COMPONENTS ANALYSIS OF A COGNITIVE BEHAVIORAL THERAPY

TREATMENT PROGRAM FOR CHILDREN AND ADOLESCENTS

WITH MAJOR DEPRESSIVE DISORDER

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DEDICATION

I would like to dedicate this work to my family and friends who have supported me throughout my time in graduate school as I pursued my professional goals, including during the writing of this project. I would not be where I am today had it not been your commitment and encouragement. I am forever grateful for your reassurance, love, and heartfelt support.

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Abstract: This study examined whether the receipt of specific CBT components in a CBT treatment program, parent or family involvement, and dosage across four domains (i.e., frequency, duration, length, and intensity) were associated with risk of occurrence of relapse among children and adolescents with Major Depressive Disorder (MDD). Children and adolescents aged 8 to 17 with MDD (*n*=75) completed a continuation phase CBT-focused treatment program after responding to an acute phase pharmacotherapy intervention. Study therapists completed session checklists following each session to

document which components were introduced during session, as well as documenting parent/family involvement, and dosage variables (e.g., length of session, etc.). Depression severity was also measured through the CDRS-R, which allowed for measurement of relapse status, which was the outcome variable for the current study. Cox Proportional Hazard Regression Models were utilized to investigate whether two primary components (i.e., Wellness, Relapse-Prevention), dosage, and parent/family involvement were related to hazard of relapse. Inclusion of Wellness and Relapse-Prevention components were not significantly related to risk of relapse. Similarly, parent/family involvement was not significantly related to hazard of relapse. Regarding dosage, however, results indicate that a higher frequency of sessions, as well as a longer period of time over which treatment is delivered (e.g., length) were significantly related to a reduced risk of relapse. However, there was no statistically significant finding regarding risk of relapse based on cumulative number of minutes spent in session. Further, when length of treatment was controlled, an increase in number of weeks that elapse between each session (e.g., intensity) was related to a higher risk of relapse, suggesting that sessions that occur closer to one another are related to a reduced risk of relapse. These findings are congruent with some of the existing research on this subject, and ultimately support the idea that treatment dosage should be measured across several domains (e.g., frequency, duration, length, intensity). Additional research with a larger sample size should be conducted regarding the influence of receipt of specific CBT components as well as parent/family involvement given the lack of statistically significant findings in the current study.

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Appendix A

Appendix B

LIST OF ABBREVIATIONS

CBT – Cognitive Behavioral Therapy

CDRS-R – Children's Depression Rating Scale-Revised

CGI-S – Clinical Global Impression-Severity

CT – Cognitive Therapy

DSM – Diagnostic Statistical Manual

GAD – Generalized Anxiety Disorder

IE – Independent Evaluator

MDD – Major Depressive Disorder

NIMH – National Institute of Mental Health

RCT – Randomized Clinical Trial

RP—CBT – Relapse Prevention Cognitive Behavioral Therapy

SSRI – Specific Serotonin Reuptake Inhibitor

TADS – Treatment for Adolescents with Depression Study

TORDIA – Treatment of SSRI-Resistant Depression in Adolescents

CHAPTER ONE

Introduction

The pervasiveness of depression in children (i.e., 8-15 years of age) and adolescents (i.e., 13-18 years of age) is substantial, with estimated 12-month prevalence rates at 2.7% for children (Merikangas et al., 2010), and adolescent lifetime and 12-month prevalence rates at 11% and 7.5%, respectively (Avenevoli, Swendsen, He, Burstein, & Merikangas, 2015), thus establishing this illness as a significant public health concern. Depression in children and adolescents is often associated with negative outcomes in many aspects of life, including academic challenges, poor physical health, difficulty establishing positive relationships, and participation in risky behaviors (Auerbach, 2015). Moreover, depression has been identified as the most significant psychiatric risk factor for adolescent suicidal behavior (Brent et al., 2009). As such, establishing effective treatment methods for child and adolescent depression is imperative.

Cognitive Behavioral Therapy (CBT) has been shown to be an effective form of psychotherapeutic treatment for depression in youth (Zhou et al., 2015). However, as CBT is a treatment modality comprised of several different treatment components, it is difficult to determine which individual components of the treatment are responsible for improvement of symptomotology, or whether it is a combination of components. A breakdown of components in studies utilizing CBT would broaden the scope of understanding those aspects of psychotherapy that are true necessities for effective treatment. Although researchers have identified this as an issue that should be addressed (Weersing, Rozenman, & Gonzalez, 2009; McCarty & Weisz, 2007; Hetrick et al., 2015), there has been little exploration of this in the child and adolescent depression literature.

Common components of CBT include psychoeducation, self-monitoring skills, relationship skills, cognitive restructuring, behavioral activation, and problem solving (McCarty & Weisz, 2007), but additional, less common components have also been utilized in extant studies, such as the inclusion of family treatment components, thus making the determination of effective treatment components even more cumbersome. In addition to the issue of specific components, little research has been conducted regarding the dosage (i.e., number of sessions, length of sessions) and intensity of treatment. With minimal knowledge surrounding these issues, it is difficult to make generalized statements regarding the most effective methods for providing CBT in specific populations.

The present study aims to conduct a secondary analysis of a randomized clinical trial of child and adolescent depression in a continuation phase treatment study in order to investigate the relationship between CBT treatment characteristics (i.e., specific CBT treatment components, session dosage, parent/family inclusion), patient characteristics (e.g., demographic information, illness information), and treatment outcomes. For the current study, treatment outcome is measured by occurrence of relapse, which has been defined as a Diagnostic Statistical Manual (DSM) episode of depression during a period of remission (Birmaher et al., 2007; Birmaher, Brent, & Kolko, 2000; Emslie et al., 1998). A secondary analysis will be completed to explore the influence of session dosage (i.e., number of total sessions, period of time over which treatment is delivered, cumulative number of minutes spent in treatment, period of time that elapsed between each individual session) on response to treatment. Results from the proposed analyses will promote greater understanding of the importance of intensity and degree of treatment and provide

information about which treatment components may be the most effective in the treatment of children and adolescents with depression.

CHAPTER TWO

Review of the Literature

Child and Adolescent Depression & the Impact of CBT Treatment

Depressive disorders in children and adolescents are widespread with 12-month prevalence rates estimated at 2.7% in children ages 8-15 years (Merikangas et al., 2010), and 7.5% in adolescents aged 13-18 years (Avenevoli et al, 2015). Indeed, depression is one of the most common mental health disorders among adolescents (Richmond & Rosen, 2005). According to the National Institute of Mental Health (NIMH, 2014), based on data from the National Survey on Drug Use and Health, an estimated 2.8 million adolescents aged 12-17 years in the United States met criteria for a depressive episode in 2014. Moreover, depression in youth has been found to be associated with a number of other impairments and long-term consequences including poor health, difficulties in school, difficulties establishing positive relationships, and an increased risk for developing comorbid conditions (Richmond & Rosen, 2005; Auerbach, 2015; Lewinsohn, Rohde, & Seeley, 1998; Birmaher et al. 1996). Extant research indicates that longer duration of depressive episodes is associated with earlier age of onset, and the rate of experiencing additional depressive episodes after recovery from an initial episode is notable, with approximately one third experiencing an additional episode within 4 years (Lewinsohn et al., 1998). As such, the expediency at which depressive symptoms are addressed through the use of effective treatments is particularly critical in a younger population. Indeed, given the notable prevalence rates as well as the long-term impact of depression on psychosocial well-being and overall quality of life, the search for effective treatments in

this population is imperative (Hetrick, Cox, & Merry, 2011; Weisz, McCarty, & Valeri, 2006).

To date, CBT is one of the most commonly studied psychotherapies for child and adolescent depression, and is largely recognized as a first-line treatment (Richmond & Rosen, 2005; Hetrick, et al., 2011; Weersing, Iyengar, Kolko, Birmaher, & Brent, 2006). Many studies exploring the effectiveness of CBT on child and adolescent depression have demonstrated positive short-term effects including results that identify CBT as a superior treatment to family therapy, nondirective supportive therapy, relaxation therapy, or receipt of referrals to outpatient mental health care (Reinecke, Ryan & DuBois, 1998; Brent et al., 1998; Compton et al., 2005; Wood, Harrington, & Moore, 1996; Weisz et al., 2006; Weersing et al., 2017). Unfortunately, despite data that identify CBT as an effective form of treatment for many adolescents suffering from depression, there remain many adolescents who fail to improve or respond to treatment (Jayson, Wood, Kroll, Fraser, & Harrington, 1998). In fact, approximately 40% of adolescents with MDD fail to sufficiently respond to first-step treatments (Asarnow et al., 2009). Although adolescents suffering from moderate depression may respond to CBT alone, those who experience more severe depressive episodes will likely require the additional treatment of antidepressants (Birmaher et al., 2007). However, some concerns have been raised about the safety of pharmacotherapy in children and adolescents, which has promoted an even greater push toward the study of effective psychotherapeutic treatment options (Weisz et al., 2006). Indeed, a "black box" warning was established by the U.S. Food and Drug Administration (FDA) on Specific Serotonin Reuptake Inhibitors (SSRI) in the treatment of adolescent depression due to possible risk for suicide (Vitiello & Swedo, 2004;

Tompson, Boger, & Asarnow, 2012). As such, further research needs to be conducted to work to identify and establish an effective psychotherapeutic treatment for those who have failed to respond to treatment in the past. The TORDIA study is one such example of treatment that explored the influence of introducing CBT to a sample of chronically depressed adolescents who had previously failed to respond to treatment with an SSRI. In this analysis, which utilized data from the TORDIA study at 24 weeks, Emslie and colleagues (2010) discovered that almost 40% of this sample achieved remission after 6 months of treatment. In order to identify effective psychotherapeutic treatments for this particular sample, it is crucial that existing treatments be explored in great depth to identify those components that are truly effective in treatment of depression and those components that are less imperative to include.

It is important to consider the course of treatment in depression when considering the timing of interventions. Emslie and colleagues (2008) discussed the concept of treatment phases in a study focused on the influence of fluoxetine versus a placebo in the prevention of relapse in children and adolescents with MDD. In this paper, Emslie and his colleagues describe 3 phases of MDD treatment: acute phase, continuation phase, and maintenance phase treatment. Acute treatment is defined as the initial treatment period that is introduced in order to reduce depressive symptoms and achieve remission. Continuation treatment is the period of treatment estimated roughly as 4-9 months following acute phase treatment, with the primary focus being prevention of symptom relapse. Finally, the maintenance treatment phase is introduced, lasting approximately 1-3 years following the continuation phase, with the primary aim being prevention of new depressive episodes. The use of antidepressants as a monotherapy in children and

adolescents during acute phase treatment is still relatively novel, but has shown to be effective in some studies (Bridge et al., 2007; Cheung, A., Emslie, G., & Mayes, T, 2005). Therefore, the notion of introducing CBT or other psychotherapeutic interventions during a continuation phase portion of treatment following, or in conjunction with the use of an antidepressant during acute phase treatment should continue to be explored to determine the most effective timeline of introduction of various forms of treatment. Some research exists that has implemented the concept of sequential treatment models with pharmacotherapy introduced as acute phase treatment. Indeed, a meta-analysis was conducted to explore the efficacy of sequential integration of pharmacotherapy and psychotherapy in the reduction of hazard of relapse and MDD recurrence (Guidi, J., Fava, G., Fava, M., & Papakostas, G., 2011). The results of this meta-analysis indicated that psychotherapy presented after pharmacotherapy as a sequencing strategy may be an ideal method of treatment delivery regarding prevention of relapse in depressed adults. Further, results from Emslie and colleagues (2008) indicated that in order to prevent relapse from occurring in a depressed child/adolescent population, continuation treatment is likely a necessity. Kennard and colleagues (2008) reported similar findings regarding the impact of continuation treatment in a pilot study with depressed adolescent population. The results of this study reported that those adolescents who received CBT during continuation phase treatment in addition to antidepressant medication had a significant reduction in risk of relapse as compared to those adolescents who received only antidepressant treatment. In a larger randomized controlled trial performed by Kennard and colleagues (2014), the authors confirmed that the addition of CBT after participants had demonstrated a response to fluoxetine, compared to fluoxetine alone, reduced the risk of relapse. Given these

promising results, the current study was designed to further explore the continuation CBT treatment used in these trials to determine the most effective components and dosage of the treatment.

