THE "IGNORED COMMON FACTOR": THE ROLE OF EXPECTANCY

IN THE TREATMENT OF ADOLESCENT DEPRESSION

by

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Since Rosenzweig's "Dodo Bird Verdict" in 1936, the "common" versus "specific" factors debate has continued to polarize the field of psychotherapy. Treatment expectancy is an important but often overlooked common factor. The current study investigated the role of treatment expectancy in the Treatment of Adolescents with Depression Study (TADS). Four-hundred three adolescents (M_{age}=14.62, SD=1.56) filled out the Treatment Expectancy for Adolescents (TEA) measure prior to treatment randomization to one of four treatments: fluoxetine (FLX), cognitive behavior therapy (CBT), their combination (COMB), and placebo (PBO). Adolescents randomized to CBT or COMB also filled out the CBT Rationale Acceptance and Expectation for Improvement (C-RAEI) form during their second session of CBT.

Before finding out their treatment assignments, adolescents endorsed higher treatment expectancies for COMB than CBT and medication only. Family income levels below $75,000 and higher levels of depression severity, hopelessness, and suicidality

were associated with lower expectations for improvement with CBT. The presence of a comorbid anxiety disorder diagnosis was associated with lower expectations for medication without CBT. Separate random coefficients and logistic regression models identified treatment expectancy as a predictor of outcome for three primary outcome measures in TADS, irrespective of treatment assignment. Severity of depression moderated this relationship; mild to moderately depressed adolescents appeared to be more sensitive to the effects of treatment expectancy than marked to severely depressed adolescents. The opposite results were found for the self-rated outcome measure in TADS based on the C-RAIE. For marked to severely depressed adolescents assigned to CBT or COMB, acceptance of treatment rationale and expectancy for improvement were associated with treatment response.

These results suggest that treatment expectancy is an important common factor of treatment for mild to moderately depressed adolescents prior to treatment initiation, although it may be especially important for initially skeptical, marked to severely depressed adolescents to "buy in" to treatment after treatment initiation. Treatment effects were still found after controlling for the effects of treatment expectancy on outcome. It seems that both the "common" factor of treatment expectancy and the "specific" factor of treatment assignment contributed to outcome in TADS.

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This is dedicated to my parents, and to Will.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER I

INTRODUCTION

For more than 50 years, researchers have speculated on the role of expectancy in psychotherapeutic outcome (Frank, 1958, 1968; Greenberg, Constantino, & Bruce, 2006). Preceding Smith and Glass' (1977) controversial meta-analysis concluding that psychotherapies produce similar outcomes due to the "common factors" of therapy (i.e. underlying factors, such as therapeutic alliance, that cut across different treatment modalities) as opposed to the "specific factors" of therapy (i.e. case formulations and techniques specific to a given therapy), Frank (1973) identified "outcome expectancy," defined as expectancy for improvement, as a common factor inherent in many forms of healing, including psychotherapy, shamanistic healing, and improvement with placebo. Related constructs in psychology include the "self-fulfilling prophecy" (Merton, 1948) and "response expectancy" *(*Kirsh, 1985), both of which describe how expectations precede and influence future events through changes in a person's behavior.

Despite early interest in expectancy and its influence on treatment outcome, research in this area has been sporadic and inconclusive. Some studies have found a positive association between expectancy and improved outcome (Sotsky et al., 1991; Chambless & Tran, 1997; Price, Anderson, & Henrich, 2008), while other studies have not demonstrated such a relationship (Borkovec, Newman, Pincus, & Lytle, 2002; Chambless, Tran, & Glass, 1997). Reasons for these discrepant findings are varied and include the lack of standard assessments of expectancy, as well as differences in definitions and conceptualizations of expectancy. For example, researchers often do not

distinguish between *overall* expectancy for improvement with or without treatment (e.g.

"I expect things will get better over time.") and expectancy particular to a given treatment

(e.g. "Tylenol will cure my headache."). This distinction is important because overall

expectancy and treatment expectancy may correlate with different variables (e.g.

hopefulness and belief in a "just world" in the case of overall expectancy and acceptance

of treatment rationale in the case of treatment expectancy), and arguably are not same

construct. Other reasons for the discrepant findings in the expectancy literature include

differences between sample participants and treatments, blinding procedures, statistical

analyses, and sequencing of assessments.

Given its potential impact on treatment outcome, surprisingly little research has

been devoted to clarifying the role of expectancy in treatment. Indeed, Weinberger and

Eig (1999) have labeled expectancy "the ignored common factor in psychotherapy" (pg.

357). This is in spite of the fact that the majority of psychotherapies, as well as

pharmacotherapies, include providing a rationale for treatment to clients (in the case of

psychology), patients (in the case of psychiatry), and participants (in the case of research)

as an important first step of treatment. For example, researchers in the area of stress

management, Shaw and Blanchard (1983), concluded,

> Giving participants a high initial expectation of therapeutic benefit from
> stress management training has significant benefit in terms of change and
> reduced physiological reactivity…the procedures, per se, are not
> especially powerful without the appropriate set (pg. 564).

However, the importance of such an "appropriate set" has not been convincingly

demonstrated; it is unclear to what extent treatment expectancy influences treatment

outcome. Also, few studies have investigated possible mediators and moderators of the relationship between treatment expectancy and outcome.

The main purpose of my dissertation is to better understand the role of treatment expectancy in determining treatment outcome through a closer examination of the Treatment for Adolescents with Depression Study (TADS). Previous expectancy research has focused primarily on adults in studies with one or two treatment conditions. TADS provides a unique opportunity to investigate the role of expectancy in adolescents with depression randomly assigned to Cognitive Behavioral Therapy (CBT), fluoxetine (FLX), the combination of the two treatments (COMB), and placebo (PBO). Despite an impressive number of studies investigating the efficacy and effectiveness of various treatments for depression over the past several decades, it is still unclear who will respond to a particular treatment and through what mechanism(s). This is particularly true for the treatment of adolescents with depression. By understanding the role of treatment expectancy in TADS, it may be possible to improve treatment matching strategies and response rates for this growing population. More broadly, this area of research has implications for blinded, randomized clinical research trials and the common versus specific factors debate in psychotherapy research.

Response Expectancy

Treatment expectancy falls under the broader category of "response expectancies." Kirsch (1997) defined response expectancy as "the anticipation of automatic, subjective, and behavioral responses to particular situational cues (pg. 69)." He discusses the power of response expectancy with the example of Southworth and

Kirsch's 1988 study on the effects of *in vivo* exposure on agoraphobia. Participants were asked to walk away from their home ten times during a two-week period until they became anxious and then to return home. Half of the participants were told that the purpose of this exercise was to reduce their anxiety over time, while the other half were told that this was part of the assessment process preceding treatment. The first group reported greater and more rapid reductions in anxiety levels compared with the latter group who were led to believe that their anxiety levels would not go down during this time. Kirsch asserts that the therapeutic effects of *in vivo* exposure can be "suppressed" by manipulating response expectancies or "disguising" a treatment's therapeutic intent (pg. 71). Alternatively, the study also suggests that response expectancy may account for a significant amount of the effects of exposure therapy.

Numerous other examples of the powerful effects of response expectancy exist in the literature, including studies indicating physiological changes and improved motor task performance (Fillmore & Vogel-Sprott, 1992; Kirsch & Weixel, 1988) and the induction of symptoms of mass psychogenic illness (Lorber, Mazzoni, & Kirsch, 2007). In Lorber, Mazzoni, and Kirsch's 2007 study, participants who believed they had inhaled environmental toxins experienced symptoms specific to the type of toxin. The investigators concluded that response expectancy is specific to one's expectations. Thus, if an individual believes that an antidepressant will improve only his/her symptoms of depression (e.g. feeling "blue"), changes in the person's anxiety levels would not be explained by response expectancy alone.

The Placebo Effect

According to Kirsch, among the various examples of response expectancy effects, the placebo effect is its "prototype" (pg. 70; Kirsch, 1997). The placebo, often consisting of little more than sugar, is commonly referred to as an "inactive" substance or treatment. However, research subjects who are assigned to the placebo condition in these studies often *actively* respond to placebo pills, presumably through response expectancy effects. While there are a growing number of researchers involved in investigating the placebo effect in pharmacological clinical research trials, most researchers continue to regard the placebo effect as a nuisance to be minimized. The placebo effect is seen as "noise," masking the effects of the comparison treatment(s) under investigation.

While the placebo effect has a relatively long history in treatment outcome research, Hrobjartsson and Gotzsche (2004) found no evidence for a placebo effect in their meta-analysis, which included studies investigating treatments for 46 clinical conditions, including nausea, smoking, and depression. Wampold and colleagues (2005) criticized this particular meta-analysis for its use of such diverse clinical conditions and separated the same studies based on adequacy of study design and the degree to which disorders were amenable to psychological factors (as rated by independent evaluators). The results of this re-analysis indicated the presence of a placebo response in studies of conditions judged to be amenable, or susceptible to psychological factors, such as depression, insomnia, and chronic pain, as opposed to bacterial infection and anemia. For conditions judged to be amenable to the placebo effect, participants assigned to placebo were more likely to improve than participants assigned to wait-list or no-treatment.

Indeed, participants receiving placebo demonstrated rates of improvement approaching those of participants receiving "active" medications, such as antidepressants.

Interestingly, research suggests that depression is particularly susceptible to the placebo effect. In an analysis of the results of meta-analyses across the major mental disorders in the mid-1980's conducted by the Quality Assurance Project (1982-1985), Andrews (2001) reported that depression had the highest rates of placebo response, followed by generalized anxiety disorder, agoraphobia, obsessive-compulsive disorder, and schizophrenia, which was not shown to have a placebo effect. Andrews speculated that depression is the most sensitive to the encouraging effect of being in treatment, highlighting depression's high spontaneous remission rates (Kendler et al., 1997; McLeod, et al. 1992).

Notably, effect sizes for the drug treatments included in Andrews' analysis ranged from .44 to more than ten times this effect size at 4.77, while the effect sizes for the placebo treatments ranged from .10 to more than twenty times this effect size at 2.28. For the psychotherapy conditions, the effect sizes ranged from .67 to 2.87, while the effects for the wait-list/no-treatment control conditions ranged from -1.45 to -.28. The wide range of effect sizes across these various treatments suggests that there are a number of factors that contribute to outcome besides the specific effects of individual treatments. One factor that may contribute to the variability of drug-placebo differences between studies is differences in integrity of the blind. Effective blinding procedures minimize expectancy effects, while ineffective blinding procedures do not.

Double-Blind, Placebo-Controlled Clinical Research Trials

Double-blind, placebo-controlled clinical research trials are the "gold standard" in treatment outcome research within the field of psychiatry (Day & Altman, 2000). Medications are deemed effective if they are able to outperform placebo in studies where treatment expectancy effects are minimized through the use of "blinded" conditions. A study is considered "double-blind" when both study participants and independent evaluators are unaware of participants' assigned treatment conditions. Based on the gold standard status of double-blind, placebo-controlled clinical research trials and the Consolidated Standards of Reporting Trials' (CONSORT) recommendation for researchers to routinely report on the integrity of study blindness (Moher, Schulz, & Altman, 2001) it seems that an underlying assumption in psychiatry (and medicine in general) is that treatment expectancy is, indeed, quite powerful and necessary to control for through the use of placebo. Yet the integrity of blind of clinical research trials is seldom assessed.

Between 1998 and 2001, only eight of 94 double-blind trials with adult populations published in four of the top-tier psychiatry journals assessed the success of blinding procedures with half of these studies indicating "imperfect" blind (Fergusson, Glass, Waring, & Shapiro, 2004). Previous studies have found that between 67-88% of independent evaluators and research participants are able to correctly identify participants' treatment conditions (Brownell & Stunkard, 1982; Margraf et al., 1991; Rabkin et al., 1986; Vitiello, Davis, Greenhill, & Pine, 2006). In an earlier review of psychotropic drug trials, Fisher and Greenberg (1993) found that 23 of 26 double-blind adult studies reported patients and/or physicians were able to differentiate active from

7

placebo conditions at rates significantly greater than chance, raising questions regarding the validity of published study results (Fisher & Greenberg, 1993).

However, since most assessments of blinding occur at the end of research trials, it is often difficult to determine if a breakdown of blind precedes or follows symptom improvement. In the latter case, independent evaluators and research participants may base their treatment attributions on symptom improvement, and the study's validity is not threatened. As stated by Senn (2004), "The whole point of a successful double-blind trial is that there should be un-blinding through efficacy… If the treatments are not distinguishable at all, then the treatments have not been proved different (pg. 1135)." Essentially, a study remains valid if attribution to active treatment occurs across conditions based on symptom improvement alone (Vitiello, Davis, Greenhill, & Pine, 2006). In contrast, rater bias (also referred to as "observer" or "ascertainment" bias) occurs when rater knowledge of treatment assignment directly affects outcome ratings and may inflate the differences between treatment and control groups (Marcus et al., 2006). If subjects are aware of their assigned conditions, the medication effect is likely to be overestimated, while the placebo effect likely to be underestimated (Sapirstein, 1995).

Despite the likelihood that treatment expectancy effects influence treatment outcome in combination with imperfect blinding procedures, thus inflating drug-placebo differences, high rates of placebo response continue to challenge the efficacy of "active" medications. The high rates of placebo response in clinical research trials of antidepressants, especially, have been used to cast doubt on the actual efficacy of these medications (Kirsch & Sapirstein, 1998; Kirsch et al., 2002). In a meta-analysis of double-blind pharmacotherapy studies for depression, Sapirstein (1995) estimated that

8

25% of the response to antidepressants is due to the passage of time, 50% to expectancy, and only 25% to the "active" ingredients of medication. Interestingly, Sapirstein found that the placebo response was proportional to the drug response (r=.87), such that the greater the drug effect, the greater the placebo effect.

Similarly, in a controversial meta-analysis, Kirsch and colleagues (2002) investigated the results of 47 randomized placebo controlled short-term efficacy trials submitted to the FDA for the six most widely prescribed antidepressant drugs approved within the study period (1987-1999). The authors concluded that the placebo response accounted for 80% of the response to these antidepressants, while the active ingredients of medication accounted for approximately a two point difference on the 17 and 21-item Hamilton Depression Scales (HAM-D-17 & HAM-D-21; Hamilton, 1960) between active medications and placebo, which is clinically insignificant. Based on their results, the investigators concluded that there is little meaningful difference between antidepressants and placebos in terms of short-term efficacy.

Previous research, however, suggests that the placebo response is less likely to occur in more severe forms of psychopathology (Shapiro & Shapiro, 1997). Indeed, the ability to treat severe depression is the most noted difference between antidepressants and placebos (Khan et al., 2002; Wilcox et al., 1992; Fairchild et al., 1986). Moreover, as Kirsch and colleagues (2002) note, pharmacological effects of antidepressants are negligible only *if drug and placebo effects are additive*. It is uncertain whether or not this is the case since two treatments that lead to the same outcome may have different mechanisms for improvement. Individuals who respond well to placebo may not respond as well to medication and vice versa.

9

In a 2002 study using functional brain imaging of depressed male inpatients randomized to six weeks of placebo or fluoxetine treatment, Mayberg and colleagues found that treatment response for both the medication and placebo conditions was associated with significant regional metabolic changes in glucose metabolism in the neocortical and limbic-paralimbic regions of the brain. Although placebo and medication responders seemed to respond equally well to treatment (as measured by the HAM-D-17), fluoxetine treatment responders generally showed greater magnitudes of change covering greater volumes of area in these regions. Fluoxetine response was associated with unique increases in brainstem metabolism and metabolic decreases in the stiratum, hippocampus, and anterior insula. The results of this study suggest different, although heavily overlapping changes in the brains of individuals who respond to placebo versus medication.

