ORIGINAL ARTICLE

Clinical Outcome After Short-term Psychotherapy for Adolescents With Major Depressive Disorder

Boris Birmaher, MD; David A. Brent, MD; David Kolko, PhD; Marianne Baugher, MA; Jeffrey Bridge, BS; Diane Holder, MSW; Satish Iyengar, PhD; Rosa Elena Ulloa, MD

Background: Cognitive behavioral therapy has been shown to be more efficacious than alternative psychosocial interventions for the acute treatment of adolescents with major depressive disorder. However, the long-term impact of brief psychosocial interventions on the course of adolescent depression is not well established.

Methods: One hundred seven adolescents with major depressive disorder randomly assigned to 12 to 16 weeks of cognitive behavioral therapy, systemic behavioral family therapy, or nondirective supportive therapy were evaluated for 2 years after the psychotherapy trial to document the subsequent course and predictors of major depressive disorder.

Results: There were no long-term differential effects of the 3 psychotherapies. Most participants (80%) recovered (median time, 8.2 months from baseline), and 30% had a recurrence (median time, 4.2 months from recovery). Twenty-one percent were depressed during at least 80% of the follow-up period. Severity of depression (at baseline) and presence of self-reported parent-child conflict (at baseline and during the follow-up period) predicted lack of recovery, chronicity, and recurrence. Despite the similarity to clinically referred patients at baseline, patients recruited via advertisement were less likely to experience a recurrence.

Conclusions: There were no significant differences in long-term outcome among cognitive behavioral therapy, systematic behavioral family therapy, and nondirective supportive therapy. While most participants in this study eventually recovered, those with severe depression and self-perceived parent-child conflict are at greater risk for chronic depression and recurrences.

Arch Gen Psychiatry. 2000;57:29-36

From the Department of Psychiatry, University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic, Pittsburgh, Pa.

ADOLESCENT major depressive disorder is a common and impairing condition that is both recurrent and persistent into adulthood.[1,2] Naturalistic studies have shown that in clinically referred samples, the median duration for a pediatric major depressive episode is approximately 8 months, with a recovery rate up to 90% over 1 to 2 years from the onset of the depressive episode and a rate of recurrence of 40% to 70% over a period of 2 to 5 years, respectively.[1,2]

The few follow-up studies after pharmacotherapy or psychotherapy trials of children and adolescents with depression[3-8] have also found that up to 80% of clinically treated patients will eventually recover, but 25% to 50% will experience a depressive relapse or recurrence over a period of 6 months to 2 years of follow-up care. Similar findings have been reported in the adult literature.[9-13]

Investigations of children and adolescents treated for depression have reported that delayed recovery is associated with initial symptom severity, functional impairment, comorbidity, double depression, cognitive distortions, and family difficulties.[4-8,14-16] These factors, along with incomplete response to treatment, were also associated with relapse and recurrence, with naturalistic and quasiexperimental studies suggesting that continuation treatment of either cognitive behavior therapy (CBT) or fluoxetine may protect against depressive relapse and recurrences.[4,16]

Given the paucity of information regarding the long-term course of children and adolescents after treatment for depression, we report the outcome of a group of adolescents with depression who were treated in a randomized clinical trial with 12 to 16 weeks of CBT, systemic behavioral family therapy, or nondirective supportive therapy[17] and then evaluated for 2 years. In this study,[17] we found that patients treated acutely with CBT showed a more rapid and complete symptomatic re-

SUBJECTS AND METHODS

SUBJECTS

As described in detail previously,[17] patients 13 to 18 years old meeting the criteria for *DSM-III-R*[19] major depressive disorder and with a BDI[20] score of 13 or higher were enrolled. Patients with ongoing physical or sexual abuse, psychosis, or bipolar, obsessive-compulsive, eating, or substance abuse disorders were excluded. Of 122 eligible patients, 107 were recruited.

The median socioeconomic score was 40 (class IV),[21] and 75.7% were female. Approximately 22%, 32%, and 21% of the patients had comorbid dysthymia, anxiety, and disruptive disorders, respectively. About one third of the patients were recruited via advertisement and the rest were recruited from a child psychiatry outpatient clinic in a university setting. The 3 treatment groups were well balanced on demographic and clinical variables (**Table 2**).

TREATMENT

The psychotherapy trial was conducted over 12 to 16 weeks, and patients were evaluated for 2 years thereafter. During the psychotherapy trial, patients were randomized to CBT, systemic behavioral family therapy, or nondirective supportive therapy, with evidence of excellent treatment fidelity.[17] After the psychotherapy trial, 62 of 78 patients who completed the psychotherapy trial received 2 to 4 "booster" treatments in the same model over as many months depending on each subject's clinical needs. The remaining 16 patients did not receive booster sessions, mainly because they required more extensive services (n = 15); 1 subject was offered booster treatment but refused to comply. There were no differences in the number of booster treatments among the 3 treatment groups.

Additional open treatment was provided to 57 (53.3%) of 107 patients: 12 (21%) during or at the end of the acute psychotherapy trial and 45 (79%) during the 2-year follow-up phase, as reported elsewhere.[22] These patients received open treatment for 1 or more of the following problems: depression (n = 40), behavior difficulties (n = 14), and family conflicts (n = 15), with 12 patients receiving help for more than 1 problem. More than half of the 57 patients (n = 33) were treated with selective serotonin reuptake inhibitors, alone or in combination with psychotherapy. There were no significant differences among the 3 treatment groups in the amount or type of additional treatment received.

ASSESSMENTS

Patients were assessed at baseline, at 6 weeks, at the end of the psychotherapy trial, at every 3 months thereafter for 1 year, and finally at 24 months after treatment ended (8 interviews in total) by a clinical interviewer with a master's degree blind to original treatment assignment. *DSM-III-R* diagnoses were rendered using the Kiddie Schedule for Affective Disorders and Schizophrenia (present and lifetime versions)[23,24] for symptoms during the time since the prior interview. Similar to the method described by Kovacs and colleagues,[25,26] if the onset or offset date of a condition could not be precisely determined, we delimited a calendar interval between the scheduled assessments and set the onset or offset at the midpoint between them. The prevailing definitions of remission, recovery, relapse, and recurrence[4,25-28] were established a priori (Table 1). Because we were interested in the effects of treatment, the rates of recovery were calculated from study entry and not from

lief of depression, with CBT resulting in a higher rate of remission (60%) (the absence of major depressive disorder and 3 consecutive scores on the Beck Depression Inventory (BDI) less than 9 sustained through the end of treatment) than either systemic behavioral family therapy (29%) or nondirective supportive therapy (36%). In this article, we address the following questions: What are the clinical and functional outcomes of these adolescents after the completion of the randomized trial? Are there any long-term differential effects among the 3 psychosocial treatments? What are the predictors of recovery and recurrence? What demographic and clinical characteristics discriminate between patients who after the psychotherapy trial continued to be either persistently depressed or persistently recovered? (**Table 1**).

On the basis of our prior findings[17] and the extant literature,[1-8,15-18] we hypothesized that patients treated with CBT will show better long-term outcome than patients treated with either systematic behavioral family therapy or nondirective supportive therapy and that patients with greater clinical severity (eg, severe depression and poor functioning), comorbid disorders, parental psychopathology, and family conflict will have longer depressive episodes, a greater likelihood of depressive recurrences, and a higher frequency of chronic and persistent depression.

RESULTS

During the follow-up period, there were no significant differences in the clinical outcome variables (including depressive symptoms, functional status, and cognitive and family variables) across the 3 psychotherapy groups. Therefore, subsequent follow-up analyses pool all 3 groups. Compared with baseline, participants' functional status did continue to improve, especially in the first 9 months of follow-up ($\chi^2_1 = 152.5$; $P = .001$)

The patients (n = 29) who did not complete the full psychotherapy trial showed higher BDI scores for the first 11 months of follow-up than those who completed the trial (n = 78) (completion group×time: $\chi^2_1 = 9.03$; $P = .003$, $\alpha/8 = .006$), but by the 12-month assessment, the BDI scores of the 2 subgroups converged. No other differences were found between these 2 subgroups.

REMISSION/RECOVERY

Eighty-seven patients (83.7%) had a remission at some point over the course of the study. The median time to remission from baseline was 5.7 months. Fifty-six (64%) of the 87 remissions occurred after the psychotherapy trial.

Of the 87 patients who had a remission, 86 went on to recover. The median time to recovery from baseline

onset of the depression. Thus, the duration of the depression depicted in this article does not reflect the total duration of the depressive episodes.

Severity of depression was assessed using the 13 depression items from the Kiddie Schedule for Affective Disorders and Schizophrenia (Dep-13) and the BDI.[20] Functional status was determined by use of the Children's Global Assessment Scale (CGAS).[29] Cognitive distortion was ascertained through the Children's Negative Cognitive Error Questionnaire (CNCEQ)[30] and the Beck Hopelessness Scale.[31] The adolescent and caretaking parent report of family environment was assessed by the Conflict Behavior Questionnaire (CBQ),[32] the Areas of Change Questionnaire,[33] and the Family Assessment Device (FAD).[34]

Parents' current and lifetime psychiatric disorders were assessed using the Schedule for Affective Disorders and Schizophrenia–Lifetime version,[35] adapted for *DSM-III-R*. Parental depressive symptoms were assessed at each interview using the BDI.

COMPLIANCE

Most of the patients (77.6% [n = 83]) completed all of the 8 interviews, 14.0% (n = 15) completed all but 1 interview, 5.6% (n = 6) completed 4 to 6 interviews, and 2.8% (n = 3) completed 2 or fewer interviews. There were no differences among the 3 treatment groups regarding proportions of missing data. Also, there were no significant baseline demographic or clinical differences between patients who completed and those who did not complete all of the interviews.

DATA ANALYSIS

The data were analyzed using an intent-to-treat approach in an attempt to preserve, as much as possible, the effects of the initial randomization. However, 3 patients whose participation was poor were excluded from all analyses over the follow-up period.

Differences between groups were analyzed using standard parametric and nonparametric univariate tests. Hazard and time to outcome were estimated using survival analyses.[36] All demographic, clinical (adolescent and parent), treatment, and family environment data collected at baseline, at the end of acute treatment, and, where specified, over the course of the study, were included in the predictor analyses. For all the above-noted analyses we had an adequate sample size to detect large (w = 0.50) and, in some cases, medium (w = 0.30) effect sizes[37] with 80% power and $\alpha = .05$ (2-tailed). Multivariate assessment of predictors of outcome and time to outcome were examined using backward-stepping logistic regression and Cox proportional hazards modeling.[38-40] The hazards models for censored survival data with fixed and time-dependent covariates were analyzed using the Stata Release 6.0 statistical software.[41] In defining a variable as a *time-dependent covariate*, it was assumed that for each subject, the value of that variable at the time of the event was the value reported at the preceding assessment.[42] In addition, it was presumed that for each subject, time-dependent variables follow a step function according to which the values were assumed to be constant between any 2 adjacent time points. Creating interaction terms between significant predictor variables tested effect modification. With respect to both time to recovery and time to recurrence, no interaction term entered the final main effect model.

For those contrasts specified in our hypotheses above, α was set at .05 (2-tailed). However, to protect against multiple comparisons, for those contrasts that were not hypothesized a priori, α values were corrected for each family of contrasts using the Bonferroni method.

was 8.2 months. Seventy-nine (92%) of the 86 patients who recovered did so after the psychotherapy trial.

Given that 86 of the 87 patients who had a remission went on to recover and that there were no differences between the predictors of remission and recovery, we present only the predictors of recovery (**Table 3**). Significant predictors of recovery at baseline included lower interviewer-rated and self-reported depression scores. At the end of the psychotherapy trial, those who recovered, compared with those who did not recover, were found to have significantly lower interviewer-rated and self-reported depression scores, fewer cognitive distortions, less self-reported and parent-reported parent-child conflict, less hopelessness, and better functioning (for all noted comparisons, $P<.05$).

Compared with those who did not recover, significantly fewer patients who recovered received additional open treatment over the course of the study (41 [48%] of 86 vs 16 [94%] of 17; $\chi^2_1 = 12.39$; $P<.001$, $\alpha/2 = .03$).

Backward-stepping Cox proportional hazards regression was used to determine the most parsimonious combination of the above-noted variables for the prediction of time to recovery. In this analysis, BDI and Dep-13 scores at baseline and at the end of the psychotherapy trial were included as fixed covariates. Time-dependent covariates included cognitive distortion (CNCEQ), functional status (CGAS), hopelessness (Beck Hopelessness Scale), open treatment, and family conflict variables. Baseline BDI and Dep-13 scores were forced into the model at each step. Lower cognitive distortion (CNCEQ: relative risk [RR], 1.003; 95% confidence interval [CI], 1.001-1.006, $P = .008$; higher scores were related to lower distortion), higher functioning (CGAS: RR, 1.06; 95% CI, 1.03-1.09; $P<.001$), and lower interviewer-rated depression at the end of the psychotherapy trial (Dep-13: RR, 0.38; 95% CI, 0.21-0.70; $P = .002$) were significantly associated with recovery. Of the 86 patients who recovered, only 7 did so by the end of acute treatment. Given that BDI and Dep-13 scores were assessed both at baseline and at the end of the psychotherapy trial, a second model was run that excluded these 7 patients. This analysis was done to estimate more precisely the impact of post-treatment BDI and Dep-13 scores as predictors of recovery. The results of this model were similar to those of the first, but self-reported parent-child conflict now emerged as an additional significant predictor (RR, 0.95; 95% CI, 0.91-0.998; $P = .04$).

RELAPSE/RECURRENCE

The 2 patients who relapsed did so very close to the time defined for recurrence. Therefore, these patients were

Table 1. Definitions*

Definite or probable MDD	4 or more *DSM-III-R* significant symptoms of MDD (including depressed mood, irritability, and anhedonia) during the present episode or within the last week
Response†	1 or no *DSM-III-R* significant symptom of MDD during the present episode or within the last week
Rapid response†	BDI score declined by 50% or more from the intake assessment to the beginning of the second treatment session
Remission†	A period of 2 weeks or more and fewer than 2 months with absence of MDD
Recovery†	A period of 2 months or more with absence of MDD
Relapse†	An episode of MDD during the period of remission
Recurrence†	An episode of MDD during the period of recovery (a new episode)
Persistent depression	Definite or probable MDD in at least 60% of the follow-up interviews and no period of sustained recovery from depression (1 or no significant symptoms during the present episode or within the last week for 2 consecutive 3-month periods)
Persistent recovery	Absence of MDD in at least 60% of the follow-up interviews and 3 or fewer significant symptoms during the present episode or within the last week at all interviews

*MDD indicates major depressive disorder; BDI, Beck Depression Inventory.
†From Frank et al.[28]

Table 2. Demographic and Clinical Characteristics of Subjects*

Characteristic	CBT (n = 37)	SBFT (n = 35)	NST (n = 35)
Mean (SD) age, y	15.7 (1.3)	15.4 (1.4)	15.7 (1.5)
Female, No. (%)	28 (76)	27 (77)	26 (74)
White, No. (%)	28 (76)	31 (89)	30 (86)
Socioeconomic distribution†			
Mean (SD)	39.9 (13.0)	39.0 (12.5)	39.6 (15.1)
No. (%)			
I	2 (5)	4 (11)	3 (9)
II	6 (16)	2 (6)	1 (1)
III	8 (22)	12 (34)	11 (31)
IV	16 (43)	16 (46)	12 (34)
V	5 (14)	1 (3)	5 (14)
Comorbid diagnoses, No. (%)			
Dysthymic disorder	6 (16)	9 (26)	9 (26)
Anxiety disorder	14 (38)	10 (29)	10 (29)
Disruptive disorder	6 (16)	8 (23)	8 (23)
Clinical referral, No. (%)	26 (70)	25 (71)	21 (60)
Booster sessions, No. (%)‡	26 (87)	19 (79)	17 (71)
Open treatment, No. (%)			
During acute phase	4 (11)	4 (11)	5 (14)
During follow-up	18 (49)	13 (37)	14 (40)

*CBT indicates cognitive behavior therapy; SBFT, systemic behavior family therapy; and NST, nondirective supportive therapy.
†From Hollingshead.[21]
‡Rates based on subjects who completed acute treatment (N = 78; 30 completed CBT; 24, SBFT; and 24, NST).

combined with those who experienced a recurrence for subsequent analyses. Of the patients who recovered, 26 (30%) of 86 patients experienced 1 and 7 (8%) of 86 experienced 2 recurrences. Among those patients who experienced at least 1 recurrence, the median time to recurrence was 4.2 months. All of the recurrences occurred after the acute phase of the psychotherapy trial.

As presented in Table 3, recurrence of depression was associated with recruitment through the clinic rather than from advertisements (92% vs 57%; $\chi^2_1 = 10.5$; $P = .001$; $\alpha/6 = .008$). Those who experienced a recurrence had a significantly lower self-reported Family Assessment Device–Affective Involvement score at baseline and higher self-reported parent-child conflict at the end of the psychotherapy trial ($P = .02$).

The most parsimonious combination of the above-noted variables for the prediction of time to recurrence was estimated using backward-stepping Cox proportional hazards regression. In this analysis, clinic referral status, self-reported Family Assessment Device–Affective Involvement scores at baseline, and BDI, Dep-13, and CGAS scores at baseline and at the end of the psychotherapy trial were included as fixed covariates. Self-reported parent-child conflict was included as a time-dependent covariate. The BDI, Dep-13, and CGAS scores at baseline and at the end of the psychotherapy trial were forced into the model at each step. Results showed that clinic referral (RR, 12.68; 95% CI, 2.57-62.63; $P = .002$) and higher self-reported parent-child conflict (RR, 1.08; 95% CI, 1.00-1.17; $P = .04$) were significantly associated with recurrence.

PERSISTENT RECOVERY VS PERSISTENT DEPRESSION

During the 2-year follow-up period, 22 (21.1%) of 104 patients were persistently depressed (mean percentage of the completed follow-up interviews with 4 or more depressive symptoms, 82.7%; median, 80.0%; range, 60%-100%). Forty (38.5%) of 104 patients had persistent recovery (mean percentage of the completed follow-up interviews with 1 or no depressive symptom, 93.7%; median, 100%; range, 60%-100%). Forty-two (40.4%) of 104 patients experienced an intermediate course (depressed on an average of 30.5% of the completed follow-up interviews; median, 29%; range, 0%-60%). Of the 86 patients who initially recovered, 6 (7%) were persistently depressed, 40 (47%) had persistent recovery, and 40 (47%) had an intermediate course. Of the 26 patients who experienced at least 1 recurrence, 4 (15%) were persistently depressed, none had persistent recovery, and 22 (85%) had an intermediate course.

As depicted in **Table 4**, the persistently depressed group, compared with the persistent recovery group, showed greater self-reported and interviewer-rated depression and greater self-reported parent-child conflict at baseline, at the end of the psychotherapy trial, and over the course of the follow-up interviews. Also, at the end of treatment, the persistently depressed group had more severe cognitive distortions and poorer functioning. The persistently depressed group was less likely to have come via advertisement and less likely to respond rapidly to treatment (Table 1) (for all noted comparisons, $P<.05$).

Using logistic regression, the most robust predictors of persistent depression at baseline were increased

Table 3. Predictors of Recovery and Recurrence*

Variables†	No Recovery (n = 18)	Recovery (n = 86)	Statistics	P
At baseline				
Dep-13	3.1 ± 0.5	2.8 ± 0.5	t_{102} = 2.64	.01
Self-reported BDI	29.0 ± 9.4	23.1 ± 7.5	1062.0‡	.01
At end of treatment				
Dep-13	2.4 ± 0.7	1.5 ± 0.5	1120.0‡	<.001
Self-reported BDI	17.8 ± 13.7	5.9 ± 7.1	1028.5‡	<.001
CGAS	56.3 ± 10.1	65.8 ± 8.5	t_{96} = 3.99	<.001
CNCEQ	87.1 ± 18.6	98.4 ± 17.8	351.0‡	.03
BHS	10.1 ± 5.8	5.7 ± 5.4	839.0‡	.01
Self-reported CBQ	11.2 ± 6.5	6.6 ± 5.8	818.5‡	.01
Self-reported ACQ	43.8 ± 24.9	26.6 ± 18.8	822.0‡	.01
Self-reported FAD-RL	2.8 ± 0.4	2.5 ± 0.4	t_{91} = 3.01	.002
Self-reported FAD-GF	2.8 ± 0.5	2.5 ± 0.5	t_{91} = 2.46	.02
Parent FAD-RL	2.8 ± 0.4	2.5 ± 0.3	820.5‡	.01
Over course of treatment				
Open treatment, No. (%)	17 (94)	41 (48)	12.39§	<.001
	No Recurrence (n = 60)	**Recurrence (n = 26)**	**Statistics**	**P**
Predictors of recurrence at baseline				
Clinic referral, No. (%)	55 (92)	15 (57)	10.50§	.001
Self-reported FAD-AI	2.4 ± 0.4	2.7 ± 0.5	494.0§	.02
Predictors of recurrence at end of treatment				
Self-reported CBQ	5.5 ± 5.4	8.9 ± 6.0	440.5‡	.02

*Values are reported as mean ± SD unless otherwise indicated. Dep-13 indicates 13 depressive items of the Kiddie Schedule for Affective Disorders and Schizophrenia; BDI, Beck Depression Inventory; CGAS, Children's Global Assessment Scale; CNCEQ, Children's Negative Cognitive Error Questionnaire; BHS, Beck Hopelessness Scale; CBQ, Conflict Behavior Questionnaire; ACQ, Areas of Change Questionnaire; FAD-RL, Family Assessment Device–Roles; FAD-GF, Family Assessment Device–General Functioning; and FAD-AI, Family Assessment Device–Affective Involvement.

†The following variables were nonsignificant predictors of both recovery and recurrence: age, sex, race, socioeconomic status, age of onset, duration of major depressive disorder, comorbid disorders assessed at baseline, and maternal and paternal psychopathology. Results available on request from the authors.

‡By Mann-Whitney test.

§By χ^2 test.

self-reported parent-child conflict (CBQ: odds ratio [OR], 1.08; 95% CI, 1.00-1.17) and severe interviewer-rated depression (OR, 1.15; 95% CI, 1.03-1.30). At the end of the psychotherapy trial, both self-reported parent-child conflict (CBQ: OR, 1.08; 95% CI, 0.98-1.19) and severe interviewer-rated depression (OR, 1.21; 95% CI, 1.09-1.34) were the most robust predictors of persistent depression. As the number of these adverse predictors increased, so did the likelihood of being persistently depressed (χ^2_1 for trend, 19.64; $P<.001$).

COMMENT

In this study, we found that, contrary to our hypothesis, CBT did not confer any long-term advantage over family or supportive therapy with regard to rates of remission, recovery, recurrence, or level of functioning. Most of the participants (84%) recovered from their index episode of depression, mostly within 1 year from baseline. Recovery was predicted by lower levels of interviewer-rated depression, negative cognitive distortions, and self-reported parent-child conflict, and by better functioning. A substantial proportion of participants (30%) experienced a depressive recurrence, with onset occurring a median of 4 months after recovery was achieved. Recurrence was predicted by recruitment through the clinical setting and by increased self-reported parent-child conflict. During the follow-up period, approximately one fifth of the patients were persistently depressed. Both increased self-reported parent-child conflict and interviewer-rated depression at baseline and at the end of treatment predicted persistent depression.

Before discussing these results, it is important to take into account the limitations of this study. Because this was a naturalistic study, it is difficult to infer causality when there was no rigorous experimental control. Consequently, the naturalistic untreated course of depression cannot be inferred from this cohort, as all 3 groups received initial treatment with psychotherapy, and more than half received additional services over the follow-up period. During the second year of follow-up interviews, there was only 1 interview covering the span from 12 to 24 months, making precise delineation of onset and offset of depression in this time more difficult. Some domains that may be predictors of relapse, recurrence, and outcome were not assessed (eg, expressed emotion, exposure to negative life events).[43-46] In addition, only 1 global measure of functional status was used. Finally, while the sample studied was typical of most controlled outpatient clinical trial samples, more complex cases (eg, comorbid substance abuse, psychosis, bipolar depression, and concomitant child abuse) that are often seen in clinical practice were excluded.

In our initial report on the acute effects of psychotherapy for the treatment of adolescent depression, we found CBT to be superior to family and supportive therapy.[17] However, this advantage did not confer any long-term benefit with regard to subsequent rates of re-

Table 4. Demographic and Clinical Predictors of Persistent Recovery or Persistent Depression During the 2-Year Follow-up Period*

Variables†	Persistent Recovery (n = 40)‡	Persistent Depression (n = 22)‡	Intermediate Course (n = 42)‡	Statistics	P
Predictors at intake					
Dep-13	2.7 ± 0.5[a]	3.0 ± 0.5[b]	2.8 ± 0.5[a]	$F_{2,101} = 3.62$	.03
Child CBQ	6.9 ± 5.6[a]	11.7 ± 6.7[b]	10.8 ± 6.2[b]	11.37§	.003
Child ACQ	27.9 ± 16.9[a]	39.2 ± 20.1[b]	35.9 ± 18.7[a,b]	5.88§	.05
Child FAD-AI	2.3 ± 0.4[a]	2.6 ± 0.5[b]	2.5 ± 0.5[b]	6.99§	.03
Predictors at end of treatment					
CGAS	66.5 ± 9.1[a]	57.8 ± 10.7[b]	64.9 ± 7.8[a]	$F_{2,96} = 6.51$	.002
Dep-13	1.4 ± 0.4[a]	2.3 ± 0.8[b]	1.6 ± 0.5[a]	21.77§	<.001
Child BDI	4.4 ± 5.2[a]	17.8 ± 14.2[a]	6.9 ± 7.2[a]	16.47§	<.001
CNCEQ	102.7 ± 16.0[a]	90.1 ± 19.4[b]	93.5 ± 18.8[b]	7.40§	.02
Child CBQ	4.2 ± 4.7[a]	10.8 ± 6.0[b]	8.8 ± 6.2[b]	18.90§	<.001
Child FAD-GF	2.4 ± 0.5[a]	2.8 ± 0.4[b]	2.5 ± 0.5[a,b]	$F_{2,91} = 4.32$	.02
Predictors over course of treatment					
Open treatment, No. (%)	13 (33)[a]	21 (95)[b]	24 (57)[c]	22.02‖	<.001
Rapid responders, No. (%)	18 (44)[a]	2 (9)[b]	14 (33)[a]	7.75‖	.02

*Values are reported as mean ± SD unless otherwise indicated. Dep-13 indicates 13 depressive items of the Kiddie Schedule for Affective Disorders and Schizophrenia; CBQ, Conflict Behavior Questionnaire; ACQ, Areas of Change Questionnaire; FAD-AI, Family Assessment Device–Affective Involvement; CGAS, Children's Global Assessment Scale; BDI, Beck Depression Inventory; CNCEQ, Children's Negative Cognitive Error Questionnaire; and FAD-GF, Family Assessment Device–General Functioning.

†The following variables were nonsignificant: age, sex, race, socioeconomic status, age of onset, duration of major depressive disorder, comorbid disorders assessed at baseline, Beck Hopelessness Scale, and maternal and paternal psychopathology. Results available on request from the authors.

‡Means with different superscript letters are significantly different at $P<.05$.

§By Kruskal-Wallis test.

‖By χ^2 test.

covery or remission. This is consistent with the finding of Wood et al,[8] who found that CBT was superior to relaxation therapy for the acute treatment of adolescent depression but that rates of recovery and relapse had converged by the 6-month follow-up. Similar findings have been reported in an adult study.[47] A recent study[16] suggests that monthly booster sessions of CBT may substantially reduce the rate of depressive relapse. Therefore, one reason for the high rate of recurrence and for the lack of sustained differential effect of CBT may have been the absence of a vigorous continuation treatment component.

Recovery was eventually achieved by most participants, along with substantial improvement in functional status. However, as reported by Puig-Antich and colleagues,[48,49] there was a lag between the clinical and functional improvement, with most subjects showing functional improvement during the follow-up phase of the study. These rates of symptomatic and functional recovery are encouraging, but they are not substantially different from those achieved by adolescent[2,7,18,27,50] as well as adult[2,10-13,47,51-53] cohorts evaluated naturalistically. Therefore, while these results indicate that the treatment of adolescents with depression should be approached with the combination of education, hope, and patience, it is also clear that more incisive interventions are required to improve the long-term course beyond what would occur without any controlled intervention. Two examples from our data illustrate this point. First, self-reported family discord retarded recovery. Therefore, future studies should target discord to improve the pace and completeness of recovery in adolescents with depression. In addition, greater depressive severity at baseline and at the end of acute treatment predicted slower recovery, suggesting the need for more aggressive and longer treatment for adolescents with more severe depression, perhaps combinations of medication and psychotherapy.

Nearly one third of participants who recovered experienced a recurrence during the 2-year follow-up interview, similar to rates of relapse and recurrence reported in other pediatric[1-8,27,50] and adult[2,47] naturalistic and treatment studies. The relatively short time between recovery and recurrence, a median of 4 months, suggests that continuation treatment might have prevented the return of depressive symptoms. Naturalistic studies of depressed youth[4,16] and controlled trials in the adult literature[47,51,54,55] strongly support the need for continuation treatment for 4 to 6 months after recovery from depression. Future controlled studies should investigate the impact of continuation treatment in adolescents with depression.

Recurrence was predicted by higher self-reported parent-child conflict and by coming to treatment via a clinic referral. Of note, child-reported parent-child conflict persisted as a predictor of recovery and recurrence, even after controlling for interviewer-rated and self-rated depression. Therefore, the relationship between conflict and depressive course is not merely an epiphenomenon of depression. Moreover, family conflict has been reported to be related to the onset, duration, and recurrence of pediatric and adult mood disorders.[1,2,45,46,56,57] Diminution of family conflict may be an important component for promoting recovery and preventing recurrences.

Patients who were recruited through advertisement had nearly a 12-fold lower rate of recurrence than those recruited through the clinic. However, except for lower hopelessness scores at baseline, there were no significant demographic, clinical, or family environmental differences between patients recruited through adver-

tisement and those recruited through the clinic.[14,17] We previously showed that those recruited via advertisement were much more likely to respond to psychotherapy than those who came via a clinical referral, and that this relationship between referral source and outcome was in part mediated by lower hopelessness scores.[17] Perhaps those recruited through advertisement had more positive expectations for improvement, which resulted in a more favorable outcome.[58,59] Whatever the reason for this finding, our results indicate the need to control for source of referral in treatment outcome studies.

We noted that approximately one fifth of participants had persistent depression over the 2-year follow-up period, despite the initial 12 to 16 weeks of psychotherapy and continuous treatment thereafter with psychotherapy and/or pharmacotherapy. Other studies have also reported the presence of protracted depression in 6% to 10% of depressed children and adolescents.[25,26,60-62] Consistent with the literature,[1-8,27] initial severity, failure to respond to treatment, and presence of ongoing self-reported parent-child conflict predicted persistent depression. Therefore, the presence at baseline and at the end of acute treatment of a cluster of these risk factors should alert the clinician and parents to the possibility of a more long-term course and may provide the clinician with a strategy for altering this course for the better. These strategies may include targeting family discord, combining psychotherapy and pharmacotherapy, and using more aggressive somatic[50,63-66] approaches to treatment-resistant depression, as described for adults with depression.[48,63-66] Future research priorities in adolescent depression should focus on helping adolescents who recover to stay well and developing and empirically testing interventions for those with treatment-resistant and chronic depression.

Accepted for publication September 17, 1999.

This work was supported by grants MH-46500 and MH-55123 from the National Institute of Mental Health, Rockville, Md (Dr Brant).

Reprints: Boris Birmaher, MD, University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, 3811 O'Hara St, Pittsburgh, PA 15213 (e-mail: birmaherb@msx.upmc.edu).

REFERENCES

1. Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J, Dahl RE, Perel J, Nelson B. Childhood and adolescent depression: a review of the past 10 years: part I. *J Am Acad Child Adolesc Psychiatry*. 1996;35:1427-1439.
2. Kovacs M. Presentation and course of major depressive disorder during childhood and later years of the life span. *J Am Acad Child Adolesc Psychiatry*. 1996; 35:705-715.
3. Clarke GN, Rohde P, Lewinsohn PM, Hops H, Seeley JR. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *J Am Acad Child Adolesc Psychiatry*. 1999;38:272-279.
4. Emslie GJ, Rush AJ, Weinberg WA, Kowatch RA, Carmody T, Mayes TL. Fluoxetine in child and adolescent depression: acute and maintenance treatment. *Depress Anxiety*. 1998;7:32-39.
5. Jayson D, Wood A, Kroll L, Fraser J, Harrington R. Which depresssed patients respond to cognitive-behavioral treatment? *J Am Acad Child Adolesc Psychiatry*. 1998;37:35-39.
6. Lewinsohn PM, Clarke GN, Hops H, Andrews J. Cognitive-behavioral group treatment for depressed adolescents. *Behav Ther*. 1990;21:385-401.
7. Vostanis P, Feehan C, Grattan E, Bickerton WL. A randomised controlled outpatient trial of cognitive-behavioural treatment for children and adolescents with depression: 9-month follow-up. *J Affect Disord*. 1996;40:105-116.
8. Wood A, Harrington R, Moore A. Controlled trial of a brief cognitive-behavioural intervention in adolescent patients with depressive disorders. *J Child Psychol Psychiatry*. 1996;37:737-746.
9. Belsher G, Costello CG. Relapse after recovery from unipolar depression: a critical review. *Psychol Bull*. 1988;104:84-96.
10. Evans MD, Hollon SD, DeRubeis RJ, Piasecki JM, Grove WM, Garvey MJ, Tuason VB. Differential relapse following cognitive therapy and pharmacotherapy for depression. *Arch Gen Psychiatry*. 1992;49:802-808.
11. Elkin I, Shea MT, Watkins JT, Imber SD, Sotsky SM, Collin JF, Glass DR, Pilkonis PA, Leber WR, Fiester SJ, Docherty J, Parloff MB. National Institute of Mental Health Treatment of Depression Collaborative Research Program: general effectiveness of treatments. *Arch Gen Psychiatry*. 1989;46:971-982.
12. Kovacs M, Rush AJ, Beck AT, Hollon SD. Depressed outpatients treated with cognitive therapy or pharmacotherapy: a one-year follow-up. *Arch Gen Psychiatry*. 1981;38:33-39.
13. Thase ME, Simons AD, McGeary J, Cahalane JF, Huges C, Harden T, Friedman E. Relapse after cognitive behavior therapy of depression: potential implications for longer courses of treatment. *Am J Psychiatry*. 1992;149:1046-1052.
14. Brent DA, Kolko D, Birmaher B, Baugher M, Bridge J, Roth C, Holder D. Predictors of treatment efficacy in a clinical trial of three psychosocial treatments for adolescent depression. *J Am Acad Child Adolesc Psychiatry*. 1998;37:906-914.
15. Clarke GN, Hops H, Lewinsohn PM, Andrews JA, Seeley MR, Williams J. Cognitive behavioral group treatment of adolescent depression: prediction of outcome. *Behav Res Ther*. 1992;34:312-321.
16. Kroll L, Harrington R, Jayson D, Fraser J, Gowers S. Pilot study of continuation cognitive-behavioral therapy for major depression in adolescent psychiatric patients. *J Am Acad Child Adolesc Psychiatry*. 1996;35:1156-1161.
17. Brent DA, Holder D, Kolko D, Birmaher B, Baugher M, Roth C, Iyengar S, Johnson BA. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive treatments. *Arch Gen Psychiatry*. 1997;54:877-885.
18. Lewinsohn PM, Rohde P, Klein DN, Seeley JR. Natural course of adolescent major depressive disorder, I: continuity into young adulthood. *J Am Acad Child Adolesc Psychiatry*. 1999;38:56-63.
19. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*. Washington, DC: American Psychiatric Association; 1987.
20. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clin Psychol Rev*. 1988;8:77-100.
21. Hollingshead AB. *Four-Factor Index of Social Status*. New Haven, Conn: Dept of Sociology, Yale University; 1975.
22. Brent DA, Kolko D, Birmaher B, Baugher M, Bridge J. A clinical trial for adolescent depression: predictors of additional treatment in the acute and follow-up phases of the trial. *J Am Acad Child Adolesc Psychiatry*. 1999;38:263-270.
23. Chambers WJ, Puig-Antich J, Hirsch M, Paez P, Ambrosini PJ, Tabrizi MA, Davies M. The assessment of affective disorders in children and adolescents by semistructured interview: test-retest reliability of the Schedule for Affective Disorders and Schizophrenia for School-age Children, present episode version. *Arch Gen Psychiatry*. 1985;42:696-702.
24. Orvashel H, Puig-Antich J, Chambers WJ, Tabrizi MA, Johnson R. Retrospective assessment of child psychopathology with the K-SADS-E. *J Am Acad Child Psychiatry*. 1982;21:392-397.
25. Kovacs M, Feinberg TL, Crouse-Novak MA, Paulauskas SL, Finkelstein R. Depressive disorders in childhood, I: a longitudinal prospective study of characteristics and recovery. *Arch Gen Psychiatry*. 1984;41:229-237.
26. Kovacs M, Feinberg TL, Crouse-Novak M, Paulauskas SL, Pollock M, Finkelstein R. Depressive disorders in childhood, II: a longitudinal study of the risk for a subsequent major depression. *Arch Gen Psychiatry*. 1984;41:643-649.
27. Emslie GJ, Rush AJ, Weinberg WA, Gullion CM, Rintelmann J, Hughes CW. Recurrence of major depressive disorder in hospitalized children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 1997;36:785-792.
28. Frank E, Prien RF, Jarret RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MM. Conceptualization and rationale for consensus definitions of terms in major depressive disorder: remission, recovery, relapse, and recurrence. *Arch Gen Psychiatry*. 1991;48:851-855.
29. Shaffer D, Gould MS, Brasic J, Ambrosini P, Fischer P, Bird H, Aluwahlia S. A children's global assessment scale (CGAS). *Arch Gen Psychiatry*. 1983;40:1228-1231.
30. Leitenberg H, Yost LW, Carroll-Wilson M. Negative cognitive errors in children: questionnaire development, normative data, and comparisons between children with and without self-reported symptoms of depression, low self-esteem, and evaluation anxiety. *J Consult Clin Psychol*. 1986;54:528-536.
31. Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol*. 1974;42:861-865.

32. Robin AL, Foster SL. *Negotiating Parent-Adolescent Conflict: A Behavioral-Family Systems Approach*. New York, NY: Guilford Press; 1989.
33. Jacob T, Seilhamer RA. Adaption of the Areas of Change Questionnaire for parent-child relationship assessment. *Am J Fam Ther*. 1985;13:28-38.
34. Epstein N, Baldwin L, Bishop DS. The McMaster Family Assessment Device. *J Marital Fam Ther*. 1983;9:171-180.
35. Endicott J, Spitzer RL. A diagnostic interview: the Schedule for Affective Disorders and Schizophrenia. *Arch Gen Psychiatry*. 1978;35:837-844.
36. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53:457-481.
37. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. New York, NY: Academic Press; 1977.
38. Cox DR. Regression models and life tables. *J R Stat Soc*. 1972;34:187-220.
39. Cox DR, Oakes D. *Analysis of Survival Data*. New York, NY: Chapman & Hall; 1984.
40. Kalbfleisch JD, Prentice RL. *The Statistical Analysis of Failure Time Data*. New York, NY: John Wiley & Sons Inc; 1980.
41. Stata Corp. *Stata Release 6.0* [computer program]. College Station, Tex: Stata Press; 1999.
42. Collet D. *Modelling Survival Data in Medical Research*. New York, NY: Chapman & Hall; 1994.
43. Garber J, Hilsman R. Cognition, stress, and depression in children and adolescents. *Child Adolesc Psychiatr Clin North Am*. 1992;1:129-167.
44. Williamson DE, Birmaher B, Frank E, Anderson BP, Matty M, Kupfer DJ. The nature of life events and difficulties in depressed adolescents. *J Am Acad Child Adolesc Psychiatry*. 1998;37:1049-1057.
45. Asarnow JR, Tompson M, Hamilton EB, Goldstein MK, Guthrie D. Family-expressed emotion, childhood onset depression, and childhood onset schizophrenia spectrum disorders: is expressed emotion a nonspecific correlate of child psychopathology or a specific risk factor for depression? *J Abnorm Child Psychol*. 1994;22:129-146.
46. Goodyer IM, Herbert J, Tamplin A, Secher SM, Pearson J. Short-term outcome of major depression, II: life events, family dysfunction, and friendship difficulties as predictors of persistent disorder. *J Am Acad Child Adolesc Psychiatry*. 1997;36:474-480.
47. Gortner ET, Gollon JK, Dobson KS, Jacobson NS. Cognitive-behavioral treatment for depression: relapse prevention. *J Consult Clin Psychol*. 1998;66:377-384.
48. Puig-Antich J, Lukens E, Davies M, Goetz D, Brennan-Quattrock J, Todak G. Psychosocial functioning in prepubertal major depressive disorders, I: interpersonal relationships during the depressive episode. *Arch Gen Psychiatry*. 1985; 42:500-507.
49. Puig-Antich J, Lukens E, Davies M, Goetz D, Brennan-Quattrock J, Todak G. Psychosocial functioning in prepubertal depressive disorders, II: interpersonal relationships after sustained recovery from affective episode. *Arch Gen Psychiatry*. 1985;42:511-517.
50. Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J. Childhood and adolescent depression: a review of the past 10 years: part II. *J Am Acad Child Adolesc Psychiatry*. 1996;33:1575-1583.
51. Blackburn IM, Eunson KM, Bishop S. A two-year naturalistic follow-up of depressed patients treated with cognitive therapy, pharmacotherapy and a combination of both. *J Affect Disord*. 1986;10:67-75.
52. Simons AD, Murphy GE, Levine JL, Wetzel RD. Cognitive therapy and pharmacotherpy for depression: sustained improvement over one year. *Arch Gen Psychiatry*. 1986;43:43-48.
53. Shea MT, Elkin I, Imber SD, Sotsky SM, Watkins JT, Collings JF, Pilkonis PA, Beckham E, Glass DR, Dolan RT, Parloff MB. Course of depressive symptoms over follow-up: findings from the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *J Consult Clin Psychol*. 1992; 49:782-787.
54. Stewart JW, Quitkin FM, McGrath PJ, Amsterdam J, Fava M, Fawcett J, Reimherr F, Rosenbaum J, Beasley C, Roback P. Use of pattern analysis to predict differential relapse of remitted patients with major depression during 1 year of treatment with fluoxetine or placebo. *Arch Gen Psychiatry*. 1998;55:334-343.
55. Frank E, Kupfer DJ, Perel JM, Cornes C, Jarrett DB, Mallinger AG, Thase ME, McEachran AB, Grochocinski VJ. Three-year outcomes for maintenance therapies in recurrent depression. *Arch Gen Psychiatry*. 1990;47:1093-1099.
56. Butzlaff RL, Hooley JM. Expressed emotion and psychiatric relapse: a meta-analysis. *Arch Gen Psychiatry*. 1998;55:547-552.
57. Hirschfeld RM. Psychosocial predictors of outcome in depression. In: Bloom FE, Kupfer DJ, eds. *The Fourth Generation of Progress*. New York, NY: Raven Press; 1995:1113-1121.
58. Keller MB, Lavori PW, Rice J, Coryell W, Hirschfeld RM. The persistent risk of chronicity in recurrent episodes of nonbipolar major depressive disorder: a prospective follow-up. *Am J Psychiatry*. 1986;143:24-28.
59. Jacobson NS, Dobson KS, Truax PA, Addis ME, Koerner K, Gollan JK, Gortner E, Prince SE. A component analysis of cognitive-behavioral treatment for depression. *J Consult Clin Psychol*. 1996;64:295-304.
60. McCauley E, Myers K, Mitchel J, Calderon R, Schloredt K, Treder R. Depression in young people: initial presentation and clinical course. *J Am Acad Child Adolesc Psychiatry*. 1993;32:714-722.
61. Sanford M, Szatmari P, Spinner M, Munroe-Blum H, Jamieson E, Walsh C, Jones D. Predicting the one-year course of adolescent major depression. *J Am Acad Child Adolesc Psychiatry*. 1995;34:1618-1628.
62. Strober M, Lampert C, Schmidt S, Morrel W. The course of major depressive disorder in adolescents, I: recovery and risk of manic switching in a follow-up of psychotic and nonpsychotic subtypes. *J Am Acad Child Adolesc Psychiatry*. 1993; 32:34-42.
63. Salee FR, Vrindavanam NS, Deas-Nesmith D, Carson SW, Sethuraman G. Pulse intravenous clomipramine for depressed adolescents: double-blind, controlled trial. *Am J Psychiatry*. 1997;154:668-673.
64. Rey JM, Walter G. Half a century of ECT use in young people. *Am J Psychiatry*. 1997;154:595-602.
65. Thase ME, Rush AJ. Treatment-resistant depression. In: Bloom FE, Kupfer DJ, eds. *Psychopharmacology: The Fourth Generation of Progress*. New York, NY: Raven Press; 1995:1081-1097.
66. Birmaher B, Brent DA. Practice parameters for the assessment and treatment of children and adolescents with children and adolescents with depressive disorders. *J Am Acad Child Adolesc Psychiatry*. 1998;37(suppl 10):63S-83S.