Overview of CBT Components & Treatment Factors Predicting Outcome

Treatment Components

CBT, defined by the Beck Institute as "a solution-focused approach to treatment that is oriented toward solving problems and learning skills," has been identified as an effective treatment for adolescent depression. It is comprised of various individual components (Kennard et al., 2009), so it is perhaps unsurprising that amongst the many studies that have utilized the overarching theoretical basis of CBT in treatment, there is considerable variability in which specific components are included. As such, it can be largely assumed that particular components likely contribute more substantially to positive treatment outcomes than others, but little research has been conducted to confirm this or identify these components (Hetrick et al., 2015). Table 1 provides a breakdown of components used in several existing CBT-based depression treatment manuals for children and adolescents to highlight those components that appear most frequently in the current literature. These particular manuals were chosen for specific review in the current study given the frequency with which they are explored and cited in the current literature. Although there are other existing CBT-based depression treatment manuals that have been utilized in research on this subject, these specific manuals are often discussed and identified as major contributors to this line of study.

Components analyses in adult depression literature show somewhat mixed results, but the majority of studies posit that completion of individual components of CBT often

prove to be equally efficacious as those treatments that require completion of all components. For instance, in studies exploring long-term follow up outcomes, cognitive therapy is shown to be equally effective as behavioral activation (Dobson et al., 2008; Hetrick et al., 2015). Jacobson and colleagues (1996) compared 3 treatment groups in an adult depressed population to study the treatment effects of providing strictly behavioral activation components versus behavioral activation and automatic thought components versus "full" traditional cognitive behavioral therapy. The results demonstrated no significant difference between these groups during short-term treatment, indicating that individual components are equally effective as "full" CBT. Gortner, Gollan, Dobson, and Jacobson (1998) explored long-term follow up effects of this study, and found comparable results, suggesting that the behavioral activation component group and the behavioral activation with automatic thought modification group boasted equivalent results as the group that received all of the traditional CBT components in prevention of relapse in depressed adults. In a meta-analysis of studies exploring the impacts of cognitive therapy in depressed adults, results indicated that cognitive therapy and behavior therapy were equally efficacious (Gloaguen, Cottraux, Cucherat, & Blackburn, 1998). However, in more recent acute treatment, some existing research indicates that behavioral activation is more efficacious than cognitive therapy (Dimidjian et al., 2006). In the adult depression population, a study by Jacobson and colleagues (1996) explored outcomes from three different treatment groups (i.e., behavioral activation alone; behavioral activation plus automatic thoughts; behavioral activation, automatic thoughts, and identifying core depressogenic schema), which demonstrated that the group that received noncognitive

behavioral-activation strategies alone showed equivalent results as those groups that received additional cognitive treatment components.

In addition to depression, components analyses of CBT have been conducted in anxiety disorders in adults, as CBT has been proven to be an effective treatment for many anxiety disorders, such as Generalized Anxiety Disorder (GAD; Borkovec, Newman, Pincus, & Lytle, 2002). Given the significant comorbidity of anxiety disorders with depression, this is a beneficial area of research to explore as well in discussion of individual component effectiveness. In a study exploring treatment options in a GAD population in adults, Borkovec et al. (2002) compared the effectiveness of three treatment groups, cognitive therapy alone (CT), self-control desensitization plus applied relaxation training (SCD), and CBT, which included all aspects of the CT and SCD groups with the exception of supportive listening. The results showed that all 3 treatment groups were equally effective in reduction of GAD symptoms. These results were maintained through a 2-year follow up.

The majority of existing research in components analyses work in child and adolescent depression appears to strictly explore the two most primary components of CBT: cognitive restructuring and behavioral activation, thus leaving much to be explored about the contribution of additional CBT components. In a meta-analysis conducted by Weisz and colleagues (2006) exploring the effects of psychotherapy on depression, the authors highlighted the finding that the vast majority of studies included in their review emphasized cognitive change as a primary component of treatment (n=33) versus those studies that did not emphasize cognitive change (n=11). In comparison of these two treatment groups (i.e., cognitive change emphasis such as CBT vs. non-cognitive change

emphasis such as relaxation training), although there were differences in effect size for both groups following intervention, a significant difference in effect size between the two groups was not discovered. Overall, Weisz and colleagues reported that treatments with non-cognitive change emphasis displayed effects that were similarly robust to cognitively focused interventions, suggesting value exists in both methods of treatment. This indicates that positive treatment outcomes for depression in children and adolescents may occur without the primary inclusion of cognitive components; however, many of the CBT treatment manuals studied in clinical trials include an emphasis on changing cognition.

Also recognizing this gap in the literature, Weersing and colleagues (2009) performed a comprehensive review of three well-established manualized CBT treatment programs for adolescent depression emphasizing the notable diversity in material and session dosage. The three studies included in their analysis were the Coping with Depression for Adolescents Course (CWD-A; Lewinsohn, Clarke, Hops, & Andrews, 1990), the Cognitive Therapy Manual from the Pittsburgh CBT trial (Brent & Poling, 1997), and the modular CBT manual of the TADS (Curry et al., 2000; Wells & Curry, 2000). This report emphasized the variance in which these 3 studies employed different components and strategies, utilized individual versus family or group therapy sessions, and the total number of sessions that occurred. Despite all being grounded in the traditional principles of CBT, these three manuals showed varying results. The notion that such variation occurred in outcome despite utilizing a similar CBT framework suggests that more investigation is needed to determine what has made some CBT programs more successful than others, whether it is use of specific components, implementation of family sessions, or sheer number of sessions attended.

Similarly, McCarty and Weisz (2007) performed a meta-analysis of studies exploring pediatric MDD and completed a components profile of successful adolescent depression treatments with the aim of identifying those strategies that were most commonly utilized across studies. Again, by performing a breakdown of components utilized in successful treatments, greater understanding is gleaned regarding which components are truly contributing to positive outcomes. For this profile, the authors created a simple matrix of 9 empirically based treatments that boasted effect sizes of 0.50 or greater, 4 of which were manualized CBT treatments. In their assessment, the authors discovered that a primary overlap in the successful CBT treatments they reviewed was the task of asking the adolescent to identify and achieve feasible goals or choosing a specific area in which they would gain competence. Furthermore, the majority of the studies being examined included components of psychoeducation, self-monitoring, communication skills, cognitive restructuring, problem solving, and behavioral activation. Despite the use of overlapping components, the necessity of inclusion of these components remains unclear, suggesting that the need for further dissemination of individual studies still remains. Although McCarty and Weisz (2007) confirmed that successful treatments tend to promote understanding of the disorder and its treatment as well as general mood and behavior modification, analyses of these specific components remain unperformed. This indicates that perhaps the most important next step for researchers is the breakdown of specific, individual manualized treatments to establish which specific components are actually directly related to treatment outcome.

In consideration of the adolescent depression population specifically, perhaps the most comprehensive components analysis conducted to date on a CBT study explores data

from the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) study by Kennard and colleagues (2009). True to the majority of CBT manuals published to date, the treatment utilized in the TORDIA study was comprised of components highlighting cognitive restructuring, behavioral activation, emotion regulation, social skills, and problem solving. Family sessions were also included throughout. Final analyses suggested that those participants who completed the problem-solving and social skills treatment components were significantly more likely to endorse better outcomes and an overall more positive response to treatment.

Another interesting component of psychosocial treatment of youth is the involvement of parents in treatment. In fact, Spielmans, Pasek, and McFall (2007) performed a meta-analysis of CBT treatments for child and adolescent anxiety and depression and discovered that "full treatments" (adolescent CBT + parent training) were not significantly more efficacious than those treatments that provided CBT to adolescents alone. Despite this, some researchers argue that successful treatment of affective disorders in adolescents or children effectively requires the involvement of parents as they may recognize relevant elements of a child's functioning that the child either fails to see or resists sharing with their treatment provider (Birmaher et al., 2007). Additionally, there is growing interest in family-focused approaches for treatment of depression in youth given that there exists a high rate of depressive disorders in the parents of depressed adolescents. Thus, the involvement of family in treatment of adolescent depression may influence family functioning, overall, and ultimately decrease the recurrence of depressive episodes across the family as a unit (Tompson et al., 2012).

In summary of this brief review of existing components literature, the results are, at times, conflicting. Several studies in adult literature suggest that cognitive and behavioral components are equally efficacious in both acute and long-term outcomes. However, despite the limited data available in child and adolescent research in this area, existing studies imply that components such as problem-solving, social skills, and goal setting trump those primary CBT components in importance. Ultimately, given the considerable variance of inclusion of components amongst these studies, as well as the mixed results, the call for further study is needed. Identification of the most effective components for treatment of pediatric depression is important, as it may provide insight into the development of treatment programs that are the most time and cost efficient, thereby reducing the burden on patient, provider, family, and society.

Session Dosage

The notion of treatment dosage of psychotherapy is of tremendous significance, yet remains minimally studied. The idea of "dosage" can be largely defined by inclusion of a few primary variables including intensity, frequency, amount of exposure, and length of treatment, with intensity accounting for the length of time between sessions, frequency accounting for the total number of sessions completed, amount of exposure accounting for the total number of minutes spent in treatment across all sessions, and length of treatment equating to the time period over which treatment is delivered (e.g., number of weeks, months, etc.). Determining the most effective dosage of therapy for child and adolescent depression will lead to the establishment of more practical, time-efficient, and ultimately better outcomes. Moreover, if research determines that brief treatments lead to better outcomes, the burden on patient, family, provider, and society is diminished.

Alternatively, if research discovers that longer, more intense treatments are most effective, advocacy for societal shifts in treatment may be warranted and may result in practice changes (Cuijpers, Huibers, Ebert, Koole, & Andersson, 2013). Despite this reasoning, consideration of treatment dosage in CBT in particular remains relatively unexplored.

The dosage literature in adult depression treatment studies is relatively mixed, with some studies reporting greater effects for longer therapies, while others find minimal differences between longer and shorter therapies (Cuijpers et al., 2013). In studies directly comparing shorter and longer therapies based on overall number of sessions, some data revealed greater improvement for lengthier treatments when depression was more severe (Shapiro et al., 1994) or upon follow up (Barkham et al., 1996), while others demonstrated no significant differences when measuring improvement of social functioning and depression severity (Molenaar et al., 2011). In a systematic review by Hansen, Lambert, and Forman (2002), the authors reported that between 13 and 18 sessions is necessary for 50% of patients to show improvement. Cuijpers and colleagues (2013) conducted a meta-analytic review of 70 randomized controlled trials to explore the association between effectiveness of psychotherapies for adult depression and several variables of treatment dosage including: number of sessions, duration of therapy, total contact time, and number of sessions per week. Using a metaregression analysis, the authors discovered that the effects increased with a higher number of treatment sessions, but only by a small effect size. They reported a strong correlation between number of sessions per week and effect size when total number of sessions remained the same with an increase in effect size of 0.45 when two sessions were completed per week instead of one. Given this data, it appears that the variable of intensity, as defined as the length of time between sessions, is

perhaps more significant than total number of sessions, overall. Interestingly, the authors observed a small negative association was discovered between duration of therapy (i.e., number of weeks spent over which treatment occurs) and effect size, showing smaller effects for longer therapies. Importantly, when performing this type of analysis, despite finding significant associations between predictors and effect size, the results do not imply causation. However, these results suggest that treatment dosage is a valuable subject of exploration and indicates that several variables related to dosage (e.g., frequency, intensity, amount of exposure, and length of treatment) may all contribute to treatment outcomes. In sum, the authors noted that although this study was strictly observational, the implications suggest that overall briefer therapies with shorter individual sessions, but with a higher intensity would lead to the best treatment outcomes. Reese, Toland, and Hopkins (2011) explored the influence of session number and session frequency on outcome of psychotherapy, and similarly identified session intensity as a critical variable. Results in their study indicated that those participants who had more time elapse between each session improved more slowly than those with shorter periods of time between sessions. Reardon, Cukrowicz, Reeves, and Joiner (2002) measured two aspects of therapy attendance (i.e., number of sessions, and total duration of treatment) in order to explore potential interactive effects of these variables of treatment dosage in predicting treatment outcome, which was measured by patient improvement via the Clinical Global Impression (CGI; Guy, 1976). The authors discovered that for those patients who attended 11 or fewer sessions, the more months they spent receiving treatment was related with worse outcomes overall, while length of treatment was not predictive of improvement for those participants who attended more than 11 sessions. Bruijniks and colleagues (2015) are currently

completing a multicenter randomized trial comparing treatment outcomes of once-weekly versus twice-weekly CBT sessions, which will provide additional important information regarding this subject. It is also important to consider that different psychological issues respond to different treatments at different rates (Hansen et al., 2002; Barkham et al., 1996). Indeed, Barkham and colleagues (1996) reported that while 50% of depressed patients showed clinically significant change in psychiatric symptoms within 8 sessions of therapy, it required 16 sessions to obtain a 40% rate of improvement in interpersonal difficulties. Ultimately, the literature suggests that mere number of sessions is perhaps an insufficient individual variable to describe therapeutic growth, as varying degrees of improvement have been found based on frequency and intensity of sessions.

While the relationship between CBT dosing and treatment outcome remain largely unexplored in child and adolescent depression, several studies have been performed regarding this issue in other clinical areas, including anxiety and sleep. Among these studies, dose-response was explored in insomnia patients to determine the impact of receiving one session, two sessions, four sessions, and eight sessions of CBT. In this study, the participant group that received four sessions had the highest number of participants achieve the greatest degree of improvement, thereby establishing four CBT sessions as "optimal dosage" (Edinger, Wohlgemuth, Radtke, Coffman, & Carney, 2007). Regarding anxiety, Abramowitz, Foa, and Franklin (2003) investigated dose-response in an obsessive-compulsive disorder (OCD) population by comparing intensive versus twice-weekly therapy sessions. Although intensive therapy boasted superior outcomes in short-term, no differences were detected between groups at follow-up, suggesting that utilization of a less burdensome therapy schedule was still effective. Indeed, the active ingredient that

was ultimately determined was the number of contacts the participants had with their therapist, as opposed to the overall length of time spent in treatment across time (e.g., 3 weeks versus 8 weeks). The relationship between CBT session intensity and anxiety has also been explored in panic disorder, where greater number of sessions was associated with fewer anxiety symptoms (Craske et al., 2006).

Specifically regarding adolescent depression, a secondary exploratory analysis of the Treatment of SSRI-Resistant Depression in Adolescents Study (TORDIA) was conducted by Kennard and colleagues (2009) and discovered that CBT dose was indeed associated with response to treatment with participants who received 9 or more sessions endorsing better outcomes. However, a "dose x technique" response was not discovered, as the data did not indicate the existence of a relationship between outcome and the number of times a participant completed a specific module.

In sum, it appears that in the adult literature, although frequency, intensity, and duration are all important variables regarding treatment dosage on outcome, perhaps the most significant element is intensity of session delivery. Given the influence of dosage on adult study participants, it may be implied that a similar degree of significance may exist in dosage for children and adolescents as well. As such, research on session dosage in the child and adolescent depression population is important to explore.

Summary

Existing research strongly supports the effectiveness of CBT as treatment for child and adolescent depression. Although literature on components analyses has begun to grow in recent years, there remain few analyses conducted on the specific pediatric depression population. Given the considerable prevalence rates of depression in this age group and

the tremendous impact depression can have on many facets of life if left untreated, identification and development of the most efficient and effective treatment is warranted. Performing a components analysis of a prominent CBT study of adolescent depression will make an important contribution to the field by expanding knowledge of the most efficacious treatment components and dosage. The overall aim of this study is to identify predictors of treatment outcome as defined by treatment characteristics including use of specific components and session dosage. Specifically, the study aims include: (1) assess the response to treatment of a CBT group to determine which specific treatment components are most greatly related to treatment outcome; (2) evaluate the relationship between treatment dosage and treatment outcome; and (3) evaluate the impact of a parent/family component on treatment outcome.

CHAPTER THREE

Aims and Hypotheses

Overall Aim

The overall aim of this study is to examine potential predictors of treatment outcome of a child and adolescent depression population, as defined by treatment characteristics (i.e., session components, session dosage, and inclusion of parent/family in treatment) of a CBT treatment study, to determine which characteristics are related to treatment outcome, as measured by occurrence of relapse.

Aims and Hypotheses

Aim 1a: Assess the response to treatment of the participants who were randomized into the CBT treatment group to ascertain which specific treatment components (e.g., psychoeducation, behavioral activation, cognitive restructuring, etc.) were related to treatment outcome (i.e., occurrence of relapse) in this population.

Hypothesis 1a: Based on existing literature in this specific population, participants who complete problem-solving and relapse-prevention components will have a lower risk of relapse.

Aim 1b: Evaluate the relationship between treatment dosage across 4 dosage domains (i.e., frequency, length of treatment, exposure to treatment, intensity) and treatment outcomes (i.e., occurrence of relapse) in this population.

Hypothesis 1b: Participants who complete a greater number of CBT sessions overall, as well as those who have greater duration of exposure to CBT, as defined by minutes in session, will have a lower risk of relapse.

Aim 1c: Examine the impact on treatment outcome, as measured by occurrence of relapse, of inclusion of parent or family sessions.

Hypothesis 1c: Those participants whose treatment included more parent or family involvement, as measured by minutes in treatment, will demonstrate a superior response to treatment, as defined by a reduced risk of relapse, than those participants who did not participate in parent or family sessions.

CHAPTER FOUR

Methods

The proposed analysis will utilize data collected as part of a single-site RCT testing the effects of a continuation phase sequential treatment strategy focused on relapse prevention. The aims for the current study will explore data exclusively from the 75 participants who were randomized to the CBT intervention group. Participants were recruited from a general pediatric psychiatry clinic at Children's Health System of Texas/Children's Medical Center in Dallas, Texas. This study was approved by the University of Texas Southwestern Medical Center (UTSW) Institutional Review Board.

Patient Recruitment

Potentially eligible individuals included children and adolescents ages 8-17 with a primary diagnosis of major depressive disorder (MDD) for a period of at least 4 weeks, a Children's Depression Rating Scale-Revised (CDRS-R; Poznanski & Mokros, 1996) score of ≥40, and a Clinical Global Impression-Severity (CGI-S; Guy, W., 1976) severity score of ≥4. Although MDD was required as the participant's primary diagnosis, additional concurrent disorders were permitted. Participants were required to be English speaking and have an English-speaking parent, be of normal intelligence, and have good general medical health. Exclusion criteria included presence of a lifetime psychotic or bipolar disorder, alcohol or substance dependence within the past 6 months, anorexia or bulimia within the past year, pregnant or lactating females, sexually active females lacking adequate use of birth control, medically unstable chronic medical illness, use of psychotropic medication, first degree relatives with bipolar I disorder, severe suicidal

ideation or behaviors requiring more intensive treatment, and a history of intolerance to or failure of fluoxetine in an adequate trial (≥4 weeks of at least 40mg).

Study Materials and Procedures

Diagnostic Evaluation & Study Enrollment

Participants and their parents completed an initial visit with study staff to receive information about the purpose and procedure of the study, risks and benefits of participation, and their rights throughout their participation, at which time written consent and assent were provided. Upon receipt of consent and assent, participants completed interviews with trained masters level independent evaluators (IEs) using the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) to determine eligibility based on diagnostic inclusion. IEs administered the CDRS-R to gather additional information about the participants' depression. Data were reviewed by a child psychiatrist at which time the participant and parents completed the CDRS-R, CGI-S, and the Columbia Suicide Severity Rating Scale—Short (C-SSRS) to determine final eligibility and appropriateness for participation in the study (Kennard et al., 2014).

Open Treatment

Those participants determined as eligible were then started on 6 weeks of fluoxetine. Dosage of fluoxetine began at 10mg/day at baseline and was increased to 20mg/day at week 1 with the exception of those participants who experienced side effects that would prevent titration. After 4 weeks, dosage could be reduced by 10mg/day or increased to 30-40mg/day, as deemed necessary by the child psychiatrist. Participants met with a child psychiatrist on a weekly basis during the open treatment phase (weeks 0-6) to

evaluate symptoms and adverse events. During this study phase, those participants who were deemed medication non-adherent (<70% of pills on two consecutive visits based on pill count) as well as those who required additional treatment were discontinued at this time.

Randomization

At completion of 6 weeks of open treatment, remaining participants were reevaluated by IEs to determine response to medication. A decrease in CDRS-R total score of ≥50% was required to be deemed a treatment responder. Those participants who were determined non-responders were discontinued from the study and provided with treatment referrals. Participants who responded to open treatment were then stratified and randomized into 2 groups: fluoxetine only (Medication Management) or fluoxetine plus Relapse Prevention CBT (Combination Treatment). Randomization was stratified by gender, age group (≥12 years; ≤11 years), and remission status (CDRS-R ≤28; CDRS-R ≥29). The focus of the present study will be exclusively on those participants who received the combination treatment. As aforementioned, the sequential treatment format of this study is unique in its design, as it is based upon the principles of acute/open phase treatment followed by continuation phase treatment as described by Emslie and colleagues (2008).

Continuation Treatment & Combination Group

Medication Management — All randomized participants, regardless of treatment group, continued to receive fluoxetine for an additional 6 months. Medication visits by IEs took place every other week for the initial 3 months and then decreased to monthly visits for the remaining time in participation.

RP-CBT (Combination Treatment)— In addition to continued receipt of fluoxetine, those participants randomized to the combination treatment group began completing CBT sessions at week 7. These sessions were designed to take place every week for the first month of treatment, were decreased to every other week for the next 2 months, and were eventually decreased to once every 4 to 6 weeks for the remaining 3 months of the study. This timeline was utilized as a model, but was adjusted as needed based on the needs of the participant. Sessions were designed to be 1 hour in length, with the first 2 sessions lasting 1.5 hours as they included a family component.

Measures

Dependent Variable

Treatment Relapse. The primary outcome for the study will be occurrence of relapse. This outcome was measured using IE ratings on the Children's Depression Rating Scale—Revised (CDRS-R; Poznanski & Mokros, 1996).

Relapse was defined as a CDRS-R score of ≥40 for at least 2 weeks or a CDRS-R<40, but with significant clinical deterioration that would suggest full relapse if alterations in treatment were not made.

The CDRS-R measures the depression severity and change in depressive symptoms for children and adolescents. It is a 17-item measure that provides a total score from 17 to 113 with those scores totaling at 40 or greater representing significant depression. It boasts strong psychometric properties in children ages 6-12 in internal consistency (Cronbach's alpha=0.85), interrater reliability (r=0.92), and test-retest reliability (r=0.78). Its convergent validity with a global depression rating has shown to be highly correlated at 0.92 (Poznanski & Mokros, 1996). Mayes, Bernstein, Haley, Kennard, and Emslie (2010)

determined psychometric properties of the CDRS-R in an adolescent population and similarly discovered good internal consistency and construct validity. These measures were administered to participants by blinded IEs at time of randomization as well as every 6 weeks throughout receiving treatment (weeks 6, 12, 18, 24, and 30).

Independent Variables

Specific Treatment Components. There were 7 individual treatment components offered in the CBT manual for this trial: psychoeducation, behavioral activation, relapse-prevention, cognitive restructuring, problem solving, emotion regulation, and wellness skills which included 6 general areas of focus (i.e., self-acceptance, social skills, success, self-goals, spiritual, and soothing). Additionally, a family communication component was also included for those participants whose families participated in treatment. Treatment was customized for each participant based on his or her individual treatment needs. Each treatment component will be a time-varying binary indicator variable (yes/no) measured at each treatment session across the 30-week continuation treatment trial. After completion of each individual CBT treatment session in this study, the study therapist completed a "therapist checklist" in addition to writing a traditional psychotherapy/research note to summarize the session. As a part of the therapist checklist, the study therapist documented the following: number of cumulative minutes spent in session; number of minutes the participant spent in session independently; number of minutes a parent/family member spent in session; whether homework from the previous session was completed; and which specific components were utilized. The therapist was required to document with a "checkmark" system which components were addressed from the aforementioned list. All of this information was then entered into a research note written by the study therapist and

documented alongside other relevant information discussed during the session. In the current study, frequency counts will be performed to establish totals of each session attended based on individual components (e.g., problem solving, cognitive restructuring, etc.). For the current study, if the checklist was not completed or was unable to be found, a chart review was completed in order to find the required information from therapy notes.

Parent/Family Involvement. The inclusion of family sessions was determined for those participants whose families participated in treatment. Each measure of parent/family involvement (e.g., total number of sessions attended, total amount of time spent in session in minutes) will be entered in a separate Cox model. As aforementioned regarding the measurement and documentation of components completed, parent/family involvement was documented through review of therapist checklists and chart/note review, when needed.

Dosage. For the purposes of this study, dosage will be defined through 4 domains: intensity, frequency, amount of exposure, and length of treatment. Intensity will represent the length of time that elapsed between each individual session. Frequency will represent the total number of sessions that was completed by each participant throughout treatment. Amount of exposure will represent the total cumulative number of minutes spent in treatment. Length of treatment will represent the time period over which the treatment was delivered, as measured by number of weeks. Treatment dosage will be determined by conducting frequency counts of total number of sessions attended by each individual participant, total number of cumulative minutes spent across each individual session, time elapsed between each session (i.e., average number of weeks for each individual

participant), and number of weeks over which the participant completed treatment (i.e., average number of weeks for each individual participant).

Demographic and Control Variables

Demographic Information. Demographic information was determined by parent report or participant self-report (i.e., age, gender, race, ethnicity).

Illness Variables/Disease Characteristics. General information regarding the course of the participant's illness and severity of depression was assessed by a child psychiatrist at baseline using the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) as well as interviews with the participant and his or her parent. Disease variables examined as potential predictors in the current study include duration of current episode and severity of depression.

Other Factors Impacting Treatment Outcome

The required use of specific treatment components in studies utilizing manualized treatments has been criticized for failing to consider the individual needs of the participant. As such, in recent years some manualized treatments have attempted to promote flexibility in treatment by providing the therapist some control in the selection of which components should be completed in order to best fit the therapeutic needs of each participant, along with the speed at which they should complete them (Spirito et al., 2009; Kendall, Cho, Gifford, Hays, & Nauta, 1998). Although this flexible approach may provide superior individualized treatment for each participant, it also puts a more substantial emphasis on the role of the therapist, whose personal selections may now impact the outcome of treatment (Spirito et al., 2009). In the current study, although the therapists maintained

some control over which components each participant received during their participation in the CBT portion of the study, overall standardization and structure was upheld throughout. Specifically, the treatment manual was designed for each participant to receive 4 core components (i.e., psychoeducation, behavioral activation, cognitive restructuring, and problem solving) during the first 4 sessions of intervention. Following the introduction of these 4 components, sessions 6-8 were largely designed as sessions for practice and application. Following these sessions, flexibility in therapist selection of additional components increased for the remainder of the participant's study completion.

Severity of Illness –Severity of depression has been identified as a predictor of response to CBT and achievement of remission status with decreased severity of illness at the beginning of treatment being related to achievement of remission (Jayson et al., 1998). As such, the severity of illness that each participant endorses at randomization in the present study may impact the components each therapist chose to complete during the child or adolescent's study participation.

Age of Participant –The age of the participant likely is a factor on which components the therapist selects to complete during treatment. Currently, the majority of research regarding psychotherapy effectiveness exists predominantly for adolescents over age 12 (Dolle & Schulte-Korne, 2013). Tompson and colleagues (2012) confirmed this report in a review of studies with preadolescent samples and noted that even in those few studies that included children 12 and under in their treatment, separate analyses between preadolescents and adolescents were not performed. Due to developmental level, empirically-based recommendations for adults will not necessarily impact children or adolescents the same way (Dolle & Schulte-Korne, 2013). For instance, Asarnow, Scott,

and Mintz (2002) reported that preadolescent children endorsed behavioral components such as problem solving and social skills as more beneficial than cognitive components. Given the degree of cognitive development that occurs between childhood and adolescence the same argument can be made for children versus adolescents (Tompson et al., 2012). Therefore, the notion that therapists would select different components or different dosages of components across ages is reasonable.

Inclusion of Family/Parent Sessions –Therapists may have different opinions regarding the importance of inclusion of family in treatment, which will impact overall amount of family participation and potentially the participants' response to treatment. Birmaher and colleagues (2007) argue that the treatment of a child or adolescent is not feasible without parental involvement as initial motivation for pursuing treatment often stems from a parent, as well as the monitoring of treatment response outside of therapy. Tompson and colleagues (2012) similarly argue that particularly for younger children, the inclusion of family-focused interventions allows parents the opportunity to provide support, generalize skills taught in treatment to the home environment, and model new behavior. Moreover, extant research suggests that adolescent depression is often accompanied by reports of low family cohesion and high family conflict, suggesting that inclusion of family or parents in treatment may assist in treatment of these issues in particular (Tompson et al., 2012).

Censored Event

The date of the "censored event" (i.e., occurrence of relapse) was established for each individual participant in the combination treatment group. A total of 7 participants experienced relapse, as measured by participant CDRS-R score (i.e., score of ≥40 for at

least 2 weeks or a score of <40, but with significant clinical deterioration that would suggest full relapse if alterations in treatment were not made), during participation of the intervention through week 30. The average time to relapse amongst these 7 participants was 18 weeks. Thus, a total of 66 participants randomized to the combination treatment group did not experience relapse by week 30 in the current study. Therefore, for these 66 participants, the identified "censored event" was established as the either the date of dropout without relapsing, or the date of the completion of treatment at week 30 without experiencing relapse. In order to identify the session number that corresponded to week 30, the baseline completion date for each participant was identified, and 30 weeks was added to this date to establish which completed session was closest to this date.

Components

Once these dates were identified, it was determined for each participant whether the receipt of each CBT component occurred up to, but not exceeding, the particular week in which the censored event took place. Further, if the component was received, the total number of times the component was received, overall, was documented. A distribution of participants not receiving the component versus participants receiving the component was needed across each component in order to establish differences in outcome and determine the influence of each specific component on occurrence of relapse. Therefore, frequencies of each component prior to, but not exceeding the occurrence of the censored event, were calculated.

As psychoeducation is an important component within CBT, it was unsurprising that every participant in the combination treatment group, who completed at least 1 session of CBT, received the psychoeducation component (n=71). Similarly, nearly every

participant (*n*=69*)* completed the behavioral activation component as well. Therefore, neither psychoeducation nor behavioral activation was explored as components in the current analyses due to lack of outcome comparisons. However, the remaining 6 CBT treatment components offered during this intervention and their relationship with relapse were examined. Results of these relationships are presented in Appendix A, Table 6. Given that the current study was originally designed as a relapse-prevention intervention, with a clinical focus on overall wellness, the Wellness and Relapse-Prevention components are discussed more thoroughly in the current analysis with regard to their specific relationship with relapse occurrence. Across the entire combination treatment group, the mean number of times the Wellness component was received prior to relapse or the censored event was 1.14 (SD=1.27, range=6 sessions). The average number of times the Relapse Prevention component was received was 0.73 (SD=1.00, range=4 sessions). Basic statistical measures on the remaining components can be found in Appendix A, Table 5.

Statistical Analyses

Following determination of the session numbers and dates that were associated with each participant's specified "censored event," analyses were performed to evaluate the descriptive statistics on treatment participation and completion, including the following: total number of CBT treatment sessions attended by each participant; total number of cumulative minutes each participant spent in CBT sessions; average number of weeks that elapsed between CBT sessions for each participant; number of weeks over which CBT treatment was completed by each participant; total number of cumulative minutes a family member or parent spent in CBT treatment with each participant; and the frequency of each individual CBT component completed by each participant. Importantly,

2 participants who were randomized to the combination treatment group were unable to be reached to schedule their first session, and therefore did not complete any sessions of CBT. Thus, these 2 participants are notable outliers in the current study's results as they influence the range and means of each of the frequencies established.

To address Aim 1a, a Cox Proportional Hazards Regression with adjustment for CDRS-R total score, age, and gender was used to estimate the hazard of Relapse from the various treatment components with the exception of psychoeducation and behavioral activation, across the 30-week continuation treatment phase. Each treatment component was entered in the Cox model as a time-varying indicator variable (yes/no). As part of the survival analysis, right censoring was used when incomplete information was available about the survival time of a given participant, while the information was considered incomplete if the participant did not have an event during the study. Hazard ratios were estimated and interpreted as the effect size estimator for the 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 considered as incomplete if the participant did not have an event during the study.

A Cox Proportional Hazards Regression similar to that described above for Aim 1a was used to address Aim 1b to estimate the hazard of Relapse from treatment dosage across the 30-week continuation treatment trial. Each measure of treatment dosage (i.e., number of total sessions, total number of cumulative minutes spent in treatment, length of treatment, intensity) was entered in a separate Cox model.

Moreover, as a sensitivity analysis, Aim 1b was addressed by utilizing a Receiver Operating Characteristic (ROC) analysis alongside the Area Under the Curve (AUC) to

determine the optimal cutpoints for treatment dosage (i.e., number of total sessions, total number of cumulative minutes spent in treatment, length of treatment, intensity) in discriminating the status of relapse at the completion of the 30 week continuation treatment trial. The AUC associated with each optimal cutpoint was tested against a nominal area of 0.50 using the Z statistic. Additionally, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for each of the optimal cutpoints.

A Cox Proportional Hazards Regression similar to that described above for Aims 1a and 1b were used to address Aim 1c to estimate the hazard of Relapse from the parent/family involvement across the 30-week continuation treatment trial. Parent/family involvement was explored through total number of sessions attended by a parent or family member, and the total number of cumulative minutes a parent or family member spent in treatment, and were entered in separate Cox models.

CHAPTER 5

RESULTS

Data related to the current study was imported into the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp, Armonk, NY) and SAS software, version 9.4 (SAS Institute, Inc., Cary, NC).

Sample Characteristics

Two hundred children and adolescents were enrolled in the open treatment phase, with a mean age of 13.8 years (SD=2.6); 54.0% of this group was female, and 78.5% identified as Caucasian. From that group, 144 participants were identified as responders to open treatment and randomized into Medication Management (*n*=69) or Medication Management + CBT (*n*=75; combination treatment group). Of the 75 participants randomized to the combination treatment group, 22 withdrew from study treatment prior to study completion (but remained in the assessment portion of the study). Refer to the CONSORT Diagram in Appendix B, Figure 1 for additional information on participant withdrawal.

In the combination treatment group (n=75), the average age of participant was 13.5 years (SD=2.7), with 50.7% of participants being female. The vast majority of participants identified as Caucasian (85.3%) and non-Hispanic (69.3%). Mean CDRS-R score for the combination treatment group at randomization (week 12) was 30.5 (SD=5.6), with an average length of current depressive episode being 41.3 weeks. Additional demographic and clinical characteristic information is provided in Table 2.

Treatment Components

A Cox Proportional Hazards Regression model was utilized to examine the first aim and hypothesis of the current study, which anticipated that those participants who completed the problem-solving and relapse-prevention treatment components would report a reduced risk of relapse compared to those participants who did not complete these components. In this analysis, the Cox Proportional Hazards Regression was adjusted for participant CDRS-R total score at randomization, age, and gender, in order to estimate the hazard of Relapse from the Wellness and Relapse-Prevention treatment components across the 30-week continuation treatment trial. Hazard ratios were also estimated and interpreted as the effect size estimator for the Cox Regression. The 2 treatment components that were explored (i.e., Wellness, Relapse-Prevention) were entered in the Cox model as time-varying indicator variables (yes/no). Cox Proportional Hazards Regression showed that there was not a statistically significant difference between those participants who received the Wellness component and those who did not receive the Wellness component (hazard ratio=0.34, 95% CI=0.071-1.636, χ^2=1.812, df=1, p=0.1783) regarding occurrence of relapse. However, although it was not statistically significant, the Cox model revealed that participants who completed the Wellness component had a lower risk of relapse than those who did not receive the Wellness component, overall, during the 30 week treatment period. Thus, although it was not statistically significant, the hazard of relapse for those who received this particular component was 0.34 times that of those who did not receive it. Similarly, Cox Proportional Hazards Regression on the Relapse-Prevention component did not report a statistically significant difference between those participants who received the Relapse-Prevention component and those who did not (hazard ratio=0.214, 95% CI=0.030-1.507, χ^2=2.3964, df=1, p=0.1216). As with the Wellness component, the hazard of

relapse, although not statistically significant for those who received the Relapse-Prevention component, had a lower risk of relapse than those who did not receive the Relapse-Prevention component during this treatment period. The hazard of relapse for those who received this component was 0.214 times that of those who did not receive it.

For completeness we did explore the other treatment components and also found no statistically significant findings when controlling for age, sex, and CDRS-R score. However, the hazard ratios for the remaining treatment components are in the correct projective direction with the exception of problem solving and family communication. The hazard ratios for the remaining components that were explored in the current analysis can be found in Table 6.

Given the lack of statistical significance discovered in the aforementioned hazard ratios, a Bayesian Cox regression with adjustment for CDRS-R total score, age, and gender was also utilized to estimate the hazard of relapse from the Wellness and Relapse-Prevention treatment components across the 30-week continuation treatment trial. Both the Wellness and Relapse-Prevention components were entered separately in a Bayesian Cox model as a time-varying indicator variable (yes/no). The posterior model parameters were estimated by Markov Chain Monte Carlo (MCMC) techniques. Maximum likelihood estimates of the model parameters were used as initial values of the Markov chain. The 10,000 burn-in samples were followed by 50,000 Monte Carlo samples. The posterior mean estimates and standard deviations of the hazard ratio along with the percentiles (25%, 50%, 75%) and 95% Highest Posterior Density (HPD) Credible Intervals, of fitting this Bayesian Cox regression model, which is an interval with a 0.95 probability of containing the parameter, are shown in Tables 10 and 11.

Treatment Dosage

The average number of sessions completed by each participant was 8.4 sessions (range=16; SD=3.51). Regarding number of cumulative minutes spent in session across the entire 30 weeks of treatment prior to the occurrence of the censored event, the average number of minutes was 500.64 (range =1110; SD=238.16). In regard to how these cumulative minutes were distributed across each session, the average length of session was 58.25 minutes, with an average of 40.90 minutes spent in session with the participant individually, and 17.15 minutes spent in session with a parent or family member. The average number of weeks that elapsed between each session was 1.88 weeks (range=4.40; SD=0.74), and the mean number of weeks over which treatment was completed was 14.87 (range=23.28; SD=7.03). This data is also presented in Appendix A, Table 4.

To address Aim 1b, several separate Cox Proportional Hazards Regression models were utilized to estimate the hazard of Relapse from treatment dosage across the 30-week continuation treatment trial. Due to the potential of multicollinearity, each of the aforementioned domains of treatment dosage (i.e., frequency, exposure, length, intensity) was entered in a separate Cox model for analysis. Beginning with session frequency, or the total number of sessions that each participant attended prior to experiencing relapse/censored event, the Cox model showed that participants who completed more sessions had a statistically significantly reduced risk of relapse (hazard ratio=0.773, 95% CI=0.615-0.971, χ^2=4.8822, df=1, p=0.0271).

A separate Cox model was used to evaluate exposure to treatment, or the total number of cumulative minutes spent in treatment prior to experiencing relapse/censored event. This model did not indicate a statistically significant effect in the risk of relapse based on this treatment variable (hazard ratio=0.997, 95% CI=0.994-1.001, χ^2=2.0704, df=1, p=0.1502).

Regarding length of treatment, or the number of weeks over which treatment was delivered prior to the occurrence of relapse/censored event, the Cox model showed that for every additional week over which treatment was delivered, the risk of relapse was reduced (hazard ratio=0.863, 95% CI=0.772-0.965, χ^2=6.7085, df=1, p=0.0096).

The Cox model on the final treatment dosage variable of intensity, or the average number of weeks that elapsed between each individual session prior to experiencing relapse/censored event, showed that there is not a statistically significant effect in the risk of experiencing relapse based on dosing intensity.

However, when length of treatment and average intensity were entered into the same Cox Proportional Hazards Regression, the model showed that when length of treatment is held constant, an increase in the average number of weeks that elapses between each individual session (i.e., intensity), the hazard of relapse also increases (hazard ratio=3.662, 95% CI=0.990-13.552, χ^2=3.7806, df=1, p=0.0518), indicating that when more time passes between individual sessions, on average, the risk of relapse increases as well.

Moreover, as a sensitivity analysis, Aim 1b was addressed by utilizing a Receiver Operating Characteristic (ROC) analysis alongside the Area Under the Curve (AUC) to determine the optimal cutpoints for treatment dosage (e.g., number of sessions, length of

sessions in minutes, length of treatment, intensity) in discriminating the status of relapse at the completion of the 30 week continuation treatment trial. The AUC associated with each optimal cutpoint was tested against a nominal area of 0.50 using the Z statistic. Additionally, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for each of the optimal cutpoints.

Regarding length of treatment, the number of observed weeks over which treatment was delivered prior to the censored event ranged from 0 to 23. The ROC analysis determined that the number of weeks over which treatment was delivered prior to the censored event with a cutoff ≤13.71 weeks (based on the Youden Index) best discriminated those who relapsed during the 30-week continuation phase (AUC: 0.756, SE: 0.073, 95% binomial exact CI: 0.643 to 0.848, *Z*=3.49, p=.0005), with 85.71% sensitivity and 69.12% specificity along with a PPV of 22.2% and NPV of 97.9%.

Regarding session frequency, the number of observed sessions completed prior to the censored event ranged from 0 to 16. The ROC analysis determined that the number of sessions completed by each participant prior to the censored event with a cutoff ≤8 sessions (based on the Youden Index) best discriminated those who relapsed during the 30-week continuation phase (AUC: 0.690, SE: 0.109, 95% binomial exact CI: 0.537 to 0.792, *Z*=1.74, p=.0819), with 85.71% sensitivity and 63.24% specificity along with a PPV of 19.4% and NPV of 97.7%.

Regarding session intensity, the average number of weeks to elapse between each individual session prior to the censored event ranged from 0 to 4.4. The ROC analysis determined that the average number of weeks to elapse between each session for each participant prior to the censored event with a cutoff ≤2 weeks (based on the Youden Index)

best discriminated those who relapsed during the 30-week continuation phase (AUC: 0.652, SE: 0.0783, 95% binomial exact CI: 0.534 to 0.759, Z=1.946, p=.0516), with 100% sensitivity and 42.65% specificity along with a PPV of 15.2% and NPV of 100%.

Regarding exposure, the number of minutes spent in treatment prior to the censored event ranged from 0 to 1110. The ROC analysis determined that the number of minutes spent in treatment by each participant prior to the censored event with a cutoff $\leq$595 minutes (based on the Youden Index) best discriminated those who relapsed during the 30-week continuation phase (AUC: 0.60, SE: 0.113, 95% binomial exact CI: 0.1474 to 0.711, Z=0.884, p=0.3765), with 85.71% sensitivity and 38.24% specificity along with a PPV of 12.5% and NPV of 96.3%.

Parent/Family Inclusion

A Cox Proportional Hazards Regression similar to the ones utilized for Aims 1a and 1b was also used to address Aim 1c. This Cox model was used to estimate the hazard of relapse from parent/family involvement across the 30-week continuation treatment trial. As a parent or family member participated in nearly every participant's treatment to some capacity (*n*=72) over the course of the 30-week treatment, parent/family involvement was measured by calculating the cumulative total number of minutes a parent or family member spent in treatment prior to the participant experiencing relapse/censored event, as opposed to cumulative number of sessions that were attended by the parent/family member. The mean number of sessions attended by a parent/family member was 6.73 (SD=3.62, range=16, median=7) with the average number of possible sessions attended reported at 8.44 (SD=3.51, range=16). The mean number of minutes that a parent/family member spent in treatment with the participant prior to the occurrence of relapse/censored

event was 149.83 minutes (SD=100.23, range=475.0 minutes). The Cox model showed that there was not a significant influence on risk of relapse based on amount of time parents or family members were involved in treatment (hazard ratio=0.998, 95% CI=0.989-1.007, χ^2=0.197, df=1, p=0.657). Further, there was not a statistically significant impact on hazard of relapse based on total cumulative number of sessions attended by a parent/family member (hazard ratio=0.219, 95% CI=0.005-8.742, χ^2=0.6521, df=1, p=0.4194).

CHAPTER 6

DISCUSSION

The overall aim of the present study was to make a contribution to the existing literature by exploring the most effective CBT treatment elements in the treatment of MDD among children and adolescents. More specifically, this study was designed to identify treatment characteristics that may serve as potential predictors of treatment outcome in pediatric depression. In doing so, this study explored the influence of individual CBT components, treatment dosage (e.g., frequency, exposure, length, and intensity), and the inclusion of parents or family members in treatment, in an attempt to determine factors related to the occurrence of relapse. Regarding the influence of specific CBT components, the primary hypothesis of the current study was that those participants enrolled in the combination treatment group who completed the problem solving and relapse-prevention components would endorse a superior response to treatment (i.e., reduced risk of relapse). In regard to treatment dosage, it was hypothesized that those participants who completed a greater number of CBT sessions overall, and those who were exposed to the greater amount of treatment, as defined by cumulative number of minutes in session, would boast a more positive treatment outcome, as measured by hazard of relapse. The final hypothesis of the current study focused on the inclusion of parent or family involvement in treatment, with the prediction that those participants whose treatment involved a more substantial amount of parent/family involvement, as measured by minutes in session, would report a reduced risk of relapse, overall.

Component Inclusion

Aim 1a of the current study was to evaluate if rate of relapse would be related to specific treatment components received in CBT treatment sessions. Based on the results of previous research on this subject, as well as the fact that this particular treatment program was specifically designed to focus on relapse prevention, it was hypothesized that those participants who completed the problem solving and relapse-prevention treatment components would be less likely to experience relapse by week 30 of their participation in the study. In the present study, there were no statistically significant findings regarding the association between receipt of specific components and the treatment outcome, which is contradictory with the findings from existing studies focused on similar populations. Specifically, in a study providing a CBT treatment intervention for adolescents with MDD, Kennard et al., (2009) reported that those adolescents who received social skills and problem-solving modules reported better outcomes at the end of treatment. In contrast, results from the current study indicate that there is not a higher risk of relapse based on which specific components are received or not received, which does not support the original hypothesis of the present study. However, it is important to recall that although the treatment offered in this treatment program was largely standardized, including introduction of core components (i.e., psychoeducation, behavioral activation, cognitive restructuring, problem solving) during the first 4 sessions, and specified time for practice and application, the intervention was also flexible in its design to fit the individual clinical needs of each participant on a case-by-case basis, as determined by the participant's assigned study therapist. As such, the direct comparison of each individual participant's treatment experience in this study is complex, and not ideal for the performed analyses, as

many of the participants may not have received several of the individual components at all depending on how long they remained in the intervention. In addition, the rate of relapse was low, which may have influenced these results, as this was the primary outcome variable explored. However, given that the average time to relapse for those 7 participants who experienced relapse within the 30 week treatment period was 18 weeks, this indicates that each of those participants had the opportunity to receive the majority, if not all, of the treatment components offered in this treatment program prior to experiencing relapse.

Given the lack of statistical significance during the original analysis, a "weight statement" was added to the Cox model during analysis to account for the varied number of sessions of each specific component completed by each participants (e.g., ratio of the number of cumulative times a session was completed, divided by the total number of times it was *possible* for a participant to receive the component prior to the occurrence of the censored event). However, due to the restricted range of possible CBT sessions, including that many participants never received specific components, the model was unable to perform this analysis. Further, as this study was not originally designed for the advanced analytic plan performed in the current study, there are limitations surrounding effect size and statistical power, which likely influenced the lack of statistical significance in this analysis. The frequency distribution of CBT sessions attended for each component can be found in Appendix B, Figure 2.

Ultimately, the specific findings of the current study indicate that neither the receipt of Wellness or Relapse-Prevention components were significantly influential regarding the hazard of relapse in this specific population. While these results imply that the receipt of specific components, or the lack of completion of specific components, will not influence

the hazard of relapse in this given population, these results are inconsistent with other studies. As such, a definitive conclusion should not be drawn regarding the importance of inclusion of specific components as it relates to the design of future interventions until further research has been conducted with a larger sample size and a design that is powered appropriately for the analyses utilized in the current study.

Treatment Dosage

The second aim of the present study was to evaluate the relationship between treatment dosage and overall treatment outcomes in this population. Similar to Aim 1a, the specific treatment outcome utilized in the current analyses was the occurrence of relapse. As aforementioned, treatment dosage was broken down into 4 primary variables: frequency (i.e., total number of sessions), exposure to treatment (i.e., total number of cumulative minutes spent in treatment), length of treatment (i.e., period of time over which treatment was delivered, as measured in weeks), and intensity of delivery of treatment (i.e., period of time between each individual session, as measured in weeks). It was predicted that those participants who completed the greatest number of sessions, as well as those who spent the most cumulative number of minutes in treatment would report a reduced hazard of relapse. Congruent with the primary hypothesis that a greater number of sessions would be associated with a reduced risk of relapse, the results of the present study indicate that those participants who attended a greater number of sessions had a smaller hazard of experiencing relapse across the 30 week treatment period. Further, based on the results of the ROC analysis, the identified cutpoint of 8 sessions indicates that a therapy client should attend at least 8 sessions of treatment in order to experience a reduced risk of relapse. This finding is congruent with results from previous research (TORDIA; Kennard

et al., 2009) that identified a cutpoint of 9 therapy sessions that was related to better outcomes. However, the second aspect of this hypothesis that predicted that the greater number of cumulative minutes one spends in session would be associated with superior outcomes was not found to be true in the current analyses. Indeed, there was not a statistically significant difference in the hazard of relapse based upon cumulative number of minutes spent in session. These results suggest that those participants who participated in a greater amount of time in session overall, did not necessarily benefit more greatly from this extended period of face-to-face interaction with his or her study therapist, as compared to those participants who spent much less time cumulatively, in minutes, in session. Thus, number of sessions appears to be more important to positive treatment outcome compared to total duration of session time, which is congruent with the observational results from a review performed by Cuijpers and colleagues (2013) that indicated that brief therapy (e.g., length of treatment) with brief session length (e.g., duration), but a higher frequency of sessions may be related to the best outcomes. As the current study examined total cumulative number of minutes spent in treatment overall (i.e., exposure), as opposed to the length of each individual session completed (e.g., 30 minute session versus 45 minute session) across the 30 week treatment, the current results do not indicate whether shorter individual sessions are superior to longer individual sessions, but merely that total exposure to treatment is not a significant factor in risk of relapse.

Ultimately, when exploring the results from the present study related to treatment dosage, although each variable independently offers important clinical information, it is perhaps even more discerning to consider how the results from each variable influence one another in treatment. For instance, the dosage variable of frequency specifically, the

current finding that receiving a greater number of sessions was associated with a reduced risk in relapse in this population bears significant clinical weight. This finding suggests to treatment providers that the greater number of times they have direct contact with each patient, the more likely their patient will be to avoid experiencing relapse. However, as was determined based on the review of the existing literature on this subject, consideration of a single dosage variable is insufficient when attempting to consider the influence of treatment dosage, as a whole. For instance, although receipt of a greater *number* of sessions demonstrated a reduced risk of relapse, the total *exposure* to treatment, as measured by minutes in treatment overall, indicated no significant influence on hazard of relapse. This is a clinically interesting finding given that a greater number of sessions would typically be associated with, or assumed to be related to, more cumulative time spent in session. This finding suggests that although experiencing a greater number of sessions is superior, the length of each individual session remains less important. When considering the age range of the current study (i.e., 8 years to 17 years), this is an important clinical finding as it indicates there is no direct benefit to demanding a child or adolescent be present in session for a long period of time, when a shorter period of time may have a similar or equivalent impact.

In addition to these two dosage variables, the influence of length of treatment (e.g., number of weeks over which treatment is delivered) is also an important consideration. The findings of the current study show that for every additional week over which treatment was delivered, the risk of relapse was reduced. By adding this finding to the aforementioned influence of frequency and exposure, it is suggested that the most influential combination of treatment dosage related to hazard of relapse is for a client to

attend a high number of sessions, regardless of length of individual session, delivered over a long period of time.

The final dosage variable to intertwine in the dosage combination is intensity of treatment (e.g., number of weeks that elapse between each individual session). Interestingly, analysis of this variable independently did not report a statistically significant relationship with hazard of relapse, which is in conflict with research that identifies intensity as an influential dosage variable (Cuijpers et al., 2013). However, upon further analysis, results suggest that when length of treatment is held constant, the greater number of weeks that elapse between each treatment session (i.e., intensity) results in an increase in the hazard of relapse. This finding indicates that when length of treatment is held constant, the greater period of time that passes between each session is related to a higher risk that relapse may occur. Overall, this suggests that it is more beneficial for a client to complete therapy sessions more closely together than to allow longer periods of time to pass (e.g., weekly sessions vs. biweekly sessions). This finding also carries important clinical weight as it relates to the other variables of dosage. Ultimately, in consideration of the four variables of treatment dosage collectively, the results from the current study imply that the most effective treatment dosage as it relates to risk of relapse in a depressed child or adolescent population, is that the client should attend a high number of sessions, regardless of length, over a long period of time, but with shorter time periods elapsing between each session.

Parent/Family Inclusion

Given that the original RCT was not powered to explore the influence of parent or family involvement, the limitations of addressing this aim are notable, and ultimately

prevent definitive conclusions from being drawn. Specifically, the vast majority of participants (*n*=72) enrolled in this study received some degree of involvement from a parent or family member during the CBT treatment portion of their participation. Analyses addressed hazard of relapse across 3 specific variations of parent/family involvement: attendance of a parent/family member at a treatment session; total (cumulative) number of sessions a parent/family member attended treatment; and total amount of time (cumulative) as measured in minutes parent/family member spent in session with the participant. Across all 3 of these separate analyses, which were entered into separate Cox models, there were no statistically significant findings regarding the influence of parent/family involvement in treatment. Given the small sample size as well as the lack of variability in number of family sessions among the sample, no formal inferences or conclusions related to family/parent involvement can be drawn at this time.

As aforementioned in the background section of this project, a notable contributing factor to the influence of parent or family involvement is the significant range in participant age. Given that each participant's treatment involved some individualization in their treatment plan as designed by their study therapist, the sheer amount of involvement of parent/family, whether measured by number of total sessions or by total number of minutes, was likely dictated by several factors. For instance, if the participant was under the age of 10, the therapist may have chosen to involve a parent or family member more frequently in order to help the child generalize skills learned in session through prompting and guidance by family at home. Further, the study therapist may have also included additional parent/family sessions for those participants who were a member of a less functional family as opposed to a family with higher levels of functioning and support.

Study Limitations

There are several limitations of the current study. Firstly, this study was not originally powered for a treatment component analysis, specifically to explore the evaluation of the relationship between receipt of CBT treatment components (as a binary indicator) and relapse status. As such, the sample size (n=75) was not large enough for this form of secondary analysis. Additionally, the current analyses were performed exclusively on those participants who were randomized into the combination treatment group, with all participants receiving psychotropic medication in addition to the CBT treatment. Therefore, the results of the current study may be confounded by the influence of psychotropic medication and not exclusively the impact of the CBT treatment. Specifically, given that all participants in the combination treatment group were prescribed medication throughout their participation in the CBT intervention, it is indeterminable what additional improvements in a participant's depression may have been due to the result of medication. If the psychotropic medication was reducing the participants' depressive symptoms, this could have impacted the existence of relapse rates. Overall, the specific influence of the medication on participants' improvement, and ultimately relapse rates, remains unknown, which is a notable limitation in the current study. Although the sample of participants in this study provided an excellent division of gender variability (i.e., 50.7% female), diversity is lacking regarding race and ethnicity, which may limit generalizability. In much the same way, age of participant is another potential limitation of the current study. As the age range for enrollment in the study was wide (i.e., 8 to 17 years), there is tremendous difference in maturity, developmental level, and family involvement across each participant. Although the vast majority of participants were over the age of 12 (>12

years = 74.7%), the remaining group of younger participants may have required additional support from family members in treatment, shorter treatment sessions due to attention level, varying severity level of depression, and additional sessions committed to psychoeducation and basic CBT principles. While age was controlled for in all analyses, a more homogenous sample may have allowed for a greater comparison of treatment. Another limitation of the current study relates to the fact that although the intervention maintained a standardized format with instruction on when to introduce core components and practice and application, several of the component modules provided to each participant past approximately session 8 were selected by the therapist. Indeed, although the modules that each therapist utilized provided the same standardized content for each participant who received them, the therapist maintained some flexibility and control over which modules each individual would receive on an as-needed, case-by-case basis. Therefore, many participants never received specific components at all, which limits the degree of comparison that can be made regarding risk of relapse. Finally, it is imperative to consider the limitation that given the unique continuation phase treatment design of the current study (e.g., acute/open treatment phase prior to continuation treatment phase), there is the potential that several participants could have already achieved a state of remission prior to the initiation of the CBT treatment phase. Additionally, given the continuation phase design of the study, the participants represent a small and specific subset of children and adolescents with depression as each participant was required to be identified as a "responder" to the acute phase pharmacological treatment in order to be randomized into the continuation phase segment of this study. Therefore, the results regarding dosage of the current study may not be generalizable to depressed children and adolescents as a

whole, particularly those youth who are being treated with acute care interventions. Furthermore, there was a very low number of participants in this sample who experienced relapse, which further limited the subset of depressed youth in this study. Ultimately, these factors limited the power and the generalizability of this study, especially to depressed youth in acute treatment settings where there is a larger range of depression severity and potential outcomes.

Clinical Implications & Directions for Future Research

Given the prevalence of depression in children and adolescents, identifying the most effective treatment content and method in which to deliver treatment across a variety of mental health settings is critical. The findings of the current study have several interesting clinical implications for development of future CBT treatment interventions for children and adolescents with MDD. Specifically, related to the variables of dosage and how treatment is disseminated to patients, given the results surrounding frequency, length, exposure, and intensity from the current study, there is much to be considered regarding how to most effectively approach the timeline and intensity of treatment.

Future psychosocial intervention studies should explore dosage and content variables that are related to positive treatment outcomes. For instance, given the results of the current study, smaller total number of minutes spent in treatment across sessions may be of equal benefit as a greater amount of time spent in treatment, when sessions are delivered more consistently and frequently. As such, this finding could influence the approach of treatment providers in how they choose to allocate their time with patients. Certainly more research is needed to further address the identification of specific CBT components that are associated with the most positive outcomes (e.g., reduced risk of

relapse, achievement of remission, reduction in symptoms, etc.), and there remains a call for other existing treatment programs to perform similar analyses to identify these components. In doing so, researchers and clinicians will be able to transform existing treatments and continue to grow in the development of the most effective treatment options available.

From a clinical perspective, the results of this study have the potential to be tremendously influential as it relates to treatment planning. For instance, based on the results of the present study, if intensity of session occurrence (e.g., weekly, bi-weekly, monthly, etc.) will reduce risk of relapsing when length of treatment is held constant, and total duration of minutes spent across treatment is less significantly related to outcome, shorter individual sessions could allow treatment providers to schedule more individual clients per day, thereby creating time to schedule sessions more closely together. Thus, from a provider perspective, the potential burden of more intense treatment for each client (e.g., less time elapsing between each session) may be limited as shorter sessions could also be implemented. Although this treatment scheduling may be less burdensome on treatment providers, the inconvenience may be more substantial for clients and their families as it would require more frequent trips to the treatment provider's office. While no cost analysis was included in this study, these findings have implications for treatment cost. Although in this circumstance, sessions would be shorter in length and therefore presumably less expensive, the increase in total number of sessions as well as the intensity at which they occur would likely contribute to an increase in treatment cost, overall. It is important for future researchers to continue to study the influence of treatment dosage on different outcome measures (e.g., remission, reduction of symptoms, etc.). If similar

findings relating dose to positive outcome are found, treatment dosage research could help support advocacy for mental health treatment compensation.

Conclusion

Although several of the hypotheses were not supported by the results in the current study, the findings presented in this project offer notable contributions to the existing body of literature related to the treatment of MDD in children and adolescents. In this study, although there were not statistically significant findings regarding the influence of specific individual CBT treatment components, the trend observed regarding hazard of relapse surrounding the components of Wellness and Relapse-Prevention indicated that those participants who received these components had a reduced risk of relapse than those participants who did not receive them.

As expected, and congruent with the hypothesis regarding dosage frequency, the results of the current study indicate that those participants who received more sessions of CBT overall demonstrated a reduced risk of relapse over a 30 week treatment period. Interestingly, however, length of overall treatment was found to be statistically significant with those participants whose treatment was longer reporting a reduced risk of relapse. Furthermore, when length of treatment was held constant, the intensity of treatment became statistically significant, with an increase in risk for relapse with increase in time between each individual session. This indicates that the greater period of time that elapses between each individual session, when overall treatment length is held constant, there is an increase in hazard of relapse. Ultimately, the results of the current study suggest that the most effective method of treatment delivery, as measured by risk of occurrence of relapse,

is a high volume of sessions over a long period of time, regardless of total exposure to treatment in minutes, with little time elapsing between each individual session.

Regarding the influence of parent or family involvement on hazard of relapse, in contrast with the original study hypothesis, there was not a statistically significant finding regarding the sheer attendance of a parent or family member in treatment, nor the amount of time a parent or family member spent in treatment (e.g., cumulative minutes in session). However, although these results were not significant, the reported hazard of relapse for those participants whose parents attended treatment was less than those participants whose parents were not involved in treatment. Overall, this finding, despite its lack of significance, suggests that additional research should be conducted with a larger sample to further pursue the true influence of parent or family involvement in treatment. Until such research is available, these findings suggest that the involvement of parents or family members in treatment likely has a positive outcome related to risk of relapse.

In sum, although several of the original hypotheses for the current study were not supported, the indications of the results are a promising contribution to the current field of literature and should be encouraging to researchers in this area of interest to continue pursuit of additional data to establish the most effective content and delivery of treatment to this specific population.

APPENDIX A

TABLES

Table 1. CBT Components used in a Select Group of Therapy Manuals Addressing Child and Adolescent Depression

	TADS (Wells & Curry, 2000)	**TORDIA** (Kennard et al., 2009)	**RP-CBT** (Kennard et al., 2014)	**CWD-A** (Lewinsohn et al., 1990)	**Pittsburg Trial** (Brent & Poling, 1997)
Psychoeducation	√		√	√	√
Cognitive Restructuring	√	√	√	√	√
Behavioral Activation	√	√	√	√	
Problem Solving	√	√	√	√	√
Parent/Family Session	√	√	√	√	√
Relaxation Training				√	
Social/Relationship Skills	√	√		√	√
Mood Monitoring			√	√	
Emotion Regulation		√			√
Communication Training				√	
Other Techniques		√	√		√

Table 2. Demographic Information & Clinical Characteristics of Combination Treatment Group (*n*=75)

Variables	N	%	Mean	SD
Age			13.5	2.7
≤11 years	19	25.3		
>12 years	56	74.7		
Gender				
Female	38	50.7		
Male	37	49.3		
Ethnicity				
Hispanic	23	30.7		
Non-Hispanic	52	69.3		
Race				
Caucasian	64	85.3		
African American	8	10.7		
Asian	1	1.3		
Multiracial	2	2.7		
Comorbid Anxiety	12	16.0		
Duration of Episode (weeks)			41.3	36.9
Number of Episodes			1.1	0.29
1	68	90.7		
2	7	9.3		
3	0	0		
4	0	0		
Number of Attempts				
0	66	88.0		
1	5	6.7		
≥2	4	5.3		
Baseline CGI Severity			5.1	0.7
Randomization CGI Severity			2.7	0.7
Baseline CDRS-R			56.8	7.1
Randomization CDRS-R			30.5	5.6

Table 3. Frequency of Delivery of CBT Components

CBT Component	**No. participants that received component**	**% participants that received component**
Psychoeducation	71	97.26
Behavioral Activation	69	94.52
Relapse Prevention	32	43.84
Cognitive Restructuring	63	86.30
Problem Solving	50	68.49
Emotion Regulation	17	23.29
Wellness	46	63.01
Family Communication	39	53.42

Table 4. Treatment Dosage Variables: Basic Statistical Measures

Dosage Variable	**Mean**	**Median**	**Range**	**Standard Deviation**
Frequency (sessions)	8.44	9.0	16.0	3.51
Exposure (minutes)	500.64	500.0	1110.0	238.1
Length of treatment (weeks)	14.87	17.0	23.29	7.03
Intensity (weeks)	1.88	1.88	4.40	0.74
Total session length (minutes)	58.25	60.0	120.0	14.20
Session length with participant only (minutes)	40.90	41.67	85.0	10.89

Table 5. CBT Components: Basic Statistical Measures *(How many total times was each component received prior to relapse/censored event?)*

CBT Component	**Mean**	**Range**	**Standard Deviation**
Psychoeducation	1.48	6.0	1.12
Behavioral Activation	2.04	9.0	1.69
Relapse Prevention	0.726	4.0	1.0
Cognitive Restructuring	1.74	6.0	1.41
Problem Solving	1.10	4.0	1.03
Emotion Regulation	0.41	4.0	0.85
Wellness	1.14	6.0	1.27
Family Communication	1.18	6.0	1.59

Table 6. Hazard Ratios for Select Individual CBT Components

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Wellness	1	-1.07906	0.802	1.812	0.178	0.340	0.071	1.636
Cognitive Restructuring	1	-1.28740	1.032	1.558	0.212	0.276	0.037	2.084
Relapse-Prevention	1	-1.54131	0.996	2.396	0.122	0.214	0.030	1.507
Problem Solving	1	0.16084	0.901	0.032	0.858	1.174	0.201	6.868
Emotion Regulation	1	-0.29993	1.008	0.089	0.766	0.741	0.103	5.344
Family Communication	1	0.05510	0.81985	0.005	0.946	1.057	0.212	5.270

Table 7. Hazard Ratios for Treatment Dosage

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Session frequency	1	-0.25792	0.11673	4.8822	0.0271	0.773	0.615	0.971
Exposure (cumulative minutes)	1	-0.00276	0.00192	2.0704	0.1502	0.997	0.994	1.001
Length (weeks)	1	-0.14751	0.05695	6.7085	0.0096	0.863	0.772	0.965
*Intensity (weeks)	1	1.29808	0.66761	3.7806	0.0518	3.662	0.990	13.552

*This data reflects intensity when length of treatment and treatment intensity are entered into the same Cox Proportional Hazards Regression, and length of treatment is held constant.