In summary, placebo response rates in double-blind, placebo-controlled clinical research trials tend to be high, despite the fact that most participants and independent evaluators are able to correctly guess participants' assigned treatments at rates exceeding chance level. The integrity of the blind in treatment outcome studies of pharmacotherapy is under-examined with the likelihood of inflated drug-placebo differences due to rater bias and/or treatment expectancy effects. Although the high rates of placebo response have cast doubt on the actual efficacy of antidepressants, it is more accurate to state that both placebo and antidepressant treatment are effective treatments for depression. A preliminary brain imaging study suggests that antidepressants and placebo response involves overlapping, though non-identical response pathways. Therefore, it is likely that there are "common" factors, such as treatment expectancy, in both antidepressants and

placebo that contribute to treatment response, and specific, non-overlapping factors, as well.

Expectancy as a "Common Factor" in Psychotherapy Research

Meanwhile, it is extremely difficult to construct a "placebo therapy" that is identical to the therapy under investigation minus the therapy's "active" ingredients. As Klein (1997) points out, a dismantling process where specific elements of a particular psychotherapy will also affect other factors, such as the therapeutic nature of the relationship (instructional vs. collaborative, etc.), and the resulting therapy control condition will not be identical to the comparison treatment in all but the "active" aspects of the treatment. For this reason, supportive counseling or treatment as usual are used as comparison treatments in psychotherapy research. Supportive counseling includes "common" ingredients/factors (e.g. warmth, authenticity, active listening on the part of the therapist, and the verbal account ad organization of experience on the part of the client, etc.) that cut across various psychotherapies (e.g. Psychodynamic Therapy, Cognitive Behavioral Therapy, Person-Centered Therapy, Dialectical Behavioral Therapy, Acceptance and Commitment Therapy, Humanistic Therapy, Interpersonal Therapy, Narrative Therapy, Relational Cultural Therapy, Gestalt Therapy, Problem Solving Therapy, Prolonged Exposure Therapy, etc.).

Rosenzweig (1936) was the first to identify common components or factors that cut across different psychotherapeutic treatment models. These so-called "common factors" of therapy include the factors listed above, as well as client motivation and expectancy, a working therapeutic relationship, client's increased mastery and self-esteem from therapy and the process of finding new ways to conceptualize one's

problems (Parloff, 1986). According to Rosenzweig, these common factors are responsible for the efficacy of psychotherapy; thus, specific treatment differences have minimal effect on outcome. To emphasize this point, he quoted the Dodo bird from Alice in Wonderland, who stated, "Everybody has won, and all must have prizes" (p. 412, Carroll 1865).

Since Rosenzweig's "Dodo Bird Verdict," a number of researchers have investigated the role of common factors in psychotherapy. Luborsky, Singer, and Luborsky (1975) reviewed the psychotherapy outcome literature and provided support for the Dodo Bird Verdict. Shortly thereafter, Smith and Glass (1977) were the first investigators to conduct a meta-analysis comparing behavioral psychotherapies to non-behavioral psychotherapies. The investigators did not find a significant difference between the two types of treatment in terms of effect sizes. In a subsequent meta-analysis, Wampold (2001) estimated that specific effects account for 8% of the variance in psychotherapy outcome, while common factors account for 70% of the variance, whereas unexplained effects account for the remainder of psychotherapy outcome variance (22%). These results were met with much criticism, including the averaging of effect sizes across outcome measures (which may blur differences in effect sizes on target measures), the preponderance of cognitive behavioral therapies included in the meta-analysis, and the inclusion of a large number of studies focusing on convenience samples (e.g. college students) with mild symptoms (e.g. test anxiety; Crits-Christoph, 1997).

The "common" versus "specific" factors of therapy debate continues to polarize psychologists in the field of treatment-outcome research. However, most would agree that common factors play a significant role in determining treatment outcome. Among a

large number of so-called "common factors," clients' expectancy for improvement seems especially important. Lambert (1992), for example, identified a four-factor model of change based upon his review of empirically based treatment outcome studies: 1) extra-therapeutic change factors, 2) common factors, 3) technique factors, and 4) expectancy factors. Based on his review, he estimated that 40% of client improvement is based on client variables and extratherapy factors (e.g. the client's environment and strengths), 15% to specific technique factors (e.g. the "empty chair" technique in Gestalt Therapy), 30% to relationship factors (e.g. therapist warmth), and the remaining 15% to expectancy effects. According to his analysis, expectancy is as important as specific treatment techniques and models, which is responsible for a relatively small though significant percentage of client improvement.

Investigating Lambert's four-factor model (dubbed "the Big Four"), Thomas (2006) asked both therapists and their clients at a university clinic to assign percentages to each of these four factors based on their perceived contribution to change during therapy. Therapists assigned percentages in the following order on average: the therapeutic relationship (35%), client's hope/expectancy (27%), client's extra-therapeutic factors (22%), and specific models/techniques (16%). The mean percentages for client ratings were hope/expectancy (30%), the therapeutic relationship (29%), specific models/techniques (28%), and extra-therapeutic factors (13%). Both the therapists and the clients in this study attributed approximately 1/3 of change in therapy to expectancy effects, which is larger than Lambert had estimated. Taken together, it seems that researchers, therapists, *and* clients believe that expectancy plays a significant role in

treatment outcome, although disagreement exists as to what extent. This disagreement is reflected in treatment expectancy research within the field of psychotherapy.

Expectancy in Psychotherapy Research Trials

In a review of 24 studies that assessed expectancy for improvement and its relationship to treatment outcome, Arnkoff, Glass, and Shapiro (2002) found support for a positive relationship in 12 studies, mixed support in seven studies, and null findings in the remaining five studies. Noble, Douglas, and Newman (2001) also reviewed the literature and found a curvilinear relationship between expectancy and outcome, where individuals with moderate expectations for improvements showed more improvement than those with very high or very low expectations. It seems that the relationship between expectancy and treatment outcome is not straightforward. As mentioned previously, differences in definitions and measures of expectancy, timing of assessments, blinding procedures, treatments, and sample characteristics offer some explanation for these discrepant findings.

Most of the research on expectancy in psychotherapy clinical research trials has focused on the treatment of anxiety. For example, in a study investigating the efficacy of group CBT for the treatment of social phobia, Safren, Heimberg, and Juster (1997) found that treatment expectancy, as measured by the Reaction to Treatment Questionnaire (RTQ; Holt & Heimberg, 1990), predicted post-treatment severity of social phobia after controlling for initial severity of symptoms. The RTQ assesses clients' confidence that treatment will eliminate their social anxiety in specific social situations. Initial RTQ ratings were negatively correlated with severity and duration of social anxiety and

14

depressive symptoms. RTQ scores were also correlated with level of education; individuals who had completed some postgraduate education had higher expectations for improvement than individuals who had not completed high school. One possible explanation for this finding is that level of education may be correlated with confidence in one's ability to master cognitive-behavioral techniques and benefit from treatment. In addition to predicting a decrease of anxiety symptoms, overall RTQ also predicted changes in depressive symptoms. It is possible that expectancy effects may not be limited to an individual's specific expectations (i.e. improvement of anxiety alone), although participants' expectancy for improvement of their depressive symptoms, or improvement in general, were not assessed.

Similarly, Chambless, Tran, and Glass (1997) assessed treatment expectancy using a four-item treatment expectancy scale (Borkovec & Nau, 1972) in a sample of participants receiving group CBT for social phobia. Participants were administered the measure, which included a question about the perceived credibility of CBT, after they had received a rationale for the treatment. Consistent with Saffren, Heimberg, and Juster's findings, higher treatment expectancies and the perceived credibility of treatment were predictive of improvement on measures of social anxiety. Since depressive symptoms were predictive of both poor outcome and lower expectations for improvement, the investigators controlled for the overlap of depressive symptoms and treatment expectancy.

Positive findings have also been demonstrated for short-term therapy for speech anxiety (Kirsh & Henry, 1977, 1979) and the treatment of specific phobias. Price, Anderson, and Heinrich (2008) conducted an analysis using hierarchical linear modeling

15

in a sample of participants receiving either virtual reality exposure (VR) or in vivo exposure for flying phobia (Rothbaum, Anderson, Zimand, Hodges, Lang, & Wilson, 2006). They adapted Borkovec and Nau's 1972 measure of expectancy to include the following three statement ratings: 1) Confidence that therapy would reduce fear of flying-related symptoms, 2) confidence that therapy would reduce other fears, and 3) how logical treatment seemed. Because the three items demonstrated less than satisfactory internal consistency, it was decided that the first item would be used alone to measure treatment expectancy. Confidence that therapy would reduce fear of flying-related symptoms predicted treatment gains made during therapy but not during follow-up.

However, in a study of participants with panic disorder and agoraphobia randomized to alprazolam and exposure (AE), placebo and exposure (PE), alprazolam and relaxation (AR), or placebo and relaxation (PR), treatment expectancy did not predict treatment outcome (Basoglu, Marks, Swinson, Noshirvani, O'Sullivan, & Koch, 1994). Participants were asked to rate their perceived benefit from "psychological treatment" and "drug treatment" prior to treatment initiation, but were not asked to differentiate between exposure and relaxation training. Additionally, they were not asked to rate their perceived benefit from combination treatment, which is important since each participant received a combination of pills and psychotherapy. In a follow-up study, higher treatment expectations for pharmacotherapy were found to be associated with greater attributions for improvement to drug treatment in treatment responders (Basoglu, Marks, Kilic, Brewin, & Swinson, 1994). Greater attribution of improvement to medications predicted more severe withdrawal effects and a relapse of symptoms during follow-up, although treatment expectancy alone did not emerge as a predictor.

16

Vogel, Hansen, Stiles, and Gotesman (2006) also failed to find a relationship between treatment expectancy and outcome in a study investigating the efficacy of CBT for Obsessive Compulsive Disorder. In their study, treatment expectancy was assessed on a scale from 0-100 with higher scores indicating greater confidence in CBT as a treatment for OCD. The investigators found a relationship between positive helping alliance and decreased severity of OCD symptoms post-treatment. It may be that expectancy has a greater variability of impact due to clients' presenting concerns/diagnoses (e.g. OCD versus social phobia), compared to the therapeutic relationship.

Relatively fewer studies have been conducted on expectancy and mood disorders. Gaudiano and Miller (2006) investigated the role of expectancy on outcome in adults treated for bipolar disorder with semi-structured pharmacotherapy with or without family psychoeducation group therapy. Utilizing the four-item Credibility and Expectancy Scale (CES; e.g. "This treatment will be successful in eliminating symptoms of bipolar disorder; Borkovec & Nau, 1972), the investigators found a significant relationship between pre-treatment expectancy levels, patient and doctor-rated alliance, and long-term outcome in bipolar patients treated with pharmacotherapy for up to 28 months following an acute episode of either mania or depression. This study is noteworthy in that the focus of the outcome was long-term and investigated the roles of both expectancy and therapeutic alliance.

Treatment expectancy, but not "global" expectancy (i.e. "How do you think things will most likely be this time of year from now?") also predicted both treatment alliance and outcome in the Treatment of Depression Collaborative Research Program (TDCRP) funded by the National Institute of Mental Health (Stotsky et al., 1991). The TDCRP

17

compared Interpersonal Therapy (IPT), CBT, imipramine plus clinical management, and placebo plus clinical management for the treatment of depression. Meyer and colleagues (2002) found that the quality of therapeutic alliance mediated the relationship between treatment expectancy and improvement of depressive symptoms in a follow-up analysis. They concluded that participants with higher expectancies for improvement were more likely to engage in session with their treatment providers, which in turn led to symptom reduction.

The hypothesis that expectancy impacts treatment outcome by increasing treatment engagement is consistent with the finding that early homework adherence mediated the relationship between *overall* expectancy and improved outcomes in adults treated with group CBT for anxiety (Westra, Marcus, & Dozois, 2007). The investigators used the Anxiety Change Expectancy Scale (ACES; Dozois & Estra, 2005) to measure expectancy, which asked participants to rate their agreement with statements such as "I feel pessimistic that my anxiety problems could ever change for the better." They found a mediation effect for Generalized Anxiety Disorder and Panic Disorder, but not for Social Phobia, perhaps due to this latter group's small sample size and poorer outcome. It is unclear if homework completion also mediates the relationship between treatment expectancy and outcome.

In addition to identifying possible mediators between treatment expectancy and outcome, attempts have been made to manipulate treatment expectancy in order to determine a causal relationship with outcome. Shaw and Blanchard (1983) randomized participants to one of three conditions: 1) "positive demand" set, 2) "neutral demand" set, and 3) waitlist control. The first two groups received a multi-component stress

management program, including psycho-education about stress, relaxation training, and cognitive coping strategies. Those randomized to the positive demand set were told that the program had been shown to be "very effective," while those randomized to the neutral demand set were told that the treatment was "experimental." The positive demand set had higher expectancies for improvement compared to the other two groups and engaged in more home practice (i.e. "homework") than the neutral demand set. Moreover, they had significantly greater reductions in systolic blood pressure reactivity post-treatment, as well as greater confidence in their ability to manage stress.

More recently, Westra and Dozois (2006) conducted a pilot study where participants were randomized to receive CBT with or without first undergoing motivational interviewing (MI). Participants who received MI reported significantly higher expectancy for anxiety control compared to participants who did not receive pre-treatment MI, and were more likely to complete homework assignments. These participants were also more likely to respond to CBT. These two studies, though preliminary, suggest that expectancy is 1) capable of being manipulated and 2) may lead to improved outcomes by increasing motivation and treatment engagement.

Expectancy in Child and Adolescent Treatment Outcome Research

The literature on expectancy and the treatment of children and adolescents with mental health problems is extremely limited. Nock and Kazdin (2001) found that mothers' expectancies of improvement for their children with oppositional, aggressive, or antisocial behavior problems were predictive of participation in treatment in that mothers with either very high or very low expectations were the least likely to drop out of

treatment. Children received problem-solving skills training, while parents received parent management training. Children's treatment expectancies were not assessed because the researchers believed that parents' expectations were more important in determining treatment outcome.

More recently, Lewin, Peris, Bergman, McCracken, and Piacentini (in press) examined the correlates of parent, child, and therapist treatment expectations in an exposure-based treatment study of childhood OCD. The investigators identified children's baseline depressive symptoms, functional impairment, externalizing behavior problems, number of comorbid psychiatric disorders, and perceptions of control as predictive of treatment expectancy in their sample of 49 youth. OCD severity was not correlated with treatment expectancy. Of note, treatment expectancy was positively associated with treatment response, homework compliance, and treatment retention in this childhood sample.

Overall, the studies discussed above suggest that treatment expectancy impacts treatment outcome for adults with mood and anxiety disorders, perhaps through increased engagement with treatment. Less is known about the importance of treatment expectancy in children and teens, although the recent study conducted by Lewin, Peris, Bergman, McCracken, and Piacentini suggests that treatment expectancy is also important for these often combined populations. Given the significant and increasingly recognized mental health needs of children and adolescents, further research is warranted in order to better understand treatment expectancy and its impact on treatment outcome.

The Treatment for Adolescents with Depression Study (TADS)

The Treatment for Adolescents with Depression Study (TADS) offers a unique opportunity to assess outcome expectancy in a multi-site study involving an adolescent population, psychotherapy, pharmacotherapy, as well as combination treatment. TADS is the first randomized control study to compare the leading treatments for depression in an adolescent sample (TADS Team, 2005). Four-hundred and thirty-nine adolescents, ages 12-17 (inclusive) who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; APA, 1994) criteria for major depressive disorder (MDD) were randomized to receive one of the following four treatments: Fluoxetine (FLX; 10-40 mg), CBT, the combination of the two treatments (COMB), and placebo (PBO).

The initial TADS findings have received considerable attention. At the end of 12 weeks of treatment, 71.0% of adolescents in COMB, 60.6% in FLX, 43.2% in CBT, and 34.8% of adolescents randomized to PBO were rated as "very much improved" or "much improved" according to the independent evaluator-rated Clinical Global Impressions Improvement scores (CGI-I, Guy, 1976; TADS Team, 2004). Teens assigned to COMB exhibited the fastest rate of recovery followed by FLX, which outperformed CBT but not PBO. No differences were found between CBT and PBO in terms of rate or response or percentage of responders. Suicidal thinking improved significantly in all four treatment conditions with suicidality improving the most in teens assigned to COMB and the least in teens assigned to FLX. Considering both the risks and benefits of treatment, the TADS Team concluded that the combination of FLX and CBT is a more effective treatment for adolescent depression than either therapy alone.

Despite convincing evidence, the "uneven blind" in TADS has been identified as a design feature that casts doubt on the strength of this conclusion (Jureidini, Tonkin, & Mansfield, 2004). The "uneven blind" refers to the fact that adolescents assigned to either CBT or COMB were not blinded to their treatment conditions, unlike adolescents assigned to "pills only" (i.e. either FLX or PBO). It has been suggested that this design feature generated meaningful differences in adolescents' expectancy for improvement, accounting for COMB's superior performance (Jureidini, Tonkin, & Mansfield, 2004). The untested assumption behind this criticism is that COMB would not outperform the other three conditions after controlling for treatment expectancy. Underlying this hypothesis is also an argument in favor of common over specific factors.

Indeed, although blinded independent evaluators were responsible for the main outcome ratings in TADS, these evaluators were able to correctly guess teens' assigned treatment conditions at rates greater than expected by chance (25%) for each of these treatment conditions at weeks 6 and 12 (Murakami et al., in progress). Additionally, teens assigned to FLX or PBO were also able to correctly guess their assigned treatment conditions at rates significantly greater than chance (50%) at both time points. While it is likely that independent evaluators based their treatment guessing on participants' treatment response, it is unclear how they were able to accurately choose teens' assigned treatment conditions between the three active TADS treatments (COMB, FLX, or CBT). Most likely, they also relied on participants' reported side effects, imperfect blinding procedures (e.g. seeing a teen enter a room with a pharmacotherapist), or participant "slip ups" (e.g. a participant stating, "I really like my therapist.") to guess correctly. These results suggest that independent evaluators' and participants' treatment expectancies may

have impacted both independent evaluator ratings (i.e. rater bias) and adolescents'

response to treatment, respectively, due to imperfect blinding procedures.

Consistent with the hypothesis that treatment expectancy accounts for the

treatment effects found in TADS, Curry and colleagues (2006) identified adolescents'

assigned treatment expectancies as a significant predictor of treatment response in a

thorough investigation of 20+ potential predictors and moderators of treatment outcome

in TADS. The investigators used a series of GLMs with CGI-I scores (responders versus

non-responders to treatment) as their outcome variable. Adolescents' assigned treatment

expectancy did not emerge as a moderator of treatment; meaning that regardless of

treatment assignment, higher expectations for improvement were associated with greater

reductions in depression after 12 weeks of treatment. Younger age, a shorter duration of

depression, a higher level of functioning, and lower levels of hopelessness and suicidal

ideation, as well as fewer melancholic features and comorbid diagnoses also emerged as

predictors of response to treatment.

Intriguingly, family income level was found to be a moderator of treatment

outcome; teens from family income levels ($\geq$\$75,000) responded as well to CBT as

COMB and FLX. The investigators noted that this finding was not mediated by verbal-

intelligence scores. Severity of depression and the presence of cognitive distortions also

emerged as moderators of treatment. In regards to severity of depression, adolescents

with marked to severe depression were as likely to respond to FLX as COMB, whereas

adolescents with mild to moderate levels of depression were more likely to respond to

COMB than FLX or CBT alone.

The identification of predictors and moderators of treatment is an important step in answering Gordon Paul's (1967) often quoted and reverberating question: "What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?" The current study builds on Curry and colleagues' findings with a closer examination of treatment expectancy in TADS. The study also seeks to clarify whether or not treatment expectancy accounts for the treatment differences initially reported by the TADS Team (TADS Team, 2004).

Study Aims and Hypotheses

Aim 1

The first aim of the current study is to investigate the relationships between treatment expectancy and adolescent demographic variables (e.g. gender, ethnicity, and family income levels), symptom characteristics (e.g. depression severity and chronicity, hopelessness, and suicidality), and treatment site in TADS. Participants in the study indicated their treatment expectations for COMB, CBT, and medication only (three separate ratings) prior to treatment randomization. However, only teens' assigned treatment expectancies (one of the three ratings) were examined in the Curry et al. paper. I will examine each of these three ratings separately for aim 1, as well as a previously unexamined measure, the CBT Rationale Acceptance and Expectation for Improvement (C-RAEI) form, which was specifically designed for TADS and administered to adolescents receiving CBT and COMB during their second CBT session.

Hypothesis 1.1

It is hypothesized that teens will have higher expectations for COMB compared to CBT and FLX. This is expected to be true both within (i.e. when comparing teens' ratings for COMB, CBT, and medication only for the whole sample) and between subjects (i.e. when comparing the teens' assigned treatment ratings.

Hypothesis 1.2

Teens with family income levels at or above $75,000 will endorse higher expectancies for CBT than teens with family income levels below $75,000. Understanding the relationship between treatment expectancy and family income level may help to clarify the relationship between family income level and response to CBT.

Hypothesis 1.3

Severity markers of illness, including severity and chronicity of depression, the presence of comorbid disorders, hopelessness, and suicidality will predict lower treatment expectations across treatment modalities.

Hypothesis 1.4

Treatment expectancy will differ by treatment site. This hypothesis is based on Simons and colleagues' (in preparation) findings that site had a significant impact on outcome. The thirteen sites in TADS differed by location, type of setting (e.g. University versus medical center), sample characteristics, and study staff characteristics (e.g. experience providing CBT), which likely impacted participants' treatment expectations.

Aim 2

The second aim of the current study is to replicate and extend Curry and colleagues' finding that assigned treatment expectancy predicts but does not moderate treatment outcome. In addition to the clinician-rated CGI-I, the primary outcome in TADS (the CDRS-R) will be used as a measure of outcome, as well as the self-rated Reynolds Adolescent Depression Scale (RADS; Reynolds, 1987). The RADS will be used as a primary outcome measure, since one might suspect that treatment expectancy would have more of an impact on a self-rated measure of depression as opposed to a clinician-rated measure. While Curry and colleagues used generalized linear model (GLM) to investigate potential moderators and predictors of treatment in TADS, random coefficient regression models (RRMs) will be used to replicate the investigators' findings. RRM is the preferred method for investigating longitudinal data given its ability to handle missing and nested data, and is consistent with the primary TADS analysis (TADS Team, 2004). RRM was not used in the Curry et al. paper due to the high number of potential predictors and/or moderators under investigation, and concerns over model convergence.

Hypothesis 2.1

Treatment expectancy will predict but not moderate treatment outcome. This is expected for both clinician-rated (CDRS-R and CGI-I) and self-rated (RADS) outcome measures.

Aim 3

The third aim of the study is to investigate whether or not treatment expectancy predicts treatment completion. Lewin, Peris, Bergman, McCracken, and Piacentini (in press) found that treatment expectancy predicted study retention in their study of CBT for the treatment of childhood OCD. For the most part, however, treatment retention has been largely ignored in the expectancy literature.

Hypothesis 3.1

It is hypothesized that treatment expectancy will predict completer status (y/n), where teens with higher expectations for improvement will be more likely to remain in treatment for the full 12 weeks than those with lower expectations for improvement.

Aim 4

Given that research suggests that the placebo effect is less likely to occur in severe depression (Shapiro & Shapiro, 1997; Khan et al., 2002; Wilcox et al., 1992; Fairchild et al., 1986), the forth aim of the current study is to investigate whether or not severity of depression moderates the impact of treatment expectancy on outcome in TADS.

Hypothesis 4.1

It is hypothesized that severity of depression will moderate the relationship between treatment expectancy and treatment outcome in TADS, where treatment expectancy will have more of an impact on treatment outcome for teens with a mild-moderate level of depression compared to teens with a severe level of depression.

27

Aim 5

The fifth aim of the current study is to investigate whether or not treatment expectancy can account of COMB's superior performance in TADS. As mentioned previously, TADS has been criticized for its "uneven" blind. Adolescents randomized to CBT and COMB were cognizant of their assigned treatment conditions, which may have impacted their treatment response. However, it is also possible that COMB will continue to outperform the other three TADS treatments after controlling for the effects of treatment expectancy.

Hypothesis 5.1

It is hypothesized that COMB will continue to outperform the other three treatment conditions after controlling for treatment expectancy. Lambert's (1992) four-factor model posits that expectancy and specific treatment effects determine treatment outcome at equivalent rates (approximately 15%). Therefore, I would expect treatment to predict outcome even after controlling for treatment expectancy.

CHAPTER II

METHOD

Participants

Four hundred and thirty-nine adolescents (M = 14.6 years, SD = 1.54 years) who met eligibility criteria for TADS were enrolled in one of the 13 academic and community sites across the United States. Participants were recruited through radio, television, and newspaper advertisements, as well as through referrals from primary care physicians, mental health providers, school personnel, and the juvenile justice system. In order to participate in the study, adolescents were required to meet criteria for a primary diagnosis of major depressive disorder according to the DSM-IV as assessed by the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). Further inclusion criteria included at least a moderate level of depression based on a Child Depression Rating Scale-Revised (CDRS-R; Poznanski & Mokros, 1996) total score of $\geq$ 45 at baseline, a current episode of depression lasting at least six weeks, and impairment in at least two out of three major contexts including home, school, and peer relationships.

Adolescents who met criteria for a comorbid Axis I diagnosis were included in the study with the exceptions of bipolar disorder, current substance abuse/dependence, severe conduct disorder, pervasive developmental disorders, and thought disorders. Adolescents were also excluded from the study if they were actively suicidal/homicidal and if they had not responded to two previous trials of selective serotonin reuptake inhibitors or a course of CBT for depression. Concurrent pharmacotherapy or

29

psychotherapy was not permitted during the study. Additionally, a full-scale IQ of at least 80 and the availability of a participating English-speaking parent or family member were required. A detailed description of the full TADS sample has been published elsewhere (TADS Team, 2005).

Of the 439 adolescents who enrolled in TADS, 403 adolescents (M_{age}=14.62, SD=1.56) filled out the Treatment Expectancy for Adolescents (TEA) form prior to treatment randomization and were included in the current study. Of the 403 adolescents, 43.9 % (n=177) were male and 56.1 % (n=226), female. The majority of participants identified their race/ethnicity as Caucasian (n=298, 73.9%), African American (n=48, 11.9%), or Hispanic, White (n=29, 7.2%). Eight participants (2%) selected Hispanic, Black, while the remaining participants selected Asian American (n=3, .7%), Pacific Islander (n=2, .5%), or other (n=15, 3.7%) as their race/ethnicity. The subsample of adolescents included in this study had a mean CDRS-R score of 60.06 (SD=10.33), which suggests a moderate level of depression. The current subsample did not differ from the full TADS sample in terms of age or severity of depression (p>.05).

Study Procedures

Adolescents were screened for participation in TADS in a three-stage process (Gates A-C). At Gate A, adolescents were assessed for eligibility using a brief screening measure by phone or in person. Adolescents and their parents were given an explanation of the study, including a brief description of each of the TADS treatments (typically no more than a few sentences, i.e. "CBT is a type of psychotherapy that has been shown to be effective for the treatment of depression"), and provided informed consent at Gate B.

In addition, adolescents were assessed using the K-SADS-PL during this visit. The majority of self-report forms, including the TEA, were filled out at Gate C prior to randomization. After confirmation of eligibility, teens were randomized to receive FLX, CBT, COMB, or PBO on a 1:1:1:1 allocation ratio with site and gender used as stratification variables. Subsequently, teens assigned to CBT and COMB were informed of their particular treatment assignments, while teens assigned to FLX and PBO were told they had been assigned to "pills only." Thus, only teens assigned to FLX or PBO were blinded to their treatment conditions. Following Gate C, adolescents entered into the acute phase of TADS (Stage I), which consisted of twelve weeks of treatment. Stage II (consolidation) consisted of six weeks of follow-up, while Stage III (continuation) and Stage IV (naturalistic) consisted of 18 weeks and one year of follow-up, respectively. The current study focuses on the results of Stage I, or the first 12 weeks of treatment.

During Stage I, participants randomized to FLX or PBO conditions met with their assigned pharmacotherapist for 20-30 minutes six times over 12 weeks. Adolescents were started on 10 mg/day, which could be raised up to 40 mg by week eight based on adolescents' treatment response and their tolerability to pills. During the acute phase of the study, participants randomized to the CBT condition received up to 15 sessions of psychotherapy lasting between 50 and 60 minutes each. These sessions included psychoeducation about depression, as well as manualized cognitive-behavioral techniques designed to increase pleasant activities and restructure dysfunctional thoughts. The rationale behind TADS CBT is that depression is either caused and/or maintained by a lack of positively reinforcing behavior and the presence of depressive thinking (Clark, Lewinson, & Hops, 1990; Brent & Poling, 1997). Additionally, two sessions were

31

devoted to psychoeducation for parents during weeks one through six, and one to three conjoint family sessions could be substituted for individual therapy sessions with teens between weeks seven and 12. COMB treatment included all of the elements of both FLX and CBT.

Independent evaluators, blinded to teens' assigned treatment conditions, conducted the outcome assessments in TADS in order to minimize experimenter bias. At every assessment point, study coordinators reminded adolescents and their parents not to disclose information (e.g. the names of teens' CBT therapists or pharmacotherapists) that might reveal teens' assigned treatment conditions to their independent evaluators. Only in cases of emergency, such as sudden worsening of suicidality, were adolescents assigned to FLX/PBO and their pharmacotherapists informed of teens' actual treatment assignments.

Baseline Measures

Demographic Information

Demographic information, including a participant's age, sex, race/ethnicity, and family income level, was collected prior to initiation of treatment. Participants' age, sex, and race/ethnicity were assessed through self-report. Gross family income over the past year was obtained through a version of the Child and Adolescent Services Assessment (CASA; Burnds, Anold, Costello, & Ascher, 1999) conducted by the study coordinator with the teen's parent(s). The CASA categorizes income from less than $5,000 to greater than $200,000. Previously, the original 12 categories were collapsed to the following five categories: $0-$19,999, $20,000-$39,999, $40,000-$74,999, $75,000-$99,999, and

>$99,999 based on the sample distribution of the original TADS sample. Because Curry and colleagues identified family income level as a moderator of treatment outcome in TADS, where teens with higher family income ($\geq$ $75,000) were more likely to respond to CBT, a separate categorical variable will be created for income based on this cutoff.

Depression Severity, Duration, and Comorbidity

Clinical Global Impression-Severity and Improvement Scales

Severity of depression was determined according to the clinician-administered Clinical Global Impressions-Severity Scale (CGI-S; Guy, 1976). The CGI-S is based on a 7-point rating of depression severity, where a score of one indicates "Normal, not mentally ill", and a score of seven indicates "Among the most extremely mentally ill." The CGI-S is among the most widely used brief assessment measures in psychiatry and is a standard used in clinical research trials for children, adolescents, and adults. In order to insure inter-rater reliability, TADS Independent Evaluator and Clinician Assessment Manuals were developed, which specify rating guidelines for the CGI-S and Clinical Global Impressions-Improvement Scale (CGI-I; Guy, 1976). Additionally, independent evaluators were required to submit their first two interviews to the coordinating site for evaluation of quality of administration and rating accuracy.

Schedule for Affective Disorder and Schizophrenia for School-Age Children

The duration of the current depressive episode and the presence of comorbid mental health diagnoses were determined by the independent evaluator based on the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime (K-SADS-PL; Kaufman et al., 1997), an extensively used semi-structured

interview that assesses for Axis I disorders included in the DSM-IV-R, including mood, anxiety, attention-deficit/ hyperactivity, disruptive behavior, eating, elimination, substance-related, and psychotic disorders. Independent evaluators interviewed both the adolescent and the parent(s), incorporating both sources of information. The K-SADS-PL has high interrater reliability (93-100%) across diagnoses and excellent test-retest reliability for major depression (.90), in particular.

In the full TADS sample, the presence of a comorbid anxiety disorder and the number of comorbid disorders both emerged as predictors of treatment response (Curry et al., 2006). Adolescents with a comorbid anxiety disorder (social anxiety disorder, separation anxiety disorder, generalized anxiety disorder, panic disorder, agoraphobia, or posttraumatic stress disorder), as well as adolescents with a greater number of comorbid disorders, were less likely to respond to treatment. Both of these comorbidity groupings and their relationship to treatment expectancy will be examined in the current study.

Expectancy-Related Measures

Treatment Expectancy for Adolescents (TEA) Form

Prior to treatment randomization, adolescents filled out the Treatment Expectancy for Adolescents (TEA) form, where they rated to what extent they thought their "depression problems" would improve with COMB, CBT, and "medication only." Since there are no measures of psychometrically validated treatment expectancy measures for children and adolescents with depression, the TEA was designed specifically for TADS. The TEA is based on a Likert scale with one indicating the most benefit from treatment ("very much improved") and seven indicating the least benefit/most harm from treatment

("very much worse"; see Appendix A). Only after filling out the TEA were adolescents randomized to one of the four treatment conditions in TADS.

Assigned Treatment Expectancy (Assigned TE)

Adolescents' assigned TE ratings were identified as the ratings that they selected on the TEA for their randomized treatment arms. For example, if a teen selected a rating of 1 ("very much improved") for COMB, 2 ("much improved) for CBT, and 3 ("much improved") for medication alone, and then was subsequently assigned to CBT, this participant had an assigned treatment expectancy of 2. For teens assigned to FLX or PBO, their treatment expectancy ratings were considered to be their expectancy ratings for treatment with medication only, since these adolescents were blinded to their conditions and expectancy for improvement with PBO was not assessed. Thus, each adolescent had an expectancy rating for COMB, CBT, and medication only; each adolescent also had an assigned TE rating based on the TEA for their assigned treatment.

CBT Rationale Acceptance and Expectation for Improvement (CBT-RAEI)

Adolescents randomized to receive CBT or COMB also filled out the CBT Rationale Acceptance and Expectation for Improvement (C-RAEI) form during their second CBT session after learning more about the rationale for CBT and what treatment entails. The C-RAEI, also designed specifically for TADS, consists of six questions (see Appendix B), three of which pertain to acceptance of treatment rationale ("The therapist's explanation of what cognitive behavior therapy is made sense to me."), and three of which pertain to treatment expectancy ("I expect to get better or become less depressed through this program."). Individuals were asked to rate each of the six

35

statements on a scale from one ("strongly disagree") to five ("strongly agree"). A total of 192 TADS participants filled out the C-RAEI. A reliability analysis revealed excellent internal consistency (α = of .918) of the measure.

Hopelessness

The Beck Hopelessness Scale (BHS; Beck & Steer, 1993) is a 20-item, self-report measure with high internal consistency (α = .82 to .93) based on a T/F format with a maximum score of 20, where higher scores indicate greater levels of hopelessness. Sample items include the following T/F statements: "I look forward to the future with hope and enthusiasm," and "All I can see ahead of me is unpleasantness rather than pleasantness." Total BHS scores were found to predict treatment response in TADS (Curry et al., 2006).

Suicidal Ideation

The Suicididal Ideation Questionnaire-Jr. High Version (SIQ-Jr; Reynolds, 1987) was used to determined adolescents' severity of suicidal ideation. The SIQ-Jr is composed of 15 items with each item rated on a Likert scale from zero ("I never had this thought") to six ["(I had this thought) almost every day"] within the past month (e.g. "I thought I would be better off if I was not alive."). An aggregate score of 31 required the assessment for further suicidal risk in TADS. The measure has been shown to have high internal consistency (α = .94) and moderate test-retest reliability in adolescents. Total SIQ-Jr scores also emerged as a predictor of treatment response in TADS (Curry et al., 2006).

Outcome Measures

Clinician-Rated Measures

Children's Depression rating Scale-Revised (Poznanski & Mokros 1995)

The Children's Depression Rating Scale-Revised (CDRS-R) is a 17-item, clinician-administered rating scale that is commonly used to assess the severity of depression in children and adolescents based on the DSM-IV-R, and is one of two measures chosen a priori as the primary outcome measure for TADS. Each item is rated on a seven-point scale for a total score from 17 to 113, with higher scores indicating greater depression severity. The 17 items cover distinct areas characteristic of depression, including social withdrawal, hypoactivity, appetite and sleep disturbance, excessive fatigue, difficulty having fun, irritability, low self-esteem, morbid/suicidal ideas, impaired schoolwork, physical complaints, excessive guilt and weeping, listless speech, depressed facial affect, and depressed mood. Previous studies suggest that the CDRS-R has high internal consistency ($\alpha = .85$), interrater reliability ($r=.92$), and test-retest reliability ($r = .78$; Poznanski & Mokros, 1996). Independent evaluators administered the CDRS-R at baseline, week six, and week 12.

Clinical Global Impressions Improvement (Guy, 1976)

The Clinical Global Impressions Improvement (CGI-I) is the second primary outcome measure chosen a priori in TADS. Independent evaluators were instructed to review the CDRS-R and the CGI-S from the adolescent's baseline evaluation, as well as assessment information from the previous assessment visit in order to remind themselves of the adolescent's baseline presentation and trajectory of symptom improvement. This

37

information enabled independent evaluators to select the most appropriate CGI-I rating

from one ("very much improved") to seven ("very much worse") with four indicating "no

change." In TADS, adolescents who received "very much improved" or "much

improved" CGI-I ratings were considered responders to treatment, while adolescents who

received "minimally improved" to "very much worse" scores were considered non-

responders to treatment. The CGI-I was administered at week six and week 12 by

independent evaluators.

Treatment Completion

Adolescents were categorized into treatment completers or non-completers based

on whether or not they completed the acute phase of TADS (12 weeks of acute

treatment).

Self-Rated Measure

Reynolds Adolescent Depression Scale (Reynolds, 1987)

The Reynolds Adolescent Depression Scale (RADS) is a self-report measure of

depression severity in teens and consists of 30-items, each rated on a Likert scale from

one ("almost never") to four ("most of the time"). Sample items include, "I feel sad," "I

feel like crying," and "I feel no one cares about me," which fall under one of four basic

dimensions of depression: dysphoric mood, anhedonia/negative affect, somatic

symptoms, and negative self-evaluation. Total scores range from 30-120 with higher

scores indicating greater depression severity. The RADS has demonstrated high internal

consistency ($\alpha = .92$) and test-retest reliability at six weeks ($r=.80$) and three months

($r=.79$). Concurrent validity has also been demonstrated with the Hamilton Rating Scale

(Hamilton, 1967). TADS adolescents filled out the RADS at baseline, week six, and week 12.

Statistical Methods

All statistical analyses were conducted using SPSS version 19.0.

Aim 1: Investigate the relationship between treatment expectancy, demographic variables, and clinical variables (e.g. hopelessness)

Pearson's correlations were calculated to measure the strength of the relationship between treatment expectancy for COMB, CBT, and medication only and the following continuous dependent variables: total C-RAEI scores, age, severity of depression (as measured by the CDRS-R), chronicity of depression, suicidality, hopelessness, and the number of participants' comorbid disorders. One-way between subjects analysis of variances (ANOVAs) were used to assess for differences in treatment expectancy based on categorical variables, including race/ethnicity, family income levels (based on five categories), severity of depression (as measured by the CGS), and the presence of a co-occurring anxiety disorder. Independent samples t-test were used to test for differences in treatment expectancy based on gender and a dichotomized family income level ($<$\$75,000 and $\geq$\$75,000).

Aim 2: Replicate and extend Curry et al.'s finding that assigned TE predicts but does not moderate treatment outcome

A random coefficients regression model (RRM) with fixed (treatment, time, site, assigned TE, and their 2-way and 3-way interactions) and random (subject and subject by time) effects was conducted with the CDRS-R as the outcome variable. A similar RRM

39

analysis was conducted with the RADS replacing the CDRS-R as the outcome variable. Random regression has been identified as an ideal approach to data analysis of continuous repeated measures with missing data, since it permits estimation of changes for missing data on both a participant and population level without using last observation carried forward (Guerorguieva & Krystal, 2004; Weinfert, 2000; Brown, 1999) or listwise deletion, and is consistent with the main analysis in TADS (TADS Team, 2004). RRM is consistent with an intent-to-treat analysis, since all randomized participants, regardless of their treatment assignment and adherence to protocol (e.g. missed appointments, percentage of homework completed, etc.) are included in the analysis.

The hypothesis that assigned TE predicts but does not moderate treatment outcome is supported if there is a main effect for assigned TE and there are no interaction effects with treatment or treatment by time. Table 1 lists the fixed and random effects that were included in the initial model (the natural log of time was used instead of linear time, which is consistent with the primary TADS analyses). Non-significant interaction effects were taken out of the final RRM. Interactions with site were not included in the model since they were not significant in the initial model and did not affect study results (TADS Team, 2004).

Table 1. Fixed and Random Effects Included in the Initial RRM for Aim 2

Fixed Effects	Random Effects
Treatment	Subject
Time	Subject*Time
Site	
Assigned TE	
Treatment*Time	
Treatment*Assigned TE	
Treatment*Assigned TE*Time	

Additionally, a first-order autoregressive covariance structure was specified in the model, since it accounts for the fact that measurements taken closer in time tend to be more highly correlated with each other than measurements taken farther apart in time. A first-order autoregressive covariance structure has been suggested as the preferred covariance structure in linear mixed models for studies that include repeated measurements over time (Neri, Kraemer, Noda, & Yung, 2005).

Consistent with the initial TADS analyses (JAMA, 2004), logistic regression with last observation carried forward (LOCF) was used to determine if assigned TE predicts responder status (yes/no) according to the CGI-I. In the full sample, the TADS Team found a main effect of treatment (Wald χ^2=33.9, p=.001) with planned pairwise contrasts demonstrating that COMB (p=.001) and FLX (p=.001) but not CBT (p=.20), outperformed PBO. COMB (p=.001) and FLX (p=.001) also outperformed CBT in the full sample; the two treatments did not differ from each other (p=.11).

RRM and logistic regression were used with total C-RAEI scores in place of assigned TE for the subsample of teens treated with CBT or COMB. RRM was also used with the CDRS-R and the RADS as continuous outcome variables, while logistic regression was used with the CGI-I as a categorical outcome variable.

Aim 3: Investigate whether or not assigned TE and C-RAIE scores predict treatment retention

A logistic regression was conducted to determine if assigned TE predicts completer status (yes/no). Again, fixed effects included treatment, time, site, assigned TE, and their 2-way and 3-way interactions (excluding site interactions). Identical

analyses were conducted with total C-RAEI scores in place of assigned TE scores for teens assigned to CBT or COMB.

Aim 4: Investigate whether or not severity of depression affects the impact of assigned TE (and possibly the C-RAEI) on outcome in TADS

Adolescents were categorized into either mild-moderate or severe depression based on their initial CGI-S scores. Adolescents with scores of three ("mildly ill") or four ("moderately ill") were included in the mild-moderate depression severity category, while adolescents with scores of five ("markedly ill"), six ("severely ill") or seven ("among the most extremely ill patients") were categorized as severely ill.

A random coefficients regression model with fixed (treatment, time, site, assigned TE, depression severity, and their 2-way and 3-way interactions) and random (subject and subject by time) effects was run with the CDRS-R as the outcome variable, followed by the RADS. The hypothesis that depression severity moderates the effect of treatment expectancy on outcome is supported if there is a significant interaction effect between assigned TE and depression severity, or if there is a three-way interaction with these two variables and time. Logistic regression was used with CGI-I as the outcome variable with identical fixed effects for categorical variables with continuous variables included as covariates. RRM and logistic regression were also used with total C-RAEI scores in place of assigned TE for the subsample of teens treated with CBT or COMB. Table 2 lists the fixed and random effects that will be included in the initial model for the purpose of aim 4.

Table 2. Fixed and Random Effects Included in the Initial RRM for Aim 4

Fixed Effects	Random Effects
Treatment	Subject
Time	Subject*Time
Site	
Assigned TE	
Severity of depression	
Treatment*Time	
Treatment*Severity of depression	
Assigned TE*Severity of depression	
Assigned TE*Severity of depression*Time	

Aim 5: Investigate whether or not assigned TE (and possibly the C-RAIE) can account of COMB's superior performance in TADS.

This hypothesis is supported if treatment by time is no longer significant in the RRM when treatment expectancy is included as a fixed effect. In the primary TADS analysis, treatment by time emerged as significant with subsequent contrasts revealing that COMB outperformed the other three treatments. I first replicated this analysis with the subsample of teens included in this study before including treatment expectancy and its interaction terms as fixed effects. Separate analyses were then run with CDRS-R, RADS, and CGI-I as outcome variables, the latter requiring the use of logistic regression.

CHAPTER III

RESULTS

Hypothesis 1.1

Prior to treatment randomization, 403 adolescents filled out the TEA, indicating their expectations for improvement with COMB, CBT, and medication only. These adolescents had the highest expectations for improvement with COMB (M=1.99, SD=1.01) followed by CBT (M=2.66, SD=.96) and medication only (M=2.54, SD=1.01) with lower scores indicating higher treatment expectancies. A repeated measures ANOVA revealed significant differences [$F(1.73,690.40)$=83.95, p<.001, η_p^2=.04] with Huyn Feldt correction. Pairwise comparisons revealed higher expectations for improvement with COMB compared to CBT (p<.001) and medication only (p<.001); no significant differences in expectancy were found between the latter two treatments.

Similarly, a one-way between-subjects ANOVA revealed differences in adolescents' assigned TEs [$F(3,399)$=9.53, p<.001, η_p^2=.067]. Posthoc analysis using Tukey's HSD demonstrated that teens assigned to COMB had higher assigned treatment expectancies than teens assigned to CBT (p<.001), FLX (p<.001) and PBO (p=.002). Table 3 lists the frequency of assigned TEs for each of the four treatment conditions. Only one participant assigned to FLX (.9%), two assigned to CBT (1.8%), two assigned to COMB (1.9%), and one assigned to PBO (.9%) believed their depression problems would worsen with treatment; these teens are not included in Table 3. As seen in the table, a large percentage of teens (43.6%) assigned to COMB believed their depression problems would be "very much improved" in comparison to teens assigned to CBT

(9.8%), FLX (11.1%), and PBO (14.9%). The majority of teens in each treatment group expected to improve at least minimally with their treatment assignment.

Table 3. Assigned TE Scores by Randomized Treatment Group

	1 "very much improved" n(%)	2 "much improved" n(%)	3 "minimally "improved" n(%)	4 "not changed" n(%)
COMB	44(43.6%)	33(32.7%)	18(17.8%)	4(4.0%)
CBT	10(9.8%)	41(40.2%)	37(36.3%)	12(11.8%)
FLX	11(11.1%)	37(37.4%)	39(39.4%)	11(11.1%)
PBO	15(14.9%)	42(41.6%)	35(34.7%)	8(7.9%)

Table 4 includes the means, standard deviations, and the results of the one-way between subjects ANOVAs for selected baseline variables by treatment group. Prior to initiation of treatment, no significant differences were found between the four treatment groups in terms of participants' mean age, duration of their current depressive episode, number of comorbid disorders, or scores on the C-RAEI, CDRS-R, RADS, and SIQ. The four treatment groups differed in their baseline hopelessness scores [$F(3,396)=3.53$, $p=.015$, $\eta_p^2=.026$] in that teens assigned to PBO had higher BHS scores than participants assigned to CBT ($p=.024$) and FLX ($p=.029$), but not COMB ($p=.30$). Curry et al. (2006) found that adolescents assigned to PBO had higher levels of hopelessness than adolescents assigned to the remaining treatment groups in the full TADS sample.

Differences in treatment expectations for COMB, CBT, and medication only based on adolescents' demographic variables were also investigated. An independent samples t-test indicated that females were more likely than males to endorse higher

Table 4. Baseline Characteristics by Treatment Group

Variable	COMB n=101 M(SD)	CBT n=102 M(SD)	FLX n=99 M(SD)	PBO n=101 M(SD)	Total n=403 M(SD)	P-Value
Age	14.65(1.50)	14.72(1.51)	14.61(1.56)	14.51(1.68)	14.62(1.56)	.83
Assigned TE	1.92(1.13)	2.56(.90)	2.54(.87)	2.41(.95)	2.35(1.00)	<.001
*C-RAEI	24.90(5.81)	23.62(5.62)			24.23(5.74)	.18
CDRS-R	60.31(11.42)	59.45(9.01)	59.20(10.21)	61.28(10.56)	60.06(10.33)	.48
RADS	79.41(13.78)	78.92(15.04)	77.09(14.62)	81.22(14.00)	79.16(14.39)	.25
BHS	9.85(5.55)	9.04(5.62)	9.07(5.30)	11.23(5.41)	9.80(5.52)	.015
SIQ	26.54(24.11)	21.93(21.06)	20.86(18.41)	23.91(21.49)	23.32(21.40)	.25
Duration of CDE**	82.13(95.78)	76.12(71.42)	68.66(83.98)	64.08(69.39)	72.77(80.80)	.40
# of comorbid disorders	.79(.99)	.76(.91)	.70(1.10)	.78(1.05)	.76(1.01)	.91

*Only participants assigned to CBT or COMB completed the C-RAEI.
**Duration of current depressive episode (in weeks)

expectations for improvement with COMB [$t(397)$=2.15, p=.03, d=.22], adjusting for inequality of variances. Male and female participants did not differ in their expectations for improvement with CBT [$t(397)$=-.339, p=.74] or with medication only [$t(400)$=1.10, p=.27]. Table 5 includes the means and standard deviations of the expectancy ratings for the three active treatment groups separated by demographic information. No significant effects of race/ethnicity were found.

Table 5. Treatment Expectancy Ratings for COMB, CBT, and Medication Only Based on Demographic Variables

Demographic variable	*n*(%)	TE for COMB *M*(SD)	TE for CBT *M*(SD)	TE for Medication Only *M*(SD)
Gender				
Male	177(43.9%)	2.11(1.17)	2.65(.98)	2.60(1.07)
Female	226(56.1%)	1.89(.85)	2.68(.95)	2.49(.95)
Race/ethnicity				
European American	298(73.9%)	1.93(.89)	2.68(.93)	2.50(.91)
African American	48(11.9%)	2.06(1.12)	2.51(1.08)	2.53(.98)
Hispanic, Black	8(2.0%)	2.38(2.13)	2.75(1.83)	2.88(1.89)
Hispanic, White	29(7.2%)	2.03(1.18)	2.66(.90)	2.62(1.18)
Asian American	3(.7%)	2.67(1.16)	2.33(1.16)	3.33(3.22)
Pacific Islander	2(.5%)	2.00(1.41)	2.00(.00)	2.50(2.12)
Other	15(3.7%)	2.50(1.45)	3.00(.56)	2.87(1.25)
Family income				
$0 - $19,999	45(11.2%)	1.96(.93)	2.56(.76)	2.42(.89)
$20,000 - $39,999	98(24.3%)	2.28(1.21)	3.03(1.12)	2.71(1.02)
$40,000 - $74,999	134(33.3%)	1.92(.98)	2.61(.93)	2.47(1.03)
$75,000 - $99,999	41(10.2%)	1.59(.67)	2.37(.83)	2.59(.92)
Over $99,999	54(13.4%)	2.07(.78)	2.56(.86)	2.57(.92)

Hypothesis 1.2

Treatment expectancies were found to differ based on family income levels for CBT [$F(4,364)=5.09$, $p<.001$, $\eta_p^2=.053$] and COMB [$F(4,365)=4.03$, $p=.003$, $\eta_p^2=.042$], but not for medication only [$F(4,366)=1.08$, $p=.367$]. Posthoc analysis using Tukey's HSD indicated that teens with family income levels from \$20,000-\$39,999 had lower expectations for CBT than teens with family income levels from \$40,000-\$74,999 ($p=.009$), \$75,000 - \$99,999 ($p=.002$), and over \$99,999 ($p=.033$). Teens with family income levels from \$20,000-\$39,999 also had lower expectations for improvement with COMB than teens with family income levels from \$40,000-\$74,999 ($p=.045$), and from \$75,000-\$99,999 ($p=.002$), but not when compared to teens with family income levels equal to or above \$99,999 ($p=.75$).

Independent samples t-tests subsequently showed that adolescents with family income levels below \$75,000 had lower expectations for improvement with CBT compared to adolescents with family income levels at or above \$75,000 [$t(368)=2.38$, $p=.018$, $d=.30$], which was not the case for COMB [$t(368)=1.83$, $p=.069$], or medication only [$t(369)=-.27$, $p=.79$], where no differences were found between the two collapsed family income groups.

Hypothesis 1.3

The hypothesis that difference severity markers of illness, including severity and chronicity of depression, hopelessness, suicidality, and the presence of comorbid disorders, would be associated with lower treatment expectations across treatment modalities was partially supported, as outlined below.

Severity of Depression

Depression severity was not correlated with treatment expectancy for CBT, COMB, or medication only (see Table 6) based on the CDRS-R. Nor was it correlated with the C-RAEI. Adolescents' self-rated depression scores (i.e. RADS scores) were found to be correlated with their expectations for improvement with COMB ($p=.014$); as participants' self-rated depression scores increased, so did their expectations for COMB treatment.

Differences in expectations for improvement with CBT were found based on the CGI-S using a one-way between subjects ANOVA [$F(4,395)=2.50$, $p=.042$, $\eta_p^2=.025$], but not for COMB [$F(4,394)=.88$, $p=.48$], or medication only [$F(4,397)=.382$, $p=.82$]. Post hoc analysis with Tukey's HSD demonstrated that teens categorized as "moderately mentally ill" had higher expectations for CBT ($M=2.49$, $SD=.824$) than teens categorized as "markedly mentally ill" ($M=2.81$, $SD=1.09$; $p=.022$). The mean scores for each of the severity groups in the TADS sample are illustrated in Figure 1 beginning with group 3 ("mildly mentally ill") up until group 7 ("among the most extremely mentally ill"). Groups 1 ("normal, not mentally ill") and 2 ("borderline mentally ill") were not represented in the TADS sample.

Chronicity of Depression

Adolescents' treatment expectancies for COMB, CBT, and medication were not correlated with chronicity of depression prior to treatment randomization. For teens assigned to COMB or CBT, total C-RAEI scores were correlated with chronicity of depression (see Table 6).

Table 6. Correlations among Treatment Expectancy and Symptom Measures

	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Treatment expectancy for COMB	.461**	.537**	-.106	.072	-.124*	.027	.009	.012	.063
2. Treatment expectancy for CBT		.117*	-.109	.095	.058	.178**	.105*	.029	.014
3. Treatment expectancy for medication only			-.088	.073	-.033	.064	.065	.042	.086
4. C-RAEI***				-.009	-.056	-.003	-.001	.147*	.083
5. CDRS-R					.404**	.229**	.334**	.116*	.137**
6. RADS						.589**	.598**	-.002	.039
7. BHS							.465**	-.043	-.038
8. SIQ								.051	.083
9. Duration of CDE****									.107*
10. Number of comorbid disorders									

*p<.05, **p<.01
***C-RAEI scores were not found to be correlated with treatment expectancy for COMB, CBT, and medication only, although they were found to be correlated with assigned TE in a follow-up analysis (R=-.186, p=.013).
****Duration of current depressive episode (in weeks)

Figure 1. Mean Expectancy Scores for CBT based on Depression Severity Groupings
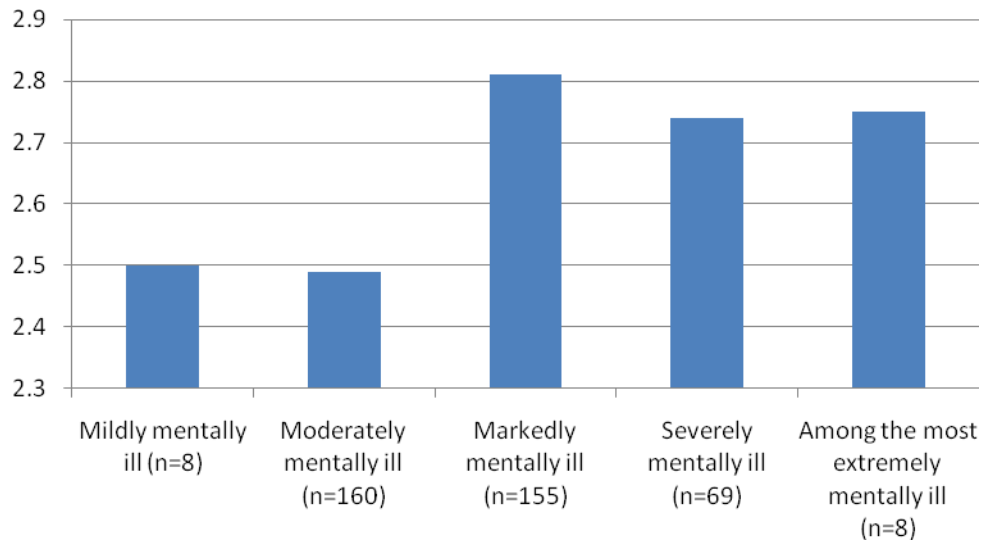
Hopelessness and Suicidality

Adolescents' expectancy scores for CBT were found to be correlated with their self-rated hopelessness ($p<.001$) and suicidality ($p=.036$) scores (see Table 6); as teens' hopelessness and suicidality increased, their expectations for improvement with CBT (but not for COMB or medication only) decreased.

Comorbidity

Previously, the presence of a comorbid anxiety disorder and a higher number of comorbid disorders were found to predict poorer response to treatment in TADS (Curry et al., 2006). While the latter was not found to correlate with treatment expectancy in this study sample, differences in treatment expectancy scores for medication were found between adolescents with and without a comorbid anxiety disorder diagnosis. Adolescents with a comorbid anxiety disorder ($n=112$) had lower treatment expectancies for medication only compared to teens without a comorbid anxiety disorder ($n=289$),

51

t(399)=-2.15, *p*=.032 (see Figure 2). Participants with and without a comorbid anxiety

disorder did not differ in their expectations for COMB [*t*(176.68)=-1.35, *p*=.177] or CBT

[*t*(397)=-1.71, *p*=.089]. Additionally, C-RAEI scores did not differ between participants

based on the presence of a co-occurring anxiety disorder [*t*(191)=.33, *p*=.74].

Figure 2. Treatment Expectancies for Adolescents with and without a Comorbid Anxiety
Disorder Diagnosis
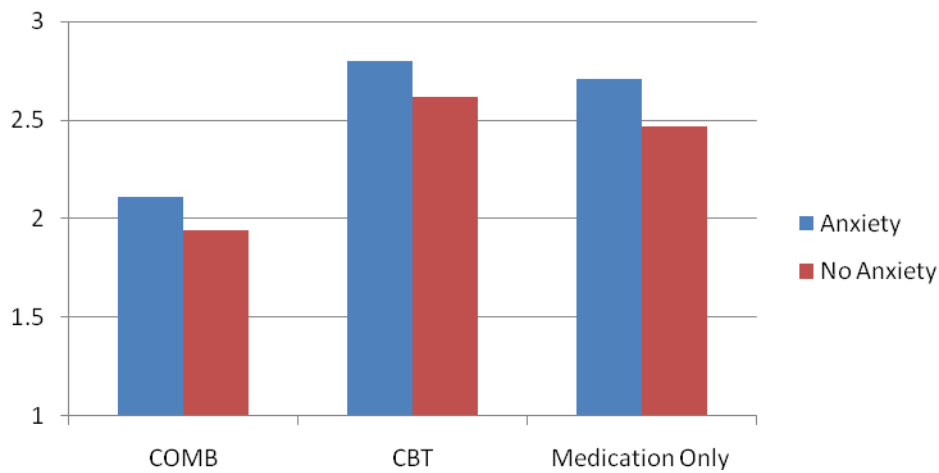
Note: Lower expectancy scores indicate higher treatment expectancies.

Hypothesis 1.4

There were no differences found in treatment expectations for COMB

F(12,386)=.84, *p*=.61], CBT [*F*(12,387)=1.22, *p*=.264], or medication only

F(12,389)=1.49, *p*=.12] between the thirteen sites. However, after randomization to

treatment, there were differences found between treatment sites in terms of participants'

expectations for their assigned treatments [*F*(12,390)=1.75, *p*=.054, η_p^2=.051] with

Tukey's HSD revealing significant differences between sites 1 and 3 (*p*=.049) and

between sites and 1 and 11 (*p*=.014); adolescents at site 1 had lower treatment

expectancies for their assigned treatment conditions compared to adolescents at site 3 and

11 (see Table 7). A one-way between subjects ANOVA did not find site differences

based on the C-RAEI [$F(12,180)=.81$, $p=.63$]. Table 8 also illustrates the differences in

enrolled subjects between the thirteen sites.

Table 7. Adolescents' Assigned TEs by Site

Site	n	M(SD)
1. New York University Medical Center	19	2.68(1.11)
2. Wayne State University Health Center	10	2.27(.72)
3. Carolinas Health Care System	19	2.30(.67)
4. University of Texas Southwestern Medical Center at Dallas	34	2.36(.71)
5. University of Nebraska Medical Center	81	2.48(.66)
6. University of Chicago Medical School	8	2.38(.74)
7. University of Oregon Psychology Department	61	2.43(.69)
8. John Hopkins University Medical Center	33	2.23(.77)
9. The Children's Hospital of Philadelphia	17	2.37(.58)
10. New York State Psychiatric Institute	32	2.49(1.18)
11. Children's Hospital Medical Center (Cincinnati, OH)	39	2.15(.58)
12. Northwestern University Medical School	18	2.52(.78)
13. Case Western Reserve University School of Medicine	27	2.43(.67)

Hypothesis 2.1

Assigned TE (CDRS-R, RADS, and CGI-I)

Random coefficients regression analyses were conducted to test the hypothesis

that treatment expectancy predicts but does not moderate treatment outcome. First, the

results of the original TADS findings (TADS TEAM, 2004) were replicated with the

current study sample. Similar to the original findings, there was a main effect for time

[$F(1,195.37)=745.29$, $p<.001$], a treatment by time interaction [$F(3,796.36)=7.52$,

$p<.001$], and a main effect for site [$F(12,388.76)=2.95$, $p=.001$].[1] Pairwise comparisons on adjusted week 12 means indicated that COMB outperformed CBT ($p=.014$) and PBO ($p=.001$), while FLX outperformed CBT ($p<.001$).

Next, RRM was used to replicate Curry and colleagues' 2006 finding that treatment expectancy predicted but did not moderate treatment outcome according to the CDRS-R. In contrast to the previous analysis using GLM, both 2- and 3-way interaction terms with treatment expectancy were included in the model and were subsequently removed from the model when they were found to be non-significant. The remaining model included significant effects of time [$F(1,212.38)=775.87$, $p<.001$], treatment by time [$F(3,805.27)=7.65$, $p<.001$], treatment expectancy [$F(5,1032.8)=3.58$, $p=.003$], and site [$F(12,398.35)=3.00$, $p<.001$]. Pairwise comparisons based on adjusted week 12 means indicated that adolescents who expected their depression problems to become "much improved" with their assigned treatments had a better outcome than adolescents who expected their depression problems to become "minimally improved" with their assigned treatments ($p=.011$). The means and standard deviations of teens' CDRS-R scores are listed in Table 9 according to teens' assigned TEs and depression severity levels.

Figure 3 provides a graphic illustration of Table 8 for adolescents who expected their depression problems to be "very much improved," "much improved," "minimally improved," and "not changed." Teens who expected their depression problems to worsen with treatment are not included in the graph due to their relatively small numbers.

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[1] In the original analysis (TADS TEAM, 2004), site was categorized as a random effect. Because the 13 sites in TADS were not randomly selected, the TADS TEAM decided to categorize site as a fixed effect in subsequent publications. The decision to include site as a fixed effect resulted in a significant finding for site, which was not found in the original analysis.

Table 8. CDRS-R Scores over Time Based on Severity of Depression and Assigned TEs

Treatment Expectancy	Severity*	n**	Week 0 M(SD)	Week 6 M(SD)	Week 12 M(SD)
1="Very much improved"	0	36	52.22(7.91)	33.40(9.73)	30.13(9.25)
	1	43	65.63(8.27)	42.53(14.07)	37.33(14.38)
	Total	79	59.52(10.49)	38.82(13.08)	34.00(12.66)
2="Much improved"	0	69	52.51(6.16)	38.90(9.56)	35.26(12.27)
	1	84	64.36(9.15)	43.13(13.68)	37.11(12.92)
	Total	153	59.01(9.89)	41.31(12.22)	36.31(12.62)
3="Minimally improved"	0	51	53.27(6.11)	40.44(11.37)	39.09(11.14)
	1	78	66.65(9.85)	48.10(11.64)	41.67(14.13)
	Total	129	61.36(10.78)	45.04(12.12)	40.78(13.06)
4="Not changed"	0	14	54.86(8.07)	36.44(8.43)	34.73(4.05)
	1	21	65.14(10.17)	44.05(11.21)	48.63(17.06)
	Total	35	61.03(10.57)	40.03(11.71)	43.53(17.01)
5="Minimally worse"	1(Total)	3	66.33(3.22)	42.67(2.89)	52.00(14.42)
7="Very much worse"	0	1	54.00	49.00	39.00
	1	2	61.50(.71)	62.00	49.00(21.21)
	Total	3	59.00(4.36)	55.50(9.19)	45.67(16.07)

Note: Adolescents who expected their depression to worsen with treatment are not included in the table due to their relatively small numbers.
**0=Mild-moderate depression, 1=Marked-severe depression*
**n reflects the number of adolescents at week 0.

Figure 4 provides a graphic illustration of Table 9 for adolescents who expected their depression problems to be "very much improved," "much improved," "minimally improved," and "not changed." Teens who expected their depression problems to worsen with treatment are not included in the graph due to their relatively small numbers.

The same process of random regression modeling and model selection was conducted with the RADS replacing the CDRS-R as the outcome variable. The following

Figure 3. CDRS-R Scores over Time Based on Assigned TEs
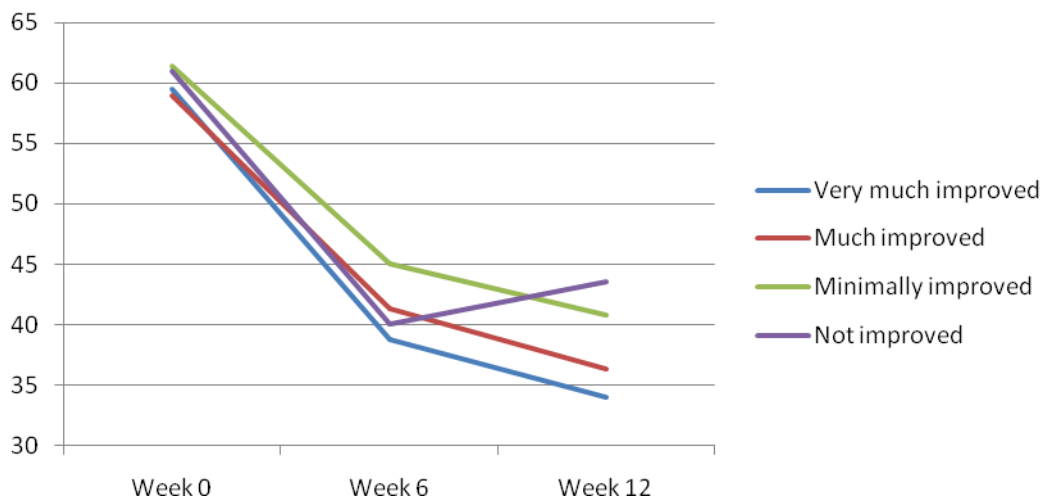
fixed effects were found to be significant: Treatment [$F(3,751.13)=2.95$, $p<.001$], time [$F(1,663.59)$, $p=.032$], treatment by time [$F(3,736.02)=3.83$, $p=.01$], site [$F(3,751.13)=2.95$, $p<.001$], and assigned TE by time [$F(5,715.67)=2.33$, $p=.04$]. The effect of treatment expectancy on outcome was not significant by itself [$F(5,761.25)=1.31$, $p=.26$]. Paired contrasts on adjusted means at week 12 showed differences in outcome between adolescents who expected their depression problems to be "very much improved" and adolescents who expected their depression problems to be "minimally improved" with treatment ($p=.053$); see Table 9 and Figure 4. As in Figure 3, adolescents who expected their depression problems to worsen with treatment were not included in the graph.

In the original TADS sample ($n=439$), the following percentages of adolescents were categorized as responders to treatment ("very much improved" or "much improved") according to the clinician-rated CGI-I: COMB (71%), FLX (60.6%), CBT,

pairwise contrasts revealed the following relationships based on treatment response:

COMB=FLX>CBT=PBO.

Table 9. RADS Scores over Time Based on Severity of Depression and Assigned TEs

Treatment Expectancy	Severity*	n**	RADS		
			Week 0 M(SD)	Week 6 M(SD)	Week 12 M(SD)
1="Very much improved"	0	36	75.06(12.20)	56.37(14.24)	49.87(12.03)
	1	43	81.47(15.25)	66.87(18.23)	59.38(17.17)
	Total	79	78.54(14.23)	62.24(17.29)	55.17(15.75)
2="Much improved"	0	68	75.24(10.49)	62.80(12.58)	57.93(13.40)
	1	83	83.53(13.33)	67.91(16.67)	63.41(16.02)
	Total	151	79.79(12.78)	65.76(15.25)	60.98(15.12)
3="Minimally improved"	0	51	74.57(15.69)	66.44(15.79)	64.51(15.68)
	1	77	82.51(13.97)	71.44(16.66)	67.70(18.61)
	Total	128	79.34(15.13)	69.47(16.43)	66.47(17.54)
4="Not changed"	0	14	67.57(16.76)	61.11(18.00)	60.27(14.60)
	1	21	84.43(14.40)	71.25(16.14)	72.55(20.24)
	Total	35	77.69(17.31)	68.10(17.09)	68.19(19.14)
5="Minimally worse"	1(Total)	3	86.00(9.17)	72.00(16.82)	75.33(8.74)
7="Very much worse"	0	1	49.00	64.00	51.00
	1	2	79.00(39.60)	114.00	99.00
	Total	3	69.00(32.92)	89.00(35.36)	75.00(33.94)

Note: Adolescents who expected their depression to worsen with treatment are not included in the table due to their relatively small numbers.
**0=Mild-moderate depression, 1=Marked-severe depression*
**n reflects the number of adolescents at week 0.

Figure 4. RADS Scores over Time Based on Assigned TEs
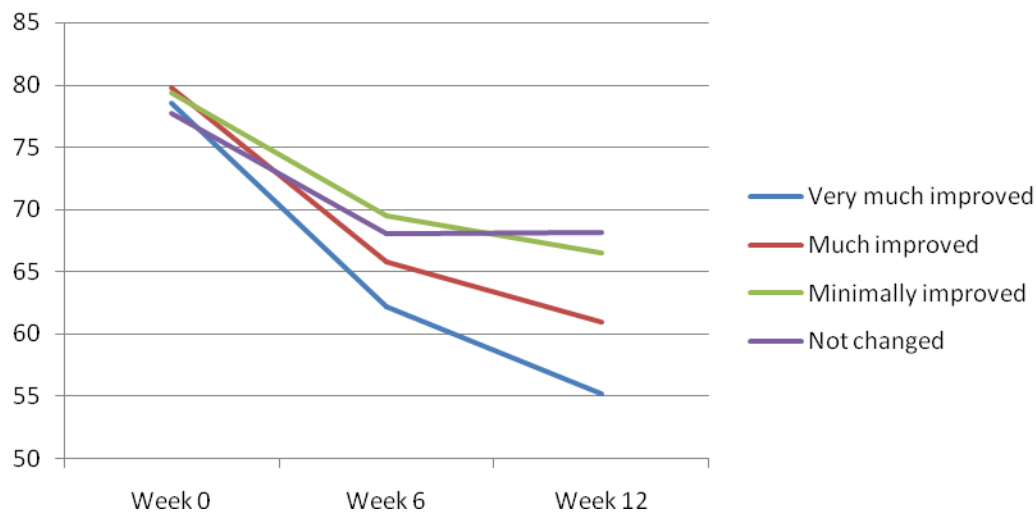
Responder rates in the current study sample were similar to the original sample for COMB (74.3%), FLX (61.6%), CBT (42.2%), and PBO (36.6%). Likewise, logistic regression revealed a significant treatment effect (Wald χ^2=37.3, p<.001) with COMB=FLX>CBT=PBO (site was not significant). When assigned TE was added to the model, both treatment (Wald χ^2=34.1, p=.001) and assigned TE contributed to the regression model (Wald χ^2=12.2, p=.03). Adolescents who expected their depression to become "very much improved" were more likely to respond to treatment than adolescents who expected minimal improvement (p=.002) or no improvement (p=.004) with treatment. Adolescents who expected their depression problems to be "much improved" were also more likely to respond to treatment compared to adolescents who expected minimal (p=.004) to no improvement (p=.014) with treatment. Figure 5 illustrates the percentage of responders to treatment for each of these four groups.

Figure 5. Percentage of Responders to Treatment Based on Assigned TEs
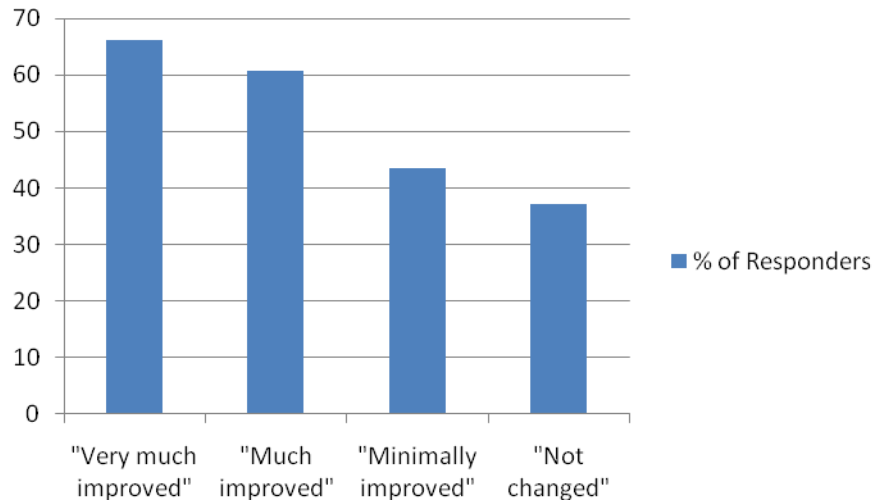
C-RAEI (CDRS-R, RADS, and CGI-I)

Attempts were made to fit a random coefficients regression model to the data using C-RAEI in place of treatment expectancy as a predictor variable for both the CDRS-R and the RADS as outcome measures. However, the models failed to converge. Subsequent analyses were performed using GLM for repeated measures. Similar results were obtained to the RRM analyses in terms of treatment, site, and treatment by time interactions. However, total C-RAEI scores did not predict CDRS-R or RADS scores over time. Additionally, total C-RAEI scores did not predict responder status, as measured CGI-I, using logistic regression.

Hypothesis 3.1

The hypothesis that assigned TE would predict completer status (yes/no) was not supported using logistic regression (Wald $\chi^2 = 3.02$, $p = .70$). Treatment and site also did not predict completer status, or alternatively, whether or not participants dropped out of

TADS. The C-RAEI also failed to predict completer status (Wald χ^2=.09, p=.77) for adolescents assigned to COMB or CBT.

Hypothesis 4.1

Assigned TE (CDRS-R, RADS, and CGI-I)

The hypothesis that severity of depression would moderate the relationship between treatment expectancy and treatment outcome was supported by the data. An RRM including treatment, time, site, severity, treatment expectancy, as well as their 2- and 3-way interactions, revealed significant effects of time [F(1, 681.86)=107.37, p<.001], treatment by time [F(3,739.68)=7.97, p<.001], site [F(12,460.21)=2.84, p=.001], severity [F(1,798.00, p<.001], and a 3-way interaction between treatment expectancy, severity, and time [F(10,744.89)=4.08, p<.001]; see Table 8. Figures 6 and 7 illustrate rates of improvement based on treatment expectancy levels for adolescents with mild to moderate depression and marked-severe depression, respectively. Rates of treatment response for adolescents with mild to moderate depression appear more sensitive to their assigned TEs when compared to adolescents with marked to severe depression.

Paired contrasts indicated that adolescents with mild to moderate depression who believed their depression problems would be "very much improved" with their assigned treatments had lower CDRS-R scores at week 12 than adolescents who believed their depression problems would be "minimally improved" with treatment (p=.003). For adolescents with marked to severe depression, adolescents who believed their depression would be "very much improved" (p=.023) and "much improved" (p=.009) with

60

treatment had lower CDRS-R scores at week 12 than adolescents who did not expect their

depression to improve ("not changed").

Figure 6. Mild-Moderately Depressed Adolescents' Improvement over Time by Assigned TEs
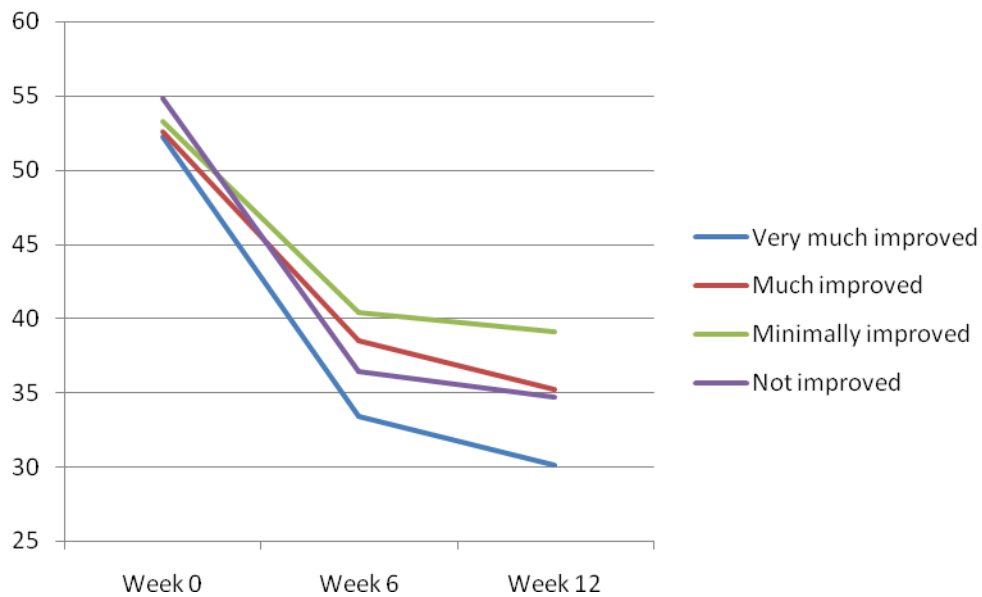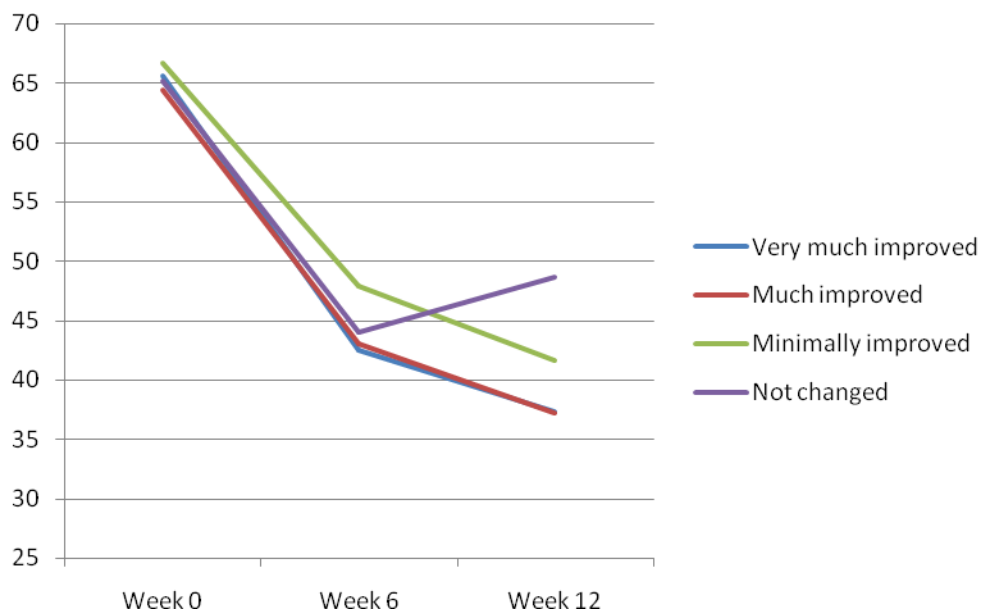

Figure 7. Moderately-Severely Depressed Adolescents' Improvement over Time by Assigned TEs

Similar results were obtained with the RADS as the outcome variable, in which the following effects were found by running a random regression model: Time [$F(1,656.25)=12.48$, $p<.001$], treatment by time [$F(3,721.48)=4.14$, $p=.006$], site [$F(12,508.82)=5.16$, $p<.001$], severity of depression [$F(1,761.83)=20.59$, $p<.001$], and a 3-way interaction between assigned TE, severity of depression, and time [$F(9,699.31)=1.98$, $p=.039$]; see Table 9. Adolescents with mild to moderate depression and the highest assigned TEs ("very much improved") had lower RADS scores at week 12 compared to adolescents who expected "much" ($p=.05$) and "minimal" ($p<.001$) improvement with their assigned treatments, while marked to severely depressed teens with the highest level of assigned TEs ("very much improved") had lower RADS scores after 12 weeks of treatment compared to adolescents who did not expect any improvement ("not changed") with their assigned treatments.

A significant 3-way interaction between treatment expectancy, severity of depression, and time was not found using logistic regression with the CGI-I (responder versus non-responder) as the outcome variable, so it was subsequently taken out of the model. The reduced logistic regression model revealed the following significant predictor variables: Treatment (Wald $\chi^2=43.44$, $p<.001$), site (Wald $\chi^2=39.36$, $p<.001$), severity of depression by treatment (Wald $\chi^2=22.22$, $p<.001$), and severity of depression by assigned TE (Wald $\chi^2=44.75$, $p<.001$). Rates of response differed between the two severity groups for adolescents who expected their depression to be "very much improved" ($p=.01$), but not for teens in the other expectancy groups (see Figure 8).

Subsequent chi-square analyses were conducted separately on the percentage of responders at week 12 for the two severity groups, excluding adolescents who expected

Figure 8. Percentage of Responders Based on Severity of Depression and Assigned TEs
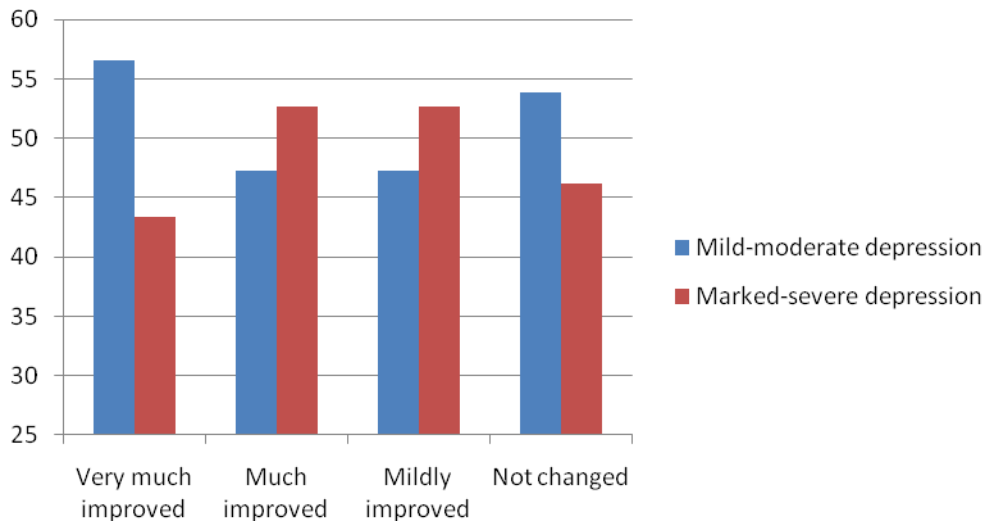
their depression to worsen with treatment. For participants with mild to moderate

depression, percentage of responders differed by treatment at rates greater than expected

by chance χ^2(3, N=170)= 19.6, p<.001. This was not the case for adolescents with

marked to severe depression. For adolescents with mild to moderate depression levels,

those who expected "very much" improvement with treatment were more likely to

respond to treatment than those with expected "mild" improvement (p<.001) or no

improvement (p=.04). Teens who expected "much" improvement also were more likely

to respond to treatment than adolescents who expected "mild" improvement (p=.003).

C-RAEI (CDRS-R, RADS, CGI-I)

General linear models for repeated measures were used to test the hypothesis that

there is an interaction between severity of depression and C-RAEI total scores. Time

[F(2,270.00)=11.38, p<.001], treatment by time [F(4,270.0)=11.01, p<.001] and site by

time [F(24.0,270.0)=1.88, p=.009] emerged as predictors for treatment outcome with

Huynh-Feldt correction, as measured by the CDRS-R. However, total C-RAEI scores did

not emerge as a predictor in the model, alone or in combination with time, treatment, or severity of depression.

The same analyses were conducted with the RADS in place of the CDRS-R with slightly different findings. In this model, the following terms were identified as significant: Treatment [$F(1,125)=5.78$, $p=.004$], site [$F(12,125)=1.87$, $p=.04$], treatment by time [$F(4,250)=11.78$, $p<.001$], and a 3-way interaction between severity of depression, C-RAIE total scores, and time [$F(2,250)=3.26$, $p=.04$]. Subsequent correlations indicated that C-RAIE total scores predicted week 12 RADS scores for teens with marked to severe depression ($R=-.25$, $p=.006$) but not for teens with mild to moderate depression ($R=-.146$, $p=.133$). Therefore, adolescents who accepted the treatment rationale for CBT and had higher treatment expectancies, as measured by the C-RAIE, were more likely to improve with treatment if they suffered from marked to severe depression.

In contrast, logistic regression identified a significant effect of treatment (Wald $\chi^2=14.52$, $p<.001$) in predicting responders versus non-responders to treatment according to the CGI-I, but did not identify any other significant main effects (site, time, C-RAIE totals) or interactions for teens assigned to COMB or CBT.

Hypothesis 5.1

Finally, the hypothesis that COMB would continue to outperform the other three treatment conditions after controlling for treatment expectancy was supported by the data. As reported in the results section (see above) of hypothesis 2.1, treatment and/or treatment by time were significant predictors of treatment response when treatment

64

expectancy was included in the model, regardless of whether outcome was measured by the CDRS-R, the RADS, or the CGI-I.

CHAPTER IV

DISCUSSION

Summary of Findings

Adolescent Characteristics and Treatment Expectancy in TADS

As hypothesized, TADS adolescents endorsed higher treatment expectations for COMB compared to CBT and medication only. The majority of adolescents (76.3%) believed that their depression problems would become "very much improved" or "much improved" with COMB, most of whom (43.6%) posited the former belief. Approximately half of the participants reported that they expected their depression problems to be at least "much improved" from a course of treatment with CBT or medication only. Expectations for improvement did not differ between these two treatments. This information is noteworthy given that very little is known about treatment expectancy in children and adolescents.

A related concept of comparison is treatment preference. Investigators recently surveyed students in a rural, Nova Scotia high school about their preferences for depression treatment *if* they were to become depressed. Students expressed a strong preference for psychotherapy over pharmacotherapy (92% of boys and 94.9% of girls) with 48% of the sample reporting that they would refuse antidepressant treatment due to its potential side effects (Bradley, McGrath, Brannen, & Bagnell, 2010). Previously, Jaycox, Asarnow, Sherbourne, Rea, LaBorde, and Wells (2006) found that adolescents who screened positive for depression in primary care preferred counseling (50%) over medication (22%). Negative attitudes about depression treatment, positive attitudes about medication treatment, as well as current anxiety symptoms were associated with

66

preference for medication. Both of these studies suggest that adolescents tend to prefer psychotherapy for the treatment of depression, while TADS teens did not report higher expectations for one over the other. Differences between these findings and the current study's findings may reflect differences between treatment preference and expectancy, study methods, and/or sample characteristics, and are not well understood.

In the current study, age and race/ethnicity were not associated with treatment expectancy for COMB, CBT, or medication only. There was a tendency for adolescent females to report higher expectations for COMB compared to adolescent males, whereas no gender differences were found in treatment expectations for either monotherapy. Interestingly, adolescents with family income levels below $75,000 reported lower treatment expectancies for CBT (but not for COMB or medication only) than adolescents with family income levels at or above this cutoff. Combined with the finding that treatment expectancy predicts outcome, this may partially explain why income moderated treatment response in TADS. Curry and colleagues (2006) found that adolescents with family income levels at or above $75,000 responded as well to CBT as COMB and FLX, and were more likely to respond to CBT than PBO. In contrast, adolescents with family income levels below $75,000 demonstrated a similar rate of response to CBT and PBO.

In Safren, Heimberg, and Juster's 1997 study investigating the efficacy of group CBT for the treatment of social phobia, the investigators found that adults who had completed some postgraduate education had higher expectations for improvement with CBT than adults who had not completed high school, which in turn, predicted higher rates of treatment response. The authors speculated that level of education may be correlated with confidence in one's ability to master cognitive-behavioral techniques and

benefit from treatment. Self-efficacy has been found to differ between adolescents based on their socioeconomic status (Hannah & Kahn, 1988). It is possible that adolescents with lower family income levels doubted their ability master CBT techniques and benefit from treatment. This may explain why adolescents with family income levels between $20,000 and $39,999 tended to have lower expectations for CBT and COMB (but not medication without CBT) than their wealthier peers; in comparison to CBT, treatment with medication is likely perceived as requiring more passive participation.

Severity of depression, hopelessness, and suicidality were similarly found to be negatively correlated with expectancy for CBT, but not for COMB or medication only. Therefore, it was not the case that these markers of illness severity predicted lower expectations for treatment in general. More severely ill adolescents in TADS may have believed that medication (either alone or in combination with CBT) was necessary in order to alleviate their depressive symptoms. The underlying assumption behind this belief is that medication is a stronger treatment for depression than CBT. Alternatively, adolescents with greater severities of illness may have conceptualized their depression as more biological in nature, thus requiring a more "biological" treatment. The fact that severity of depression was positively associated with higher treatment expectations for COMB suggests that despite lower expectations for CBT, adolescents with more severe depression perceived additional benefit with CBT in combination with medication.

The only factor found to be associated with treatment expectancy for medication without CBT was the presence of a comorbid anxiety disorder. Adolescents with a co-occurring anxiety disorder diagnosis had lower expectations for improvement with medication than their peers. This is not entirely explained by anxiety over medication

side effects, since there were no differences in expectations for COMB based on comorbidity. Perhaps, adolescents prone to anxiety had more concerns about medication without the additional monitoring of a therapist. Taken together, these results suggest that treatment expectancy varies by treatment and adolescent characteristics. More research is needed in order to understand how an adolescent's knowledge of treatment, perceived self-efficacy, and perceived treatment fit (e.g. whether or not the treatment is seen as addressing one's problems) contribute to treatment expectancy.

Treatment Expectancy Predicts Treatment Response

Curry and colleagues (2006) initially reported that treatment expectancy predicts but does not moderate treatment outcome. This appears to be a robust finding, appearing in generalized linear, randomized coefficient, and logistic regression models with both clinician-rated and adolescent-rated measures of treatment response. Regardless of treatment, adolescents' expectations for improvement with their assigned treatments impacted their treatment response. Perhaps most noticeably, the percentage of responders to treatment (based on the CGI-I) decreased in a linear fashion as participants' treatment expectations went down (see Figure 5).

Lewin, Peris, Bergman, McCracken, and Piacentini (in press) also demonstrated that treatment expectancy was positively associated with treatment response in a study of exposure-based treatment for childhood OCD. The investigators found that children's baseline depressive symptoms, but not their severity of OCD symptoms, were associated with treatment expectancy. In addition to treatment response, expectancy predicted homework compliance and study completion. Homework was not examined in the current study, and is currently being examined in a separate TADS paper (Simons et al.,

in progress), while treatment expectancy did not predict study completion in TADS. Combined with Lewin et al.'s results, TADS provides initial evidence that treatment expectancy is an important consideration in the treatment of mood and anxiety disorders in children and adolescence.

For the most part, the finding that treatment expectancy predicts treatment outcome in TADS is consistent with the adult literature. As mentioned previously, Arnkoff, Glass, and Shapiro (2002) found support for a positive relationship between expectancy and outcome in 12 studies, mixed support in seven studies, and null findings in five studies. These 24 studies are difficult to compare to each other due to their different populations, treatments under investigation, measurements of expectancy, timing of assessments, and statistical procedures. For example, of the studies reviewed in my introduction, only one study utilized hierarchical linear modeling (Price, Anderson, & Heinrich, 2008) similar to the statistical methods employed in the current study. The researchers found that treatment expectancy predicted treatment gains during therapy but not during follow-up in a study of virtual reality exposure and in vivo exposure for the treatment of flying phobia.

Notably, the investigators found poor internal consistency for their initial measure of expectancy, which included the following three items: 1) confidence that therapy would reduce fear of flying-related symptoms, 2) confidence that therapy would reduce other fears, and 3) how logical treatment seemed. They subsequently decided to use the first item alone as their measure of treatment expectancy given its high face validity. As Lorber, Mazzoni, and Kirsch (2007) advocate, response expectancy is specific to one's expectations. It is unclear why participants would expect treatment for flying phobia to

70

reduce other fears (item 2), while item 3 appears to target acceptance of treatment

rationale rather than treatment expectancy.

Borkovec and Nau's 1972 credibility/expectancy questionnaire, which consists of

four questions, includes one question that measures treatment credibility ("At this point,

how logical does this therapy seem to you at this point?"). This measure has been shown

to predict treatment response (e.g. Chambless, Chan, & Glass, 1997). Almost thirty years

after its creation, Devilly and Borkovec (2000) investigated the psychometric properties

of this measure, and derived two predicted factors from the measure, a cognitively based

credibility factor and a more affectively based measure of expectancy. The measure was

found to have high internal consistency within each factor, and test-retest reliability

across different populations. The expectancy, but not the credibility factor, was found to

be associated with outcome. The investigators hypothesized that credibility scales are

cognitively related, while expectancy scales are more affective-based. It is possible that

the Treatment Expectancy for Adolescents (TEA) and the CBT Rationale Acceptance and

Improvement Expectancy (C-RAIE) measures, both specifically designed for TADS,

tapped into different constructs, which subsequently led to different findings.

C-RAIE Scores Do Not Predict Treatment Outcome

While the single-item measure of treatment expectancy (derived from the TEA)

predicted treatment response in TADS, total C-RAIE scores for adolescents assigned to

CBT or COMB did not. The C-RAIE consists of six items, three of which were designed

to measure acceptance of treatment rationale. The measure was found to have high

internal consistency in the current study, which is indicative of one latent variable.

Therefore, it is unlikely that non-significant findings for the C-RAIE can be attributed

71

solely to its inclusion of items designed to measure acceptance of treatment rationale. Moreover, acceptance of treatment rationale has been found to predict treatment outcome in studies of CBT for depression (Addis & Jacobson, 2000; Fennell & Teasdale, 1987). Differences found between the TEA and the C-RAIE, rather, can be attributed to discrepancies in the timing of the two assessments and their statistical power; while the TEA was administered to the entire study sample prior to adolescents finding out their randomized treatment assignments, the C-RAIE was only administered to adolescents assigned to CBT or COMB (half the sample) during their second session of CBT.

Adolescents filled out the TEA with very little treatment information (typically no more than a couple of sentences for each of the treatment arms) provided by study staff (e.g. "CBT is a type of psychotherapy that has been shown to be effective for the treatment of depression."). Presumably, adolescents varied greatly in terms of their knowledge of CBT, antidepressant medication, and the combination of the two treatments when they entered TADS. The C-RAIE, in comparison, was administered after adolescents were made aware of their treatment assignments and had experienced some exposure to CBT. Specifically, session 1 included the following goals: 1) to begin to establish a collaborative therapeutic relationship, 2) to review briefly the major findings from assessment and relate these to the model of depression, 3) to explain rationale for CBT; rationale for family involvement; and how this treatment can help, 4) to elicit adolescent's and parents' initial goals for treatment, and 5) to review no-suicide contract and answer questions about treatment (Curry et al., 2000).

TADS therapists provided an extensive amount of information to adolescents and their parents at session 1, including written handouts. Furthermore, in the TADS' CBT

treatment manual, therapists were encouraged to convey hopefulness to adolescents during this session, and were instructed to describe depression as a learned pattern that is capable of being changed, thus instilling further hope for improvement. Therapists were specifically instructed to point out to adolescents receiving COMB that medication can also change this pattern ["It (medication) can especially help to get the changes started as adolescents learn new skills. Then, the new skills can take over and the medication will not be necessary."]. Adolescents were reminded of the treatment rationale for CBT in session 2, prior to filling out the C-RAIE.

How might this account for the finding that the C-RAIE did not predict treatment response for adolescents assigned to CBT, either alone or in combination with FLX? One hypothesis is that treatment expectancy is more important prior to treatment initiation. Research suggests that treatment gains early in therapy predict treatment outcome, especially when these gains are "sudden" (occurring between two sessions; Tang & Deurbeis, 1999). For example, Kelly, Robert, and Ciesla (2005) found that sudden gains occurring in the first third of CBT for depression treatment led to larger symptom reductions over time and treatment response. In a more nuanced study, Busch, Kanter, Landes, and Kohlenberg (2006) compared sudden gains that occurred after initial assessment, after one session of cognitive therapy, and single-session gains that occurred after at least two sessions of therapy. First-session gains and gains that occurred in the first half of treatment predicted positive outcome in adults with depression.

Since early sudden gains often occur before the "specific" interventions of treatments are administered (e.g. thought records in CBT), some researchers have speculated that placebo/expectancy and other common factors of treatment account for

73

early sudden gains (Haas, Hill, Lambert, & Morrell, 2002). However, Tang and DeRubeis initially reported that CBT clients demonstrated cognitive changes (a primary target of CBT) in the session directly prior to their sudden gains, which they attributed to clients' symptom reduction.

Based on the current study's findings, it is hypothesized that treatment expectancy may be more predictive of early response to treatment, while other factors may account for improvement later on in treatment. Future research is necessary in order to draw any firm conclusions about the importance of treatment expectancy in different stages of treatment. Since the TEA was not re-administered in conjunction with the C-RAIE after starting CBT, it is unclear whether or not the information provided in session 1 of CBT increased or decreased adolescents' expectations for improvement with CBT. Some teens may have been disappointed to learn that CBT requires significant effort (e.g. homework) with an emphasis on learning (much like school) if they had mostly wanted and expected psychotherapy to consist of someone compassionate to talk (i.e. supportive therapy), while other teens' expectations may have improved after learning about CBT's focus on the present and its inclusion of problem-solving.

Severity of Depression Moderates the Effect of Treatment Expectancy on Outcome

The hypothesis that severity moderates the relationship between treatment expectancy and outcome was supported by the TADS data. Two- or three-way interactions between adolescents' expectation for improvement with their assigned treatment condition (i.e. assigned TE), severity of depression (mild-moderate versus marked-severe depression), and time (in the case of three-way interactions) were found to be significant for each of the primary outcome measures in TADS using random

74

coefficients and logistic regression. If it is true that mild to moderately depressed adolescents are more sensitive to the effects of expectancy, we would expect to see increasingly smaller rates of recovery as treatment expectancy decreased ("very much improved">"much improved">"minimally improved">"not changed"), which is indeed evidence in Figure 6. The same pattern was not evident for adolescents with marked to severe depression, although there were differences in outcome between the groups farthest apart from each other ("very much improved">"not changed"), which implies that treatment expectancy still matters for these teens.

These results are consistent with research suggesting that the placebo response is less likely to occur in more severe forms of psychopathology (Shapiro & Shapiro, 1997); it is also consistent with research indicating that antidepressants are especially likely to outperform placebo for individuals with more severe forms of depression (Khan et al., 2002; Wilcox et al., 1992; Fairchild et al., 1986), where expectancy effects are less powerful, thus requiring the more "active" ingredients of medication. To my knowledge, this is the first study to examine severity of depression as a moderator of treatment expectancy on outcome; although preliminary, it is notable that for all of the three primary measures of expectancy, significant interactions were found between severity of depression and adolescents' expectations for improvement with their assigned treatment conditions.

When total C-RAIE scores replaced assigned TEs in the random coefficients and the logistic regression analyses, a significant interaction between total C-RAIE scores and severity of depression was found for the TADS' self-rated outcome measure (i.e. RADS), but not for the two primary clinician-rated measures. The C-RAIE was associated with

75

treatment outcome for marked to severely depressed teens, but not for mild to moderately depressed teens. This finding is perplexing and raises further questions about the methods and timing of assessment of treatment expectancy. What is seems to suggest, however, is that it may be especially important for marked to severely depressed adolescents to "buy-in" to CBT after their initial session, perhaps in order to increase treatment engagement. There may also be a difference between severely depressed adolescents who, after hearing about the rationale for CBT, accept the rationale and have higher expectations for improvement than adolescents who are exposed to the same rationale and remain skeptical about CBT.

A study conducted by Fennell and Teasdale (1987) is of particular relevance to this finding. The investigators examined clients' acceptance of treatment rationale in a treatment outcome study for depression with CBT. After reading Beck and Greenberg's 1974 *Coping with Depression* booklet (designed to provide clients with an introduction to CBT), clients were asked to share their reactions to the booklet. Acceptance of treatment rationale, as coded by independent evaluators based on clients' recorded reactions, predicted client outcomes at three and six months. Interestingly, the investigators also found that higher levels of "depression about depression" early in treatment were associated with both acceptance of treatment rationale and subsequent response to CBT.

"Depression about depression" refers to beliefs consistent with the idea that depression is untreatable, one's own fault (e.g. based on a character flaw), and not capable of being understood. Although it is not often identified in the more recent studies of depression, "depression about depression" is an important concept given its correlation with depression severity (Fennell & Cambell, 1984). Fennell and Teasdale speculated

that adolescents depressed about their depression may have received considerable benefit (e.g. symptom reduction and increased feelings of hope) from increased insight into their depression after reading *Coping with Depression* and learning more about the CBT model. The same reasoning can be applied to severely depressed TADS participants. It is possible that severely depressed TADS adolescents who endorsed acceptance of treatment rationale and higher expectations for improvement with CBT *after* learning about the CBT model may have suffered from "depression about depression" prior to treatment initiation. For these adolescents, we might expect a clear and convincing treatment rationale to be particularly important, both in terms of raising treatment expectations and increasing treatment engagement.

Treatment Expectancy and Treatment Effects Contribute Separately to Outcome

The final aim of the current study was to investigate whether or not treatment expectancy accounts for COMB's superior performance in the acute phase of TADS. As previously discussed, the "uneven blind" in TADS has been criticized as a flawed design of the study (Jureidini, Tonkin, & Mansfield, 2004). The uneven blinding in TADS refers to the fact that adolescents assigned to COMB and CBT were cognizant of their treatment assignments, while adolescents assigned to one of the "pills only" conditions were unaware of whether they were receiving FLX or PBO. Thus, treatment expectancy effects were presumably controlled for in the "pills only" conditions, but not for adolescents receiving CBT (alone or in combination with medication). Given that independent evaluators and adolescents were able to guess teens' assigned treatment conditions at rates greater than expected by chance alone, it is likely that expectancy influenced both clinician- and self-rated measures of outcome.

77

The current study found that both treatment expectancy and treatment (either alone or in combination with time) predicted treatment outcome for the study's three primary outcome measures. It seems that treatment differences cannot be attributed to treatment expectancy alone. This finding is consistent with Lambert's four-factor model, which attributes similar, separate, and modest (15%) effects of hope/expectancy and specific models/techniques. However, it is important to note that these effects are not easily divorced. For example, some treatments might simply make more *sense* than other treatments, and perhaps are more congruent with a person's culture. In this case, does treatment expectancy function as a common or a specific factor? Similarly, certain treatment methods (e.g. CBT's emphasis on "collaborative empiricism") may engender a stronger treatment alliance, which in turn, may impact treatment outcome. In other words, the process of change likely involves a combination of common and specific factors that are highly interrelated and dependent on each other.

Limitations and Future Directions

There are several limitations in the current study that can be used to guide future research. First, although treatment expectancy was not shown to be associated with participants' ethnicity/race, the TADS sample was predominantly Caucasian Americans and the findings of this study may not generalize to other populations. More efforts should be made in the future to overcome barriers that may prevent minority adolescent populations from participating in treatment outcome research, such as TADS.

Second, while 100% of teens assigned to COMB or CBT knew their assigned treatment conditions, a significantly smaller percentage of teens assigned to FLX or PBO could identify their assigned treatment conditions. At week 12, 63.9% of teens assigned

to FLX and 64.4% of teens assigned to PBO correctly guessed their assigned treatment condition. Therefore, it is likely that treatment expectancy impacted treatment outcome to a greater extant in COMB and CBT compared to FLX and PBO. While it is difficult to pinpoint the effects of treatment expectancy in blinded clinical research trials, it is certainly more difficult in studies with uneven blinding procedures. Future research studies in this area should include multiple measurements of expectancy over time without the use of blinding procedures, or alternatively, might include the use of blinding as a design feature to manipulate expectancy levels.

Third, treatment expectations for PBO were not assessed (or, alternatively, adolescents' expectations for improvement over time without treatment). Therefore, adolescents' expectations for improvement with medication only were used as their assigned TEs for the purposes of this study. It is unclear how much of an adolescent's expectations for improvement with a certain treatment could be accounted for by their overall expectation for improvement in general. For example, teenagers who believe their depression problems will be "much improved" over time without treatment, who then indicate that they expect to be "very much improved" with COMB treatment, perhaps only expect minimal improvement with COMB in addition to the effects of time. It would be helpful for future research studies to include a more nuanced approach to conceptualizing and measuring expectancy in its various forms. This would also help to clarify the "active" ingredients (e.g. self-efficacy, acceptance of treatment rationale, etc.) in different definitions of expectancy (e.g. overall versus treatment expectancy).

Fourth, although adolescents were asked about their expectations for improvement with COMB, CBT, and medication only, independent evaluators, CBT

therapists, and pharmacotherapists were not asked to rate their expectations for the TADS treatments. This implies that adolescents' expectations are more important than the investigators' or the treatment providers' expectations, which has not been demonstrated. In fact, it has been estimated that the correlation between researchers' therapeutic allegiance and treatment outcome may be as high as .85 (Luborsky et al., 1999), and accounts for treatment outcome more than any other factor that has been investigated so far (common or specific; Wampold, 2001). By assessing investigators' treatment expectancies, it may be possible to determine the extent of rater bias in randomized, clinical research trials.

Fifth, the measures of expectancy in TADS were designed for the study. Therefore, very little is known about the psychometric properties of the measures, which complicates the comparison of these results to the results of other similar studies. Moreover, although the TEA measure appears to have face validity, it is not entirely clear if the measure is actually measuring treatment expectancy, or if it is a measure of a related or alternative construct (e.g. agreeableness). More research is needed in order to validate these measures and clarify the construct of treatment expectancy. Also of interest is the test-retest reliability of the TEA and the C-RAIE. Is treatment expectancy (and its related constructs) stable within an individual, or is it variable over time? Also, how easily is treatment expectancy manipulated? What are the best ways of increasing treatment expectancy? If expectancy has an affective component as Devilly and Borkoved (2000) suggest, how can clinicians improve the treatment expectations of their clients on an emotional level, especially for adolescents who may be skeptical about treatment?

Other areas for future research include the following: 1) identifying treatment expectancy's mechanisms of change (e.g. through increased treatment engagement), 2) utilizing treatment matching strategies based on participants' expectancies/preferences in order to improve outcome, 3) manipulating expectancy in randomized clinical research trials (assigning high versus low expectancy treatment conditions within participants' treatment assignments), and 4) investigating the long-term impact of treatment expectancy. Basoglu, Marks, Kilic, Brewin, and Swinson (1994), for example, found that higher treatment expectations for pharmacotherapy were found to be associated with greater attributions for improvement to drug treatment in treatment responders. Greater attribution of improvement to medications predicted more severe withdrawal effects and a relapse of symptoms during follow-up, although treatment expectancy alone did not. This study suggests that treatment expectancy indeed matters after treatment is completed. One question of interest is whether assigned TE or total C-RAIE scores predict outcome in the later stages of TADS.

Finally, it is important to consider the context in which treatment expectancy develops, changes, and is maintained. How might trauma, for example, affect adolescents' expectations for particular treatments? For adolescents attempting to cope with chaotic living situations, it may be necessary for mental health providers to directly address these situations in order to increase adolescents' treatment expectations and engagement early on in treatment. Also, it is likely that adolescents will endorse higher expectations for treatments that appear to address their problems directly. More research is needed in order to understand how adolescents' environmental and historical contexts,

explanations for their depression problems, treatment expectations, and depressive symptoms influence each other over time.

Conclusions

Despite the study limitations outlined above, very little is known about the treatment expectancies of children and adolescents and how it impacts treatment outcome. Treatment expectancy, which has been called the "ignored common factor," appears to predict outcome for adolescents treated for depression, regardless of treatment. Adolescents had the highest expectations for improvement with COMB with the more severely depressed teens reporting lower expectations for CBT, in particular. The current study results suggest that treatment expectancy may be especially important for adolescents prior to treatment initiation with mild to moderate depression, although it may become more important (in combination with acceptance of treatment rationale) for those with marked to severe depression after treatment has begun. In TADS, both treatment expectancy and treatment assignment predicted treatment response. Therefore, it is not the case that the former accounts for COMB's superior performance in TADS. Rather than seeing treatment expectancy as a factor that must be controlled to isolate the effects of treatment (e.g. through blinded clinical research trials), it is perhaps more fruitful to view expectancy as an active ingredient in psychotherapy, and instead find ways to increase its potency.

APPENDIX A

TEA

How much do you expect your depression problems to improve with each of the following treatments? Circle your answers below.

1=Very much improved

2=Much improved

3=Minimally improved

4=Not changed

5=Minimally worse

6=Much worse

7=Very much worse

1. Cognitive Behavior Therapy

1   2   3   4   5   6   7

2. Medication only

1   2   3   4   5   6   7

3. Combined Cognitive Behavior Therapy with medication

1   2   3   4   5   6   7

APPENDIX B

C-RAIE

Please rate each of the following items on a scale of 1 ("strongly disagree") to five ("strongly agree") based on your agreement with the statement.

1=Strongly disagree
2=Somewhat disagree
3=Neutral
4=Somewhat agree
5=Strongly agree

    1. What depression is made sense to me.

1   2   3   4   5

    2. What CBT is made sense to me.

1   2   3   4   5

    3.   How CBT will help made sense to me.

1   2   3   4   5

    4. I expect I will have control over my depression through this treatment.

1   2   3   4   5

    5. I expect to get better or less depressed through this treatment.

1   2   3   4   5

    6. I expect life to get better through this treatment.

1   2   3   4   5

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