An Exploratory Analysis of the Impact of Family Functioning on Treatment for Depression in Adolescents

Norah C. Feeny,
Department of Psychology, Case Western Reserve University

Susan G. Silva,
Duke Clinical Research Institute, Duke University Medical Center

Mark A. Reinecke,
Department of Psychiatry, Northwestern University

Steven McNulty,
Duke Clinical Research Institute

Robert L. Findling,
Department of Psychiatry, Case Western Reserve School of Medicine

Paul Rohde,
Oregon Research Institute

John F. Curry,
Department of Psychiatry, Duke University Medical Center

Golda S. Ginsburg,
Division of Child and Adolescent Psychiatry, Johns Hopkins University School of Medicine

Christopher J. Kratochvil,
Department of Psychiatry, University of Nebraska Medical Center

Sanjeev M. Pathak,
Cincinnati Children's Hospital Medical Center

Diane E. May,
Department of Psychiatry, University of Nebraska Medical Center

Betsy D. Kennard,
Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas

Anne D. Simons,
Department of Psychology, University of Oregon

Karen C. Wells,
Department of Psychiatry, Duke University Medical Center

Michele Robins,
Children's Hospital of Philadelphia

David Rosenberg, and
Department of Psychiatry, Wayne State University

Correspondence should be addressed to Norah C. Feeny, Department of Psychology, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106. norah.feeny@case.edu.

John S. March
Department of Psychiatry, Duke University Medical Center

Abstract

This article explores aspects of family environment and parent–child conflict that may predict or moderate response to acute treatments among depressed adolescents ($N = 439$) randomly assigned to fluoxetine, cognitive behavioral therapy, their combination, or placebo. Outcomes were Week 12 scores on measures of depression and global impairment. Of 20 candidate variables, one predictor emerged: Across treatments, adolescents with mothers who reported less parent–child conflict were more likely to benefit than their counterparts. When family functioning moderated outcome, adolescents who endorsed more negative environments were more likely to benefit from fluoxetine. Similarly, when moderating effects were seen on cognitive behavioral therapy conditions, they were in the direction of being less effective among teens reporting poorer family environments.

In the last decade, researchers have learned a great deal about the efficacy of both pharmacological and psychosocial interventions for major depressive disorder (MDD) in children and adolescents. Studies have shown that cognitive behavioral therapy (CBT) is an efficacious treatment for MDD in youth (see Butler, Chapman, Forman, & Beck, 2006; Compton et al., 2004; Curry, 2001; Kaslow & Thompson, 1998; and Reinecke, Ryan, & DuBois, 1998, for reviews), though its impact on depression may be modest (Weisz, McCarty, & Valeri, 2006). Results of clinical trials have also supported the efficacy of medications, in particular fluoxetine (FLX), in the treatment of depressed youth (Emslie et al., 1997; Treatment for Adolescents with Depression Study [TADS] Team, 2004). Most recently, in the TADS, acute (12-week) treatment response rates among teens with MDD were 71% for the combination of CBT and FLX (combination [COMB]), 60.6% for FLX alone, and 43.2% for CBT alone (TADS, 2004). Thus, even the best treatments for depression are effective in only 60 to 70% of treated youth. Given this, it is essential to better understand factors that influence treatment outcome in depressed adolescents.

A developing body of research highlights the role of family relationships and interactions as variables that may be relevant to understanding MDD in adolescents. Disturbances in family functioning have long been recognized as important contributors to the development of child and adolescent psychiatric disorders (e.g., Cummings, Davies, & Campbell, 2000). Indeed, a relatively large body of literature supports the relation between child mental health problems and various aspects of impaired family functioning: general family functioning (e.g., Stark, Humphrey, Crook, & Lewis, 1990), parent–child conflict (e.g., Barrera, Chassin, & Rogosch, 1993), and martial conflict (Davies & Cummings, 1994; Gottman & Notarius, 2000). Similarly, having a family member with a psychiatric disorder is consistently predictive of poor family functioning and/or impaired relationships (e.g., Joffe, Offord, & Boyle, 1988; Keitner & Miller, 1990; Tamplin, Goodyer, & Herbert, 1998).

Specific to adolescent depression, family environments characterized by high levels of conflict are predictive of higher levels of depression (Formoso, Gonzales, & Aiken, 2000; McCleary & Sanford, 2002). In a large study of adolescents and their mothers, less supportive and more conflictual family environments were associated with greater levels of depressive symptoms both concurrently and prospectively (Sheeber, Hops, Alpert, Davis, & Andrews, 1997). Depressed youth also display substantially more problematic family interactions with both their mothers and fathers than youth at risk to develop depression (Birmaher et al., 2004). Similarly, parent–child conflict has been associated with vulnerability to (Kaslow, Deering, & Racusin, 1994), severity of (Goodyer, Herbert, Tamplin, Secher, & Pearson, 1997), and persistence of (Sanford et al., 1995) depression in

youth. Higher levels of parental marital conflict have also been associated with a higher risk for development of MDD in adolescents (Unger, Brown, Tressell, & McLeod, 2000). Of importance, increases in both marital distress (i.e., dissatisfaction and unhappiness) and marital conflict (i.e., open hostility between parents) have been demonstrated to predict increases in adolescents' depressive symptoms over time in a recent prospective study (Cui, Conger, & Lorenz, 2005).

Among adults, studies have demonstrated that unhealthy family functioning including high levels of criticism is associated with decreased likelihood of recovering from depression and increased risk of relapse (Hooley, Orley, & Teasdale, 1986; Keitner et al., 1995). There is also significant evidence (see Hooley & Gotlib, 2000) to support that such family conflict variables, or expressed emotion, are powerful predictors of outcomes and relapse for other serious psychiatric illnesses such as schizophrenia and bipolar disorder (e.g., Butzlaff & Hooley, 1998; Marom, Munitz, Jones, Weizman, & Hermesh, 2005; Miklowitz, Goldstein, Nuechterlein, Snyder, & Mintz, 1988). Less is known, however, about the impact of such family relationship factors on treatment outcome (psychosocial or pharmacological) among depressed adolescents. Data suggest that adolescents who report higher levels of parent–child conflict are less likely to recover from depression despite treatment (Birmaher et al., 2000). In a recent article exploring a variety of potential moderators of outcome in the TADS sample, family conflict levels, as measured by the Conflict Behavior Questionnaire (CBQ; Robin & Foster, 1989), were not found to predict or moderate acute treatment outcomes (Curry et al., 2006). However, this was not a fine-grained analysis of the impact of family environment: Only one measure of parent reported conflict was included, family functioning per se was not examined, and no adolescent reported data were examined. Given the evidence that family variables are predictive of treatment efficacy among adults, they warrant further investigation among adolescents.

In this article, we explore the impact of general family functioning and parent–child conflict on response to treatment for depression in the TADS sample. We are interested in identifying family variables prior to treatment that either predict outcome or moderate outcome, both in terms of depression severity and general functioning. Predictors and moderators are variables that are present prior to treatment and are independent of treatment assignment (Kraemer, Wilson, Fairburn, & Agras, 2002). A predictor is a variable that has a main effect on outcome regardless of treatment condition. By contrast, a moderator variable has an interactive effect with treatment condition on treatment outcome. We hypothesized that poor family functioning and high levels of parent–child conflict will be predictive of worse response for both depression and functioning across the interventions within TADS. We also examined, on an exploratory basis, whether these variables moderate outcome across individual treatment groups: FLX, CBT, COMB, or clinical management with pill placebo (PBO).

METHOD

TADS Sample

The TADS design, methods, and sample characteristics have been described previously (TADS Team, 2003, 2004, 2005). TADS was a randomized controlled trial funded by the National Institute of Mental Health, conducted at 13 academic and community clinics in the United States, which enrolled 439 outpatients, age 12 to 17 years ($M = 14.6 \pm SD$ 1.5 years) with a current primary *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). diagnosis of MDD (American Psychiatric Association, 1994). Fifty-four percent of the sample was female, and 74% were Caucasian. All patients and at least one parent provided written informed consent. The coordinating center at Duke University Medical Center and the Institutional Review Board at each site approved and monitored the protocol, and

quarterly review was performed by the Data and Safety Monitoring Board of the National Institute of Mental Health.

In the TADS, patients were randomly assigned to one of four treatment conditions: FLX, CBT, COMB, or PBO. These interventions have been described in detail in previous published reports (TADS Team, 2003, 2004, 2005). Two primary outcome measures, depression severity and end-of-treatment status (responder: much or very much improved), were collected by a blinded independent evaluator (IE). During the acute (12-week) treatment phase, the trial was double-blind for the FLX and PBO conditions and single-blind for the CBT and COMB conditions. On the primary outcome measure, the rate of improvement from baseline to Week 12 based on the total depression score, COMB was significantly more effective than PBO or either monotherapy. On IE-rated depression severity and response status, COMB and FLX alone proved superior to PBO and CBT, which were not statistically different, in producing symptomatic improvement (TADS Team, 2004).

Measures: Baseline Measures

As described in more detail elsewhere (TADS, 2003), pretreatment assessments were conducted through an initial telephone screening (Gate A), followed by a diagnostic interview (Gate B), and a final eligibility and baseline assessment that included a battery of measures (Gate C). Baseline measures selected as candidate predictor or moderator variables are described here.

CBQ (Robin & Foster, 1989)—Adolescents (CBQ-A) and parents (CBQ-P) both completed the CBQ. The CBQ is a self report questionnaire designed to assess conflict and negative communication. Items are rated as "true" or "false." The CBQ yields two scores: (a) perception of the other's conflict behavior (e.g., teen's perception of mother's conflict behavior; "My mom picks on me") and (b) perception of the dyad's conflict behavior (e.g., "My mom and I sometimes end our arguments calmly"); both scores were used for each respondent. The CBQ-P contains 75 items related to conflict behavior (e.g., "My teen sulks after an argument") and the CBQ-A contains 73 items (e.g., "My mom stays calm during a discussion"). Although adolescents completed the CBQ-A separately for each parent, their reports of mother behavior were used for these analyses, as mothers represented 88% of respondents, fathers 10%, and other caregivers 2%. If both parents completed the CBQ-P (about the teen), the mother's score was used to represent the parent's view. The CBQ has internal consistencies of .90 and above for mother and teen report on each scale, good test–retest reliability (rs ranging.37–.85), and shows treatment sensitivity (Foster, Prinz, & O'Leary, 1983; Robin, 1981). Higher scores indicate greater levels of conflict and negative communication.

Issues Checklist (IC; Robin & Weiss, 1980)—The IC is a 44-item self-report measure of parent–child conflict with moderate test–retest reliability among distressed families (e.g., Foster et al., 1983; $r = .65$ for maternal quantity, $r = .49$ for teen quantity). Both the adolescent (ICA) and a parent (ICP) completed this measure. For the ICP, the majority of the respondents were mothers (87%). This measure assesses (a) frequency of parent–adolescent conflict across 44 areas (e.g., doing homework, cleanliness, talking back to parents) during the past 2 weeks, and (b) intensity of conflicts regarding these issues ranging from 1 (*calm*) to 5 (*angry*). Number of conflicts and mean intensity ratings were used for each respondent, with higher scores indicating higher intensity.

Family Assessment Measure–III General Scale (FAM; Skinner, Steinhauer, & Santa-Barbara, 1983)—The FAM is a 50-item questionnaire that asks questions about

the family environment as a whole. The FAM has good internal consistency (overall score, $\alpha = .93$, subscales median $\alpha = .73$). The measure was filled out by both the parent (FAM-P) and the adolescent (FAM-A). For the FAM-P, the majority of the records are from the mother figure (87%). For each statement, the individual determines how well the statement applies to his or her family (e.g., "We have the same views on what is right and wrong"). Responses are rated on a 4-point scale ranging from *strongly agree* to *strongly disagree*. Higher scores indicate worse family environment (positive items are recoded). The FAM has seven subscales: Task Accomplishment (e.g., "We spend too much time arguing about what our problems are"), Role Performance (e.g., "Family duties are equally shared"), Communication (e.g., "When I ask someone what they mean, I get a straight answer"), Affective Expression (e.g., "When someone in our family gets upset, we don't know if they are really angry, scared, or what"), Involvement (e.g., "You don't get a chance to be an individual in our family"), Control (e.g., "When I ask why we have certain rules, I don't get a good answer"), and Values and Norms (e.g., "We have the same views on what is right and wrong"). For the teen and the parent, each subscale was included as a potential moderator/predictor of acute outcome. Thus, 14 FAM variables (seven subscales per reporter) were included in analyses.

Measures: Outcome Measures

Children's Depression Rating Scale–Revised (CDRS–R; Poznanski & Mokros, 1996)—The CDRS–R is a 17-item clinician rated measure of depression severity with items rated on a scale of 1 to 7 (15 items) or 1 to 5 (2 items). Scores ranged from 17 to 119 with higher scores indicating more severe depression. The CDRS–R was completed by an IE who was unaware of the treatment assignment at baseline, Week 6, and Week 12. The total score at each assessment was based on the synthesis of information from interviews with the adolescent and the parent. Interrater reliability on the CDRS–R at baseline was high (intraclass correlation coefficients of .95; TADS Team, 2005). The entry criterion for TADS was IE rated total score of 45 or higher.

Reynolds Adolescent Depression Scale (RADS; Reynolds, 1987)—The RADS is a 30-item adolescent self-report measure of current depressive symptomatology. It utilizes a 4-point Likert scale. Higher scores indicate more severe levels of depression. Scores range from 30 to 120. Due to missing data, the RADS had 11 scores imputed with the median baseline value of 80.5. It has excellent internal consistency, good test–retest reliability (12-week interval reliability coefficient = .79; Reynolds, 1987) and good sensitivity (89%), and specificity (90%) for diagnoses of depression (Reynolds & Mazza, 1998).

Children's Global Assessment Scale (CGAS; Shaffer et al., 1983)—Overall level of functioning during the past week was measured with the CGAS. On this scale, scores above 70 usually indicate no clinically significant functional impairment, whereas scores of 70 and below are associated with increasingly severe dysfunction. Clinically referred patients usually have scores below 61 (Bird et al., 1990). The CGAS has good interrater reliability (intraclass correlation coefficient of .84; Shaffer et al., 1983), has good test–retest reliability (6-month interval, reliability coefficient = .85; Shaffer et al., 1983), and is sensitive to change during treatment of depression (Mufson et al., 2004). The CGAS was completed by the IE.

Statistical Analyses

Primary endpoint—The primary outcomes for all predictor/moderator analyses were the Week 12 predicted score on the CDRS–R, RADS, or CGAS. The predicted values are estimated scores derived from the linear random coefficients regression model. Such scores are adjusted for the fixed (treatment, time, Treatment × Time, site) and random (patient,

Patient × Time) effects based on available data for all 439 intent-to-treat cases. Using this method, Week 12 predicted scores were generated for all 439 randomized teenagers regardless of whether they completed Stage 1, completed the Week 12 assessment, or were compliant with treatment. Unlike the last observation carried forward imputation method, this approach provides less biased estimated scores that are consistent with the observed scores for teenagers who completed the Week 12 assessment.

A comparison of the Week 12 predicted CDRS–R scores for the 439 randomized teenagers and the observed scores for the 378 who completed a Week 12 CDRS–R assessment indicated that the means for the observed versus predicted scores within each treatment arm were nearly identical. The standard deviations were slightly smaller for the predicted scores due to a larger sample size and a reduction in the standard error when the scores are adjusted for random and fixed effects. The means (standard deviations) for the CDRS–R predicted scores were as follows: COMB 33.8 (8.3), FLX 36.4 (7.9), CBT 41.7 (8.8), PBO 41.7 (7.7); the means (standard deviations) for the 378 observed scores at Week 12 were as follows: COMB 33.4 (11.9), FLX 36.8 (12.7), CBT 41.4 (14.2), PBO 41.4 (13.4).

Analytic Plan

An intent-to-treat analysis was conducted to examine the impact of general family functioning (FAM-A, FAM-P) and parent–child conflict (CBQ-M, & -A; ICP / ICA) on the predicted CDRS-R, RADS, and CGAS scores at Week 12. The final list of candidate variables included baseline family measures for which data was available for 85% or more of the TADS sample. This criterion was set to ensure adequate representation of the TADS sample in this secondary analysis and variation in results due to degree of missingness on each measure. The intensity subscale of the IC (parent and teen version) was dropped because of 15% or greater missing cases. Cases that were dropped because of missing IC data did not differ at baseline on main IE-rated outcomes (CDRS-R and C-GAS) from those who were retained in the analyses.

For the final list of 20 candidate measures (see Table 1 for baseline scores), the baseline median score for the measure under consideration was imputed when the baseline score was missing. This procedure was used to prevent listwise deletion of cases due to missing data and to ensure that all 439 enrolled patients were included in this intent-to-treat analysis. Among the 20 candidate variables, most had 20 or fewer observations imputed, and the maximum was 32 values imputed.

Predictor and moderator analyses—Analysis of covariance methods were conducted using the General Linear Model (GLM) procedure in SAS 8.2. Analysis of covariance, controlling for site and the baseline value of the outcomes under consideration, was employed to examine the main effects of treatment and each candidate variable, and their interaction on each of the three primary outcomes. A separate model was conducted for each of the candidate variables. To be consistent with the primary efficacy analysis (TADS Team, 2004) and the primary moderators' articles (Curry et al., 2006), site was included as a covariate to adjust for possible site effects. For each Week 12 outcome, the respective baseline score was also included as a covariate, as baseline and 12-week scores were significantly correlated. Because these analyses were considered exploratory, the traditional alpha level of .05 was retained for all statistical tests.

Applying Kraemer et al.'s (2002) definitions of predictors and moderators, baseline measures yielding a significant main effect on outcome in the absence of a significant Treatment × Candidate interaction effect were classified as predictors of treatment outcome. A significant Candidate Variable × Treatment interaction effect with or without a main

effect of candidate variable indicates that the baseline measure is a moderator of treatment outcome.

For each significant moderator identified, the youth were divided into moderator subgroups and a GLM analysis, controlling for baseline scores and site, was conducted to test for treatment differences within each subgroup for each of the three outcome measures. A posteriori pairwise treatment comparisons using least square means t tests were conducted only if the main effect of treatment was significant within the subgroup. This analytic strategy was adapted from the definitions and procedures recommended by Kraemer and colleagues (2002). For purposes of subgroup analyses, simple product terms and regression analysis methods described by Aiken and West (1991) were used to examine treatment effects when the level of the moderator was 1 standard deviation above and below the mean. Table 4 includes results of the subsequent comparisons along with Week 12 predicted CDRS–R least square means and SDs for each treatment group at each level of the moderator.

RESULTS

Preliminary Analyses

We used GLM or chi-square to test for prerandomization differences in the treatment arms (COMBO, FLX, CBT, PBO) on any of the family variables of interest. If the overall treatment effect was significant, then a posteriori t tests were conducted to further examine between-group differences prior to treatment. The only significant finding was that prior to randomization, on the adolescent completed FAM, the norms and values subscale scores were higher in the group subsequently assigned to FLX than in those assigned to COMBO, $F(1, 435) = 6.08$, $p = .0141$, or PBO, $F(1, 435) = 4.34$, $p = .0377$.

Baseline Intercorrelations: Family Measures and Depression Severity

As part of our preliminary analyses, we examined correlations among family functioning, parent-child conflict, severity of depression (CDRS–R and RADS) and functioning (CGAS) at baseline (see Table 2). We used a Pearson r of .20 or greater as an index of meaningful (low-moderate or higher; for rs .20 and above, all ps <.05) intercorrelation (Curry et al., 2006).

None of the family functioning or conflict variables (according to teen or parent report) were associated meaningfully with depression severity (CDRS–R) or functioning (CGAS) as assesed by the independent evaluator. However, depression severity as measured by the RADS (adolescent report), was moderately associated with family functioning (rs ranging .20–.33 on all subscales of FAM) as reported by the adolescent. Parent report of conflict and family functioning were not meaningfully associated with depression severity on the RADS.

Overall, conflict behavior on the CBQ and family functioning on the FAM showed patterns of moderate to strong positive association within reporter (i.e., parent–parent report and adolescent–adolescent report). However, number of reported conflicts (ICA, ICP) by both the adolescent and the parent were not meaningfully associated with any other family variables examined. With regard to agreement between informants, parent and teen reports of conflict behavior on the CBQ (rs = .36–.44) and IC (r = .25) were moderately positively associated, while associations between parent and teen report of family functioning were quite weak (rs = .04–.17).

Moderator and Predictor Analyses

CDRS–R results: prediction—Table 3 summarizes the significant results from the set of GLMs conducted to determine whether each variable was either a predictor or a moderator of treatment outcome. Of the 20 candidate variables tested for outcome on the CDRS–R, one was determined to be a predictor of treatment outcome (see summary on Table 3). Notably, the frequency of parent–adolescent conflicts as reported by mothers predicted outcome. Adolescents with mothers who reported high levels of conflict improved less by Week 12 than did those whose mothers reported less conflict.

CDRS–R results: moderation—Four adolescent-reported family functioning variables moderated the effect of assigned treatment: the adolescent's values and norms, family communication, family involvement, and control, all as measured by the FAM (see summary on Table 3). Table 4 includes results of the subsequent subgroup comparisons along with Week 12 predicted CDRS-R least square means and standard deviations for each treatment group at each level of the moderator. Adolescent values and norms moderated outcome such that among those who reported low scores, COMB was more effective than PBO, FLX, and CBT. FLX was superior to CBT but was not different from PBO. However, among those with high scores, indicating less clarity and agreement on norms, rules, and values, COMB was not more effective than FLX, and FLX was more effective than both CBT and PBO. The pattern for the three other moderators, communication, family involvement and control, was the same. Among teens who reported low scores on these subscales (i.e., better communication and family involvement, more clear rules/control), COMB was more effective than PBO and both active treatments, and FLX was superior to CBT but not different from PBO. However, among those with high scores, indicating worse communication, family involvement, and control, COMB was not more effective than FLX, and FLX was more effective than both CBT and PBO.

RADS results: prediction—Significant predictor results are summarized in Table 3. Of the candidate variables tested, one was determined to be a predictor of treatment outcome. In parallel to the CDRS–R results, frequency of parent–adolescent conflicts as reported by mothers again predicted outcome. Adolescents with mothers who reported high levels of conflict improved less by Week 12 than did those whose mothers reported less conflict.

RADS results: moderation—One variable moderated the effect of assigned treatment: the adolescent's reported values and norms as measured by the FAM (see Table 3). Results of subsequent GLMs and paired comparisons are shown in Table 4. This table includes Week 12 predicted RADS least square means and standard deviations for each treatment group at each level of the moderator, along with results of paired contrasts. As with results seen on the CDRS–R, adolescent values and norms moderated outcome such that among those who reported low scores (i.e., more clarity and agreement on norms, rules, and values), COMB was more effective than PBO, FLX, and CBT. Also among those with low scores, FLX, CBT, and PBO did not show differential efficacy. Among those with high scores (i.e., less clarity and agreement on norms, rules, and values), COMB was not more effective than FLX, and FLX was more effective than both CBT and PBO.

CGAS results: prediction—Significant predictor analyses are summarized in Table 3. Of the candidate variables tested, one was determined to be a predictor of treatment outcome. Consistent with the CDRS–R and RADS analyses, frequency of parent–adolescent conflicts as reported by mothers predicted outcome on the CGAS. Adolescents with mothers who reported high levels of conflict improved less with regard to overall functioning by Week 12 than did those whose mothers reported less conflict.

CGAS results: moderation—As indicated on Table 3, two variables moderated the effect of assigned treatment: the Role Performance and Involvement subscales on the FAM as reported by the adolescent. Results of subsequent GLMs and paired comparisons are shown in Table 4. The patterns for both of the moderators were similar, and in line with findings on the CDRS–R and RADS. Among adolescents who reported low scores (i.e., good functioning) on the Role Performance and Involvement subscales on the FAM, COMB was superior to FLX, and FLX and PBO did not separate. For those with lower scores on role performance, FLX and CBT did not differ, whereas for those with low scores on family involvement, FLX was superior to CBT. For both moderators, among those who reported high scores (i.e., worse functioning) COMB was not more effective than FLX, and FLX was more effective than both CBT and PBO.

DISCUSSION

Although multiple studies have documented the association between unhealthy family environments and psychopathology including depression (e.g., Barrera et al., 1993; Kaslow et al., 1994; Sheeber et al., 1997, Stark et al., 1990), few have investigated the impact of family environments on treatment outcome. On an exploratory basis, we examined the impact of family functioning and parent–child conflict on acute depression and functioning outcomes. Across outcomes (IE ratings of depression, self-reported depression, and IE-rated functioning) indicators of some of these family variables looked to play a role in both predicting and moderating treatment outcome. These findings complement and expand those reported in the main moderator analyses of TADS outcome (Curry et al., 2006) in which only parent report of family conflict was examined (using the CBQ) and found not to predict or moderate outcome.

Across all outcome measures, maternal report of quantity of parent–adolescent conflict was predictive of outcome. As hypothesized, after 12 weeks of treatment, those adolescents with mothers reporting more conflict fared more poorly than their counterparts, irrespective of the type of treatment they received. Our confidence in this finding is strong given that the measure was a significant predictor across all three outcome measures. Parental report of conflict levels appear to be more predictive of recovery than adolescent report.

Contrary to our expectations of the family functioning and conflict variables examined, this is the only parent-reported variable that contributed to outcome. In contrast to our hypothesis that poor family functioning would predict poor outcome, none of the family functioning variables reported by adolescents or their parents were predictive of acute outcome. Notably, in Brent et al.'s (1998) investigation of predictors of treatment response (responders vs. nonresponders) across three psychosocial interventions for adolescent depression, neither family climate nor levels of family conflict (as measured by the CBQ) were predictive of outcome. However, when longer term outcomes of this treatment study were examined, adolescent reported parent–child conflict emerged as a predictor of both recovery (period of at least 2 months without MDD) and recurrence of MDD (Birmaher et al., 2000). Perhaps teens' perceptions of family conflict are particularly important in their influence on risk for relapse and maintenance of gains.

Adolescent-reported family functioning showed an interesting pattern of outcome moderation across measures. Those adolescents who perceived aspects of their family environment to be problematic or unsatisfactory were those who were more likely to benefit from FLX. Rather than CBT being more effective in these teens as one might expect, when there were moderating effects on CBT containing conditions (CBT or COMB) they were in the direction of being less effective among those teens who reported poorer family environments. These findings are similar in pattern to those seen in the Curry et al. (2006)

TADS moderator paper with regard to depression severity at baseline, where COMB was more effective than FLX for mild to moderate depression but not for severe depression. TADS moderator analyses at 12 weeks also indicated that CBT alone may work best for adolescents from higher income families (Curry et al., 2006). Thus, to better understand our findings, we also explored whether family functioning and conflict were meaningfully associated with income levels in the TADS sample, and they did not appear to be (rs ranged .01–.12).

Specifically, on the CDRS–R, four family functioning variables moderated outcome: values and norms, family communication, family involvement, and control. The pattern across all of the moderators was such that among teens who reported better family functioning, FLX and PBO did not separate, but among those who reported poor family functioning on these subscales, FLX was superior to PBO. For all four of the moderators COMB was superior to FLX among teens who reported good family environments but not among those who indicated problematic functioning in these areas.

When we examined the impact of family functioning and conflict on self-reported depression, results were similar to those seen on the CDRS–R. Those adolescents who reported less agreement and clarity about family values, norms, and rules benefited more from FLX. Alternatively, those who endorsed better agreement and clarity about family values, norms, and rules benefited more from combination therapy than those endorsing poorer functioning in this area. Two family functioning variables, role performance and family involvement, moderated functional outcomes. As seen on the 12-week IE and teen ratings of depression severity, those teens who reported poorer family environments on these subscales benefited more with regard to functioning from FLX than their counterparts.

Although exploratory, these results suggest several implications. First, mothers' reports of the amount of conflict they experience with their adolescent children may be a useful and simple prognostic indicator of how much benefit to expect from acute depression treatment. Perhaps conflict levels should routinely be assessed, even when treatment involves only the adolescent. Second, it is our hope that these preliminary findings of the impact of family environment on patterns of outcome foster more refined examinations of family conflict and environment, ideally including behavioral observation of family interaction among depressed youth. Such investigations may further clarify the potentially important role of family among those receiving treatment for depression. It is important to note that, as seen across TADS articles thus far (e.g., Curry et al., 2006; TADS Team, 2004; Vitiello et al., 2006), the efficacy of COMB was robust even among those reporting aspects of family functioning as problematic; monotherapy was never superior to COMB.

As alluded to earlier, one of the limitations of this study may have been the measures of family functioning and conflict themselves. The TADS was not designed specifically to examine family variables and their impact on outcome, and did not include an independent assessment of the family environment, nor did it include a measure of expressed emotion. All measures were based on parent or adolescent report; others (e.g., Holden & Edwards, 1989) have highlighted that self-report measures of family environment may not correspond well to actual behavior. Thus, future research could be augmented by observational coding of the family interaction patterns. Though the largest study of its kind to date, TADS was not powered for moderator analyses. As such, these results should be considered exploratory. Although we included a wide age range of adolescents in this study, we did not focus on developmental differences in family functioning or conflict. Future work with depressed adolescents should carefully explore patterns of family environment and interaction as they relate to age and developmental stage. In addition, future research should investigate the impact of treatment on family functioning itself. Perhaps family functioning

would improve more with CBT than with medication, given CBT's focus on building skills such as problem solving and communication. The impact of family functioning and conflict on relapse and recurrence should also be explored.

Acknowledgments

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TABLE 1

Baseline Scores by Treatment Group

Baseline Variable	COMB[a] M ± SD	FLX[b] M ± SD	CBT[c] M ± SD	PBO[d] M ± SD	p for Testing Baseline Differences
Family Functioning					
FAM-A: Task Accomplishment	8.0 ± 2.5	7.5 ± 2.4	8.1 ± 2.6	7.8 ± 2.3	0.30
FAM-A: Role Performance	8.1 ± 2.6	7.4 ± 2.2	8.0 ± 2.4	8.0 ± 2.3	0.12
FAM-A: Communication	8.0 ± 2.4	7.5 ± 2.3	7.7 ± 2.5	7.8 ± 2.4	0.44
FAM-A: Affective Expression	7.9 ± 2.1	7.7 ± 2.4	7.8 ± 2.1	7.8 ± 2.4	0.94
FAM-A: Involvement	7.2 ± 3.1	6.3 ± 3.0	6.6 ± 3.0	7.1 ± 2.5	0.07
FAM-A: Control	7.8 ± 2.6	7.4 ± 2.4	7.6 ± 2.8	7.6 ± 2.5	0.65
FAM-A: Values & Norms	8.1 ± 2.7	7.3 ± 2.6	7.5 ± 2.5	8.0 ± 2.4	0.04
FAM-P: Task Accomplishment	6.7 ± 2.3	6.8 ± 2.3	7.3 ± 2.1	6.2 ± 1.9	0.13
FAM-P: Role Performance	8.0 ± 2.5	8.5 ± 2.4	8.7 ± 2.5	8.0 ± 2.0	0.06
FAM-P: Communication	6.3 ± 2.1	6.5 ± 2.0	6.7 ± 1.9	6.4 ± 1.9	0.39
FAM-P: Affective Expression	6.3 ± 2.3	6.5 ± 2.1	6.5 ± 2.0	6.2 ± 1.9	0.69
FAM-P: Involvement	4.8 ± 2.5	5.1 ± 2.4	5.4 ± 2.4	5.0 ± 1.7	0.34
FAM-P: Control	5.9 ± 1.9	5.9 ± 1.9	5.9 ± 2.0	5.7 ± 1.8	0.79
FAM-P: Values & Norms	5.7 ± 2.1	6.1 ± 2.1	6.1 ± 1.9	5.7 ± 1.9	0.22
Parent–Child Conflict					
CBQ-A: Adolescent Report Mother Behavior	18.8 ± 13.1	18.1 ± 12.2	18.8 ± 12.4	21.1 ± 12.3	0.32
CBQ-A: Adolescent Report Dyadic Behavior	8.6 ± 5.9	8.0 ± 5.2	8.8 ± 5.4	9.5 ± 5.2	0.25
CBQ-P: Parent Report Adolescent Behavior	25.3 ± 11.0	25.2 ± 10.5	26.2 ± 11.2	25.9 ± 10.0	0.88
CBQ-P: Parent Report Dyadic Behavior	8.3 ± 5.3	8.3 ± 4.7	8.6 ± 5.0	8.3 ± 4.4	0.98
ICA: Quantity of Issues (Adolescent)	18.7 ± 11.7	16.2 ± 10.1	16.6 ± 10.5	16.7 ± 11.0	0.33
ICP: Quantity of Issues (Parent)	22.4 ± 7.5	23.1 ± 10.1	21.5 ± 8.2	21.4 ± 8.2	0.42
Depression					
CDRS–R: IE-Rated Total Depression Score	60.7 ± 11.6	59.0 ± 10.2	59.6 ± 9.2	61.1 ± 10.5	0.38
RADS: Adolescent Report Total Depression Score	79.9 ± 13.7	77.1 ± 14.5	78.9 ± 14.6	81.2 ± 13.7	0.17
Functioning					
CGAS: IE-Rated General Functioning	50.0 ± 7.5	49.5 ± 7.3	50.0 ± 7.6	49.1 ± 7.6	0.79

Note: Sample baseline median for the measure was imputed in the event of missing values. COMB = combination; FLX = fluoxetine; CBT = cognitive behavioral therapy; PBO = placebo; FAM-A/FAM-P = Family Assessment Measure adolescent completed or parent completed; CBQ-A/CBQ-P = Conflict Behavior Questionnaire, adolescent completed or parent completed; ICA/ICP = Issues Checklist

adolescent completed or parent completed; CDRS–R = Children's Depression Rating Scale–Revised; IE = independent evaluator; RADS = Reynolds Adolescent Depression Scale; CGAS = Children's Global Assessment Scale.

[a] $N = 107$.

[b] $N = 109$.

[c] $N = 111$.

[d] $N = 112$.

TABLE 2

Pearson Correlation Coefficients Among Family Functioning and Conflict Variables at Baseline

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. CBQ-A: Adolescent Report of Mother Behavior		.85	.36	.38	.52	.44	.55	.37	.58	.52	.48	.17	.13	.17	.16	.21	.09	.23	.12	.06
2. CBQ-A: Adolescent Report of Dyadic Behavior			.39	.44	.51	.37	.52	.35	.56	.44	.47	.21	.14	.20	.16	.23	.09	.22	.13	.07
3. CBQ-P: Parent Report of Adolescent Behavior				.82	.22	.18	.23	.09	.24	.24	.16	.37	.29	.47	.24	.35	.29	.27	.04	.27
4. CBQ-P: Parent report of Dyadic Behavior					.24	.16	.28	.11	.24	.22	.15	.39	.25	.45	.25	.40	.29	.29	.03	.16
5. FAM-A: Task Accomplishment						.52	.67	.53	.60	.51	.53	.10	.13	.14	.04	.10	.08	.17	.08	.01
6. FAM-A: Role Performance							.58	.42	.54	.56	.50	.13	.13	.13	.07	.15	.12	.17	.11	−.03
7. FAM-A: Communication								.53	.69	.61	.62	.08	.01	.12	.09	.14	.08	.18	.09	.01
8. FAM-A: Affective Expression									.53	.42	.41	.04	.06	.10	.10	.06	.08	.16	.03	−.01
9. FAM-A: Involvement										.66	.64	.09	.03	.11	.09	.17	.10	.20	.10	.04
10. FAM-A: Control											.63	.11	.05	.12	.06	.14	.15	.20	.11	.06
11. FAM-A: Values & Norms												.09	−.01	.10	.09	.15	.11	.22	.15	.04
12. FAM-P: Task Accomplishment													.52	.66	.52	.61	.46	.47	.10	.05
13. FAM-P: Role Performance														.47	.41	.41	.40	.38	.07	.12
14. FAM-P: Communication															.54	.57	.53	.53	.04	.04
15. FAM-P: Affective Expression																.49	.40	.45	.00	−.05
16. FAM-P: Involvement																	.49	.55	.05	.04
17. FAM-P: Control																		.61	.06	.07
18. FAM-P: Values & Norms																			.03	.05
19. ICA: Quantity of Issues																				.25
20. ICP: Quantity of Issues																				

Note. CBQ-A/CBQ-P = Conflict Behavior Questionnaire, adolescent completed or parent completed; FAM-A/FAM-P = Family Assessment Measure adolescent completed or parent completed; ICA/ICP = Issues Checklist adolescent completed or parent completed.

TABLE 3

Summary of Predictors and Moderators of Treatment Outcome

Candidate Variable	Week 12 Outcome	Site p Value	Treatment p Value	Baseline Outcome p Value	Candidate p Value	Candidate × Treatment p Value	Determination
FAM-A: Role performance Subscale	CDRS–R	.0822	.0412	<.0001	.8968	.1998	—
	RADS	.3367	.0921	<.0001	.6820	.9247	—
	CGAS	.0010	.0293	<.0001	.3567	.0377	Moderator
FAM-A: Communication Subscale	CDRS–R	.0408	.0033	<.0001	.7142	.0318	Moderator
	RADS	.3129	.0416	<.0001	.4309	.4350	—
	CGAS	.0012	.0447	<.0001	.3919	.3147	—
FAM-A: Involvement Subscale	CDRS–R	.0501	.0001	<.0001	.6919	.0170	Moderator
	RADS	.4018	<.0001	<.0001	.4729	.1943	—
	CGAS	.0007	<.0001	<.0001	.4173	.0423	Moderator
FAM-A: Control Subscale	CDRS–R	.0547	.0223	<.0001	.8955	.0317	Moderator
	RADS	.3915	.0575	<.0001	.2948	.2280	—
	CGAS	.0007	.0123	<.0001	.5812	.2118	—
FAM-A: Values & Norms Subscale	CDRS–R	.0376	.2005	<.0001	.9800	.0276	Moderator
	RADS	.3541	.0244	<.0001	.8114	.0478	Moderator
	CGAS	.0005	.1393	<.0001	.3208	.4629	—
ICP: Quantity of Issues	CDRS–R	.0426	.0003	<.0001	.0186	.1724	Predictor
	RADS	.3204	.0152	<.0001	.0159	.1530	Predictor
	CGAS	.0004	.0002	<.0001	.0152	.3548	Predictor

Note: Results from general linear models. The *p* values for Type III Sum of Squares. Moderator = Candidate × Treatment interaction (p .05). Predictor = candidate main effect only (p .05). FAM-A = Family Assessment Measure adolescent completed; CDRS–R = Children's Depression Rating Scale–Revised; RADS = Reynolds Adolescent Depression Scale; CGAS = Children's Global Assessment Scale; ICP = Issues Checklist parent completed.

TABLE 4

Moderators of Treatment Outcomes: Subgroup Analysis Results

Moderator	COMB M ± SD	FLX M ± SD	CBT M ± SD	PBO M ± SD	Paired Contrasts
CDRS–R: IE-Rated Total Depression Score					
FAM-A: Values & Norms Subscale					
1 *SD* Below Mean	32.6 ± 18.1	36.9 ± 15.3	41.0 ± 15.3	39.4 ± 15.9	COMB >(FLX >CBT) = PBO
1 *SD* Above Mean	33.1 ± 14.7	25.4 ± 16.4	41.4 ± 15.6	41.9 ± 15.7	COMB = FLX >CBT = PBO
FAM-A: Communication Subscale					
1 *SD* Below Mean	31.5 ± 16.5	37.1 ± 15.8	41.1 ± 15.8	39.9 ± 16.1	COMB >(FLX >CBT) = PBO
1 *SD* Above Mean	33.7 ± 15.7	35.2 ± 15.9	41.1 ± 15.5	41.4 ± 15.4	COMB = FLX >CBT = PBO
FAM-A: Involvement Subscale					
1 *SD* Below Mean	31.9 ± 18.4	37.1 ± 14.0	40.8 ± 15.3	40.0 ± 18.2	COMB >(FLX >CBT) = PBO
1 *SD* Above Mean	33.2 ± 15.5	35.6 ± 17.4	41.4 ± 15.7	41.1 ± 15.0	COMB = FLX >CBT = PBO
FAM-A: Control Subscale					
1 *SD* Below Mean	32.4 ± 17.1	37.5 ± 16.2	40.8 ± 16.0	40.4 ± 15.4	COMB >FLX = CBT = PBO
1 *SD* Above Mean	33.0 ± 15.6	35.8 ± 15.9	41.6 ± 15.2	40.8 ± 15.8	COMB = FLX >CBT = PBO
RADS: Adolescent Report					
Total Depression Score					
FAM-A: Values & Norms Subscale					
1 *SD* Below Mean	54.2 ± 21.6	61.6 ± 18.3	65.2 ± 18.3	62.6 ± 18.9	COMB >FLX = CBT = PBO
1 *SD* Above Mean	56.9 ± 20.1	60.4 ± 22.5	67.1 ± 21.4	67.1 ± 21.5	COMB = FLX >CBT = PBO
CGAS: IE-Rated Functioning					
FAM-A: Role Performance Subscale					
1 *SD* Below Mean	66.1 ± 13.8	62.1 ± 12.2	59.8 ± 12.9	61.3 ± 14.2	COMB >FLX = CBT = PBO
1 *SD* Above Mean	66.3 ± 13.8	63.1 ± 14.8	59.1 ± 13.5	59.1 ± 13.2	COMB = FLX >PBO = CBT
FAM-A: Involvement Subscale					
1 *SD* Below Mean	67.7 ± 16.0	61.8 ± 12.2	60.8 ± 13.3	61.9 ± 15.8	COMB >(FLX >CBT) = PBO
1 *SD* Above Mean	65.4 ± 13.3	63.2 ± 14.8	58.5 ± 13.4	59.1 ± 12.8	COMB >FLX >PBO = CBT

Note: General linear models (GLM) least squares means and standard deviations: GLM adjusted for the effects of site and the baseline values of the outcome measure (CDRS–R, RADS, or CGAS) score.
CDRS–R = Children's Depression Rating Scale–Revised; IE = independent evaluator; FAM–A = Family Assessment Measure adolescent completed; COMB = combination treatment; FLX = fluoxetine;
CBT = cognitive behavior therapy; PBO = placebo; RADS = Reynolds Adolescent Depression Scale; CGAS = Children's Global Assessment Scale.