54	78.3		
African American	15	10.4	8	10.7	7	10.1		
Asian	1	0.7	1	1.3	0	0		
American Indian	1	0.7	0	0	1	1.5		
Multiracial	9	6.3	2	2.7	7	10.1		
Number of Episodes								
1	127	88.2	68	90.7	59	85.5		
2	25	10.4	7	9.3	8	11.5		
3	1	0.7	0	0	1	1.5		
4	1	0.7	0	0	1	1.5		
Attained Remission by Week 6	54	37.5	29	38.7	25	36.2		
Baseline CGI Severity								
4	25	17.4	16	21.3	9	13.0		
5	69	47.9	38	50.7	31	45.0		
6	50	34.7	21	28.0	29	42.0		
Randomization CGI Severity								
1	3	2.1	1	1.3	2	3.0		
2	48	33.3	27	36.0	21	30.4		
3	76	52.8	39	52.0	37	53.6		

Variables	Treatment Group					
	All Randomized (N=144)		Medication Management + CBT (N=75)		Medication Management Only (N=69)	
Categorical	N	%	N	%	N	%
4	16	11.1	7	9.4	9	13.0
5	1	0.7	1	1.3	0	0
Comorbid anxiety disorder	32	22.2	12	16.0	20	28.9
Comorbid behavior disorder	48	33.7	26	34.7	22	31.9
Comorbid dysthymia	24	16.7	10	13.3	14	20.3
Baseline Suicidal Ideation						
None	42	29.2	26	34.7	16	23.2
Morbid thoughts/death wishes	23	16.0	10	13.3	13	18.8
Suicidal thoughts	53	36.8	28	37.3	25	36.2
Suicidal plans	5	3.5	2	2.7	3	4.4
Suicide attempts	21	14.6	9	12.0	12	17.4
Number of Suicide Attempts						
None	123	85.4	66	88.0	57	82.6
1	12	8.33	5	6.7	7	10.1
2	9	6.33	4	5.3	5	7.3
Continuous	Mean	SD	Mean	SD	Mean	SD
Age	13.8	2.6	13.5	2.7	14.2	2.4
Duration of Episode (weeks)	43.7	38.6	41.3	36.9	46.4	40.4
Number of Episodes	1.1	0.4	1.1	0.29	1.2	0.52
Baseline CDRS-R	58.0	7.2	56.8	7.1	59.2	7.0
Randomization CDRS-R	30.9	5.7	30.5	5.6	31.4	5.9
Baseline CGI Severity	5.2	0.7	5.1	0.7	5.3	0.69
Randomization CGI Severity	2.8	0.7	2.7	0.7	2.8	0.71