Table 8. Hazard Ratios for Parent/Family Involvement

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Parent/family attendance (number of sessions)	1	-1.51922	1.88137	0.6521	0.4194	0.219	0.005	8.742
Parent/family involvement (minutes)	1	-0.00210	0.00472	0.197	0.657	0.998	0.989	1.008

Table 9. Parent/Family Involvement: Basic Statistical Measures

Parent/Family Variable	Mean	Median	Range	Standard Deviation
Total sessions attended	6.73	7.0	16.0	3.62
Possible number of attended sessions	8.44	9.0	16.0	3.51
Session length with parent/family member and individual (minutes)	17.15	17.14	75.0	8.49

Table 10. Posterior summary results from fitting a Bayesian logistical regression model to relapse as a function of the Wellness treatment component from 50,000 Monte Carlo Samples

Relapse Response						
			Percentiles			
Posterior parameter	Mean estimate	Standard deviation	25%	50%	75%	95% HPD Credible Interval
Wellness component received	0.5129	0.5573	0.2002	0.6289	0.6341	0.0119 to 1.4246

Note. The 95% Highest Posterior Density (HPD) Credible Interval is an interval (or region) with a 0.95 probability of containing the posterior mean parameter. The Geweke test statistics (not shown) indicated convergence of the Markov chain Monte Carlo (p's > 0.57).

Table 11. Posterior summary results from fitting a Bayesian logistical regression model to relapse as a function of the Relapse-Prevention treatment component from 50,000 Monte Carlo Samples

Relapse Response						
			Percentiles			
Posterior parameter	Mean estimate	Standard deviation	25%	50%	75%	95% HPD Credible Interval
Relapse-Prevention component received	0.2171	0.2694	0.0531	0.1312	0.2784	0.00148 to 0.7055

Note. The 95% Highest Posterior Density (HPD) Credible Interval is an interval (or region) with a 0.95 probability of containing the posterior mean parameter. The Geweke test statistics (not shown) indicated convergence of the Markov chain Monte Carlo (p's > 0.62)

APPENDIX B

FIGURES

Figure 1. CONSORT Diagram of Study Participants

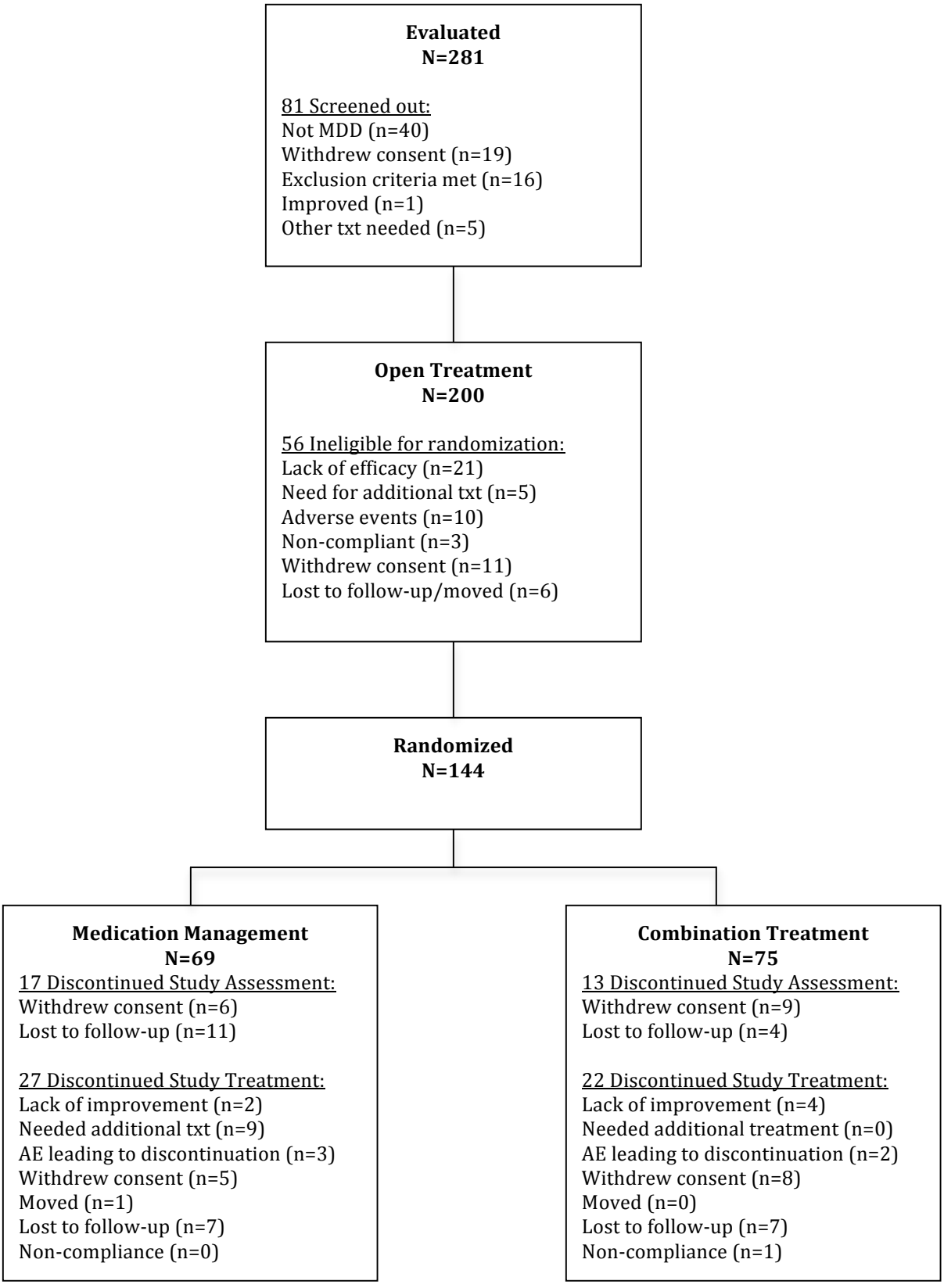
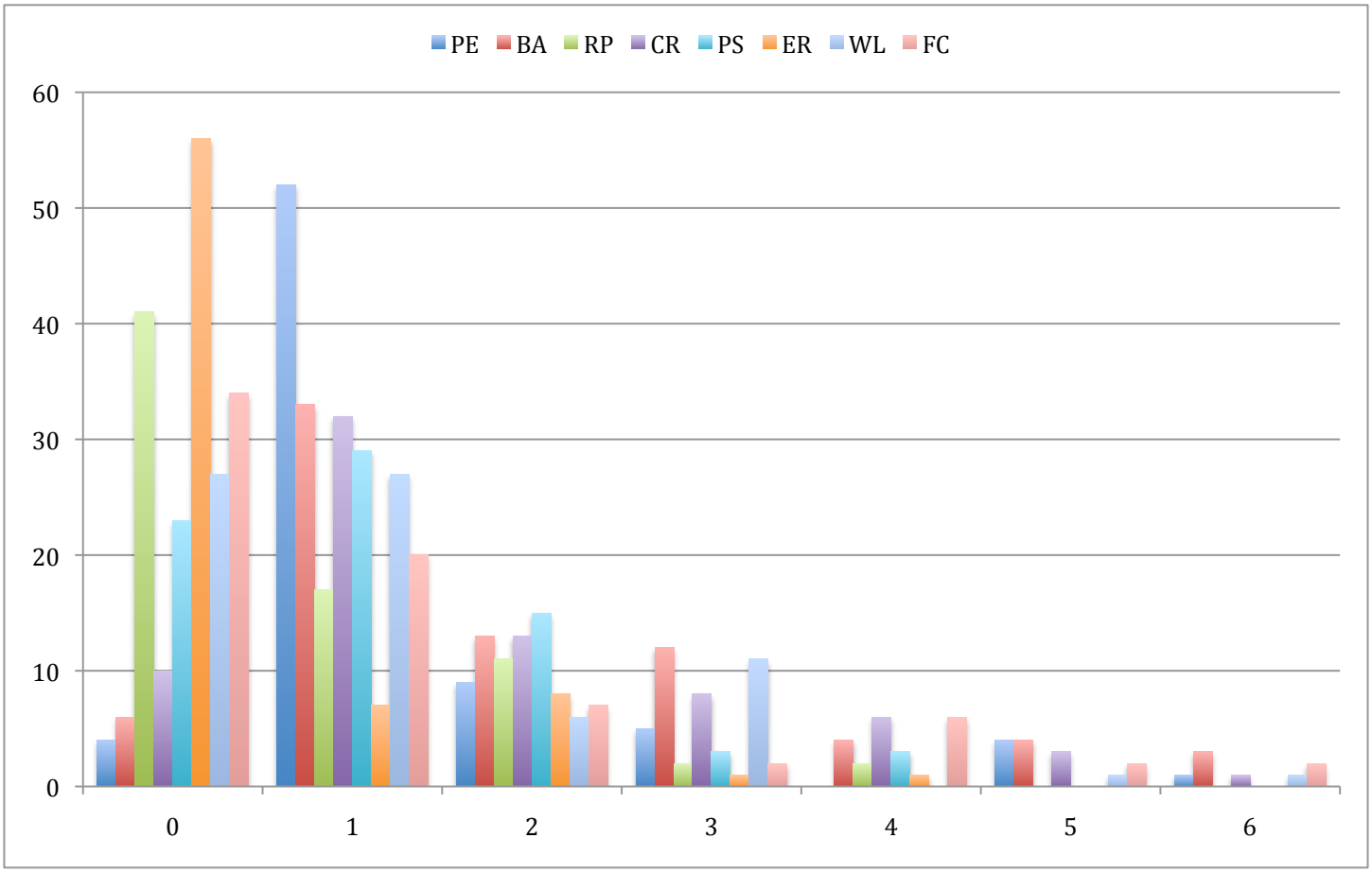


Figure 2. Total Number of Times CBT Components were Completed by Study Participant Prior to Censored Event

(PE = psychoeducation; BA = behavioral activation; RP = relapse-prevention; CR = cognitive restructuring; PS = problem solving; ER = emotion regulation; WL = wellness; FC = family communication)



X axis: Number of times a session was completed
Y axis: Number of participants who completed the session

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