Published in final edited form as:

Am J Psychiatry. 2005 November ; 162(11): 2131–2138.

Treatment Matching in the Posthospital Care of Depressed Patients

Ivan W. Miller, Ph.D., Gabor I. Keitner, M.D., Christine E. Ryan, Ph.D., David A. Solomon, M.D., Esteban V. Cardemil, Ph.D., and Christopher G. Beevers, Ph.D.

From Brown University School of Medicine, Providence, R.I.; the Psychosocial Research Program, Butler Hospital; Rhode Island Hospital, Providence, R.I.; and Clark University, Worcester, Mass

Abstract

Objective—This study assessed the efficacy of 1) matching patients to treatments and 2) adding additional family therapy or cognitive therapy in a group of recently discharged patients with major depression.

Method—Patients with major depression were recruited during a psychiatric hospitalization. After discharge, they were randomly assigned to one of four treatment conditions that were either “matched” or “mismatched” to their pattern of cognitive distortion and family impairment. The four treatment conditions were 1) pharmacotherapy alone; 2) combined pharmacotherapy and cognitive therapy; 3) combined pharmacotherapy and family therapy; and 4) combined pharmacotherapy, cognitive therapy, and family therapy. Randomly assigned treatment continued for 24 weeks on an outpatient basis.

Results—Among patients with at least moderate depressive symptoms at hospital discharge, low rates of remission (16%) and improvement (29%) were obtained. Matched treatment led to a significantly greater proportion of patients who improved and greater reductions over time in interviewer-rated depressive symptoms than mismatched treatment. However, matched treatment did not produce greater change in self-reported depression or interviewer-rated suicidal ideation. Treatment that included a family therapy component also led to a greater proportion of patients who improved and to significant reductions in interviewer-rated depression and suicidal ideation than treatment without family therapy.

Conclusions—These results suggest that 1) current treatments are not very efficacious in the aftercare of hospitalized depressed patients, 2) treatment matching moderately improves outcome for patients who are symptomatic at hospital discharge, and 3) inclusion of family therapy improves the outcome of posthospital care for depressed patients.

Recognition of the prevalence and seriousness of depressive disorders has led to the development of numerous treatments for depression, including medications, individual psychotherapies, marital/family therapy, as well as combinations of pharmacological and psychosocial treatments. In general, all of these treatments have been found to be efficacious. However, there has been considerable variability in absolute response rates. Conclusions about possible differences between treatments are unclear, with the most common finding being equivalence among active treatments (1).

Our knowledge about treatments for depression has a number of significant additional limitations. First, there is a high degree of heterogeneity among individuals labeled

¹ Address correspondence and reprint requests to Dr. Miller, Psychosocial Research Program, Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; ivan_miller@brown.edu (e-mail).

Supported by NIMH grants MH-44778 and MH-58866.

“depressed,” with descriptions ranging from the mildly depressed “worried well” to psychotic, suicidal patients. Despite this heterogeneity, a majority of treatment research in depression has been conducted on a relatively homogeneous group of moderately depressed outpatients. Patients whose depression was severe enough to require hospitalization, who had a significant risk of suicide, or who had psychiatric or medical comorbidity typically have been excluded.

Second, we have little knowledge of what type of treatment works best for which patient. Although clinicians make decisions about matching treatment to patient characteristics on a daily basis, virtually all research studies have treated patients as if they were homogeneous and have not investigated how to best match the large number of available treatments for depression to the needs of individual patients.

Third, despite the common use of combined psychosocial and pharmacological treatments in clinical practice, compared to studies of pharmacotherapy or psychotherapy alone, relatively few studies have investigated the efficacy of combined treatments for depression (2). Furthermore, reviews of this literature have reached conflicting conclusions regarding the benefits of combined treatments (2).

Fourth, although most researchers would accept that depression is a “biopsychosocial” disorder and that there is evidence that family dysfunction is predictive of treatment response and course of illness (3), there have been few studies investigating the efficacy of family treatments for depression (4–7) and virtually none that have integrated family interventions with pharmacological and individual treatments.

The present study was designed to address these limitations. More specifically, the goals of the current study were 1) to investigate the efficacy of matching treatments to patient characteristics in the posthospital outpatient care of a group of depressed hospitalized patients and 2) to investigate the efficacy of adding cognitive or family therapy to pharmacotherapy in this group.

Our primary a priori hypothesis was that patients receiving “matched” treatment would have better outcomes than those receiving “mismatched” treatment. We had two secondary hypotheses. First, the patients receiving additional cognitive therapy would have better outcomes than the patients who did not. Second, the patients receiving additional family therapy would have better outcomes than the patients who did not.

Method

Participants

A total of 121 patients were initially recruited from the inpatient or partial hospital units of a private psychiatric hospital if they met all of the following criteria: 1) currently living with one or more family members, 2) a DSM-III-R diagnosis of major depressive disorder according to the Structured Clinical Interview for DSM-III-R—Patient Version (SCID) (8), 3) a score greater than 17 at admission on the 17-item Modified Hamilton Rating Scale for Depression (9), and a score greater than 17 on the Beck Depression Inventory (10), 4) ages 18 to 65 years, 5) sufficient English reading skills to complete questionnaires, and 6) informed consent provided by the patient and family to participate in the project. Patients were excluded from the study if they 1) met DSM-III-R criteria for a current episode of bipolar disorder, alcohol or drug dependence, somatization disorder, or schizophrenia, 2) had significant cognitive impairment, or 3) had medical illness severe enough to contraindicate antidepressant medication.

The patients' levels of depression and suicidal ideation were reassessed within 2 days of discharge from the hospital. Forty-five (37%) of the 121 patients did not have clinically significant levels of depression (a modified Hamilton depression scale score ≥ 14 or a Beck Depression Inventory score ≥ 16) before discharge. In fact, the mean level of depression for this group was in the nondepressed range (a modified Hamilton depression scale score=6.8, SD=3.5; a Beck Depression Inventory score=8.6, SD=4.9). Because hospital treatment was not controlled and the goal of this study was to evaluate different strategies for treating depression, these patients with low levels of symptoms before treatment assignment were excluded, leaving a group of 76 patients to be included in this report. All participants received a complete explanation of the study and provided written informed consent.

Stratification

The patients who met these criteria were grouped according to two classes of variables: 1) cognitive distortion and 2) family impairment. The procedures used for this grouping were as follows.

Consistent with our previous studies (11,12), the subgroup with high cognitive distortion was defined by scores on two measures of cognitive distortion: 1) the Dysfunctional Attitude Scale (13) and 2) the Cognitive Bias Questionnaire (14). A patient was included in the subgroup with high cognitive distortion if he or she scored greater than one standard deviation above a mean derived from previously published reports for nondepressed subjects on both the Dysfunctional Attitude Scale (mean=119) (13) and the Cognitive Bias Questionnaire (mean=3) (14).

High and low family impairment was determined on the basis of the general functioning subscale of the interviewer-rated Mc-Master Clinical Rating Scale (15,16). Because a majority of families with a depressed member will manifest some dysfunction, particularly during an acute episode, we used the median score of 3.0 for depressed families on the general functioning subscale of the McMaster Clinical Rating Scale from our previous studies of hospitalized depressed patients as a cutoff score.

Based on these criteria for cognitive distortion and family impairment, the patients were classified into one of four subgroups: 1) high cognitive distortion and high family impairment, 2) high cognitive distortion and low family impairment, 3) low cognitive distortion and high family impairment, and 4) low cognitive distortion and low family impairment.

Description of Treatment Conditions

All study treatments began after discharge from the hospital and continued for a 24-week period.

Pharmacotherapy—The pharmacotherapy condition consisted of a semistructured medication protocol and clinical management sessions with one of two board-certified psychiatrists. The medication protocol required prescription of an antidepressant approved by the Food and Drug Administration at recommended therapeutic dosages for at least a 4-week trial. The treating psychiatrist chose the specific antidepressant. This flexibility was particularly useful, given that many of the patients had previous medication trials. If the patient did not respond to the first trial of medication, subsequent trials with different antidepressants were initiated. The clinical management sessions with the psychiatrist followed the clinical management guidelines, as described by Fawcett et al. (17). The scheduling of the psychiatric visits was determined by the clinical judgment of the psychiatrist, with a maximum of 10 visits during the 24-week treatment period.

Combined cognitive therapy—The combined cognitive therapy condition consisted of pharmacotherapy, as described, plus individual cognitive therapy administered according to the manual by Beck et al. (18). The scheduling of cognitive therapy visits was determined by the clinical judgment of the cognitive therapist, with the goal of 20–24 therapy sessions.

The cognitive therapy was provided by one of three Ph.D. clinical psychologists with at least 5 years of clinical experience who had been trained as cognitive therapists. Before treating patients in the study, all of the therapists were certified as competent by an external cognitive therapy expert (Dr. Margorie Weishaar). In addition, all of the therapists received ongoing supervision from another highly experienced cognitive therapist (Dr. Stephen Bishop).

Combined family therapy—The combined family therapy condition consisted of pharmacotherapy plus family therapy based on the problem-centered systems therapy of the family (19). The problem-centered systems therapy of the family model is a short-term multidimensional family treatment that focuses on comprehensive assessment, problem identification, and task-oriented problem solving. The scheduling of sessions was at the discretion of the family therapist, with the goal of 8–10 therapy sessions.

The family therapy was provided by one of two M.S.W. family therapists with at least 5 years of clinical experience who were certified as competent in problem-centered systems therapy of the family by one of the developers of the model (Dr. Duane Bishop). In addition, both family therapists received ongoing supervision from this same family therapy expert.

Combined cognitive and family therapy—The combined cognitive and family therapy condition consisted of pharmacotherapy plus cognitive therapy plus family therapy, as described previously.

Assignment to Treatment

The patients were randomly assigned to a treatment condition that was theoretically “matched” or “mismatched” to the patients’ pattern of deficits. The matching was based on a “deficit remediation” model; that is, it was hypothesized that patients with deficits in a specific area would benefit most from a treatment that directly addressed those deficits. Based on this model, a matched and mismatched treatment condition was derived for each of the four patient subgroups. Thus, patients with high levels of cognitive distortion were hypothesized to respond best to a treatment that included cognitive therapy. Similarly, patients from highly impaired families were hypothesized to respond better to a treatment condition that included family therapy. The matching algorithm can be seen in Figure 1. It should be noted that this design was only 50% of a full factorial (four-by-four [patient group-by-treatment]) design. Thus, although the design allowed an efficient test of the matching hypotheses, comparisons between individual treatment conditions were confounded with patient groupings (see Data Analysis).

An urn randomization procedure (20) was used to balance the matched and mismatched conditions for potentially confounding variables, including gender, patient role in family, severity of depression (Modified Hamilton Rating Scale for Depression score >23), axis I disorder in a family member, presence of comorbid dysthymic disorder or personality disorder in the patient, and recruitment site (inpatient versus partial hospitalization). As expected, there were no differences in these variables between treatment groups.

Assessments

Upon admission to the hospital, the patients were administered the patient version of the SCID (8), the Dysfunctional Attitude Scale (13), the Cognitive Bias Questionnaire (14), the McMaster Clinical Rating Scale (16), the Modified Hamilton Rating Scale for Depression (9), the

Beck Depression Inventory (10), the Modified Scale for Suicidal Ideation (21), as well as other measures not included in this report. The measures of depressive symptoms (the Modified Hamilton Rating Scale for Depression, the Beck Depression Inventory, and the Modified Scale for Suicidal Ideation) were readministered in person at discharge from the hospital and at week 12 and week 24 of outpatient treatment. The assessors were clinical raters trained to at least 0.80 reliability who were blind to the match/mismatch status of the patients but not to assignment to cognitive or family therapy.

Data Analysis

Treatment discontinuation—We categorized patients who dropped out of randomly assigned treatment as either “treatment failures” or “dropouts.” “Treatment failures” were defined as patients who manifested significant symptom deterioration or constituted a serious suicide risk and were removed from the study by the investigators. This decision was made at a weekly meeting attended by all study clinicians and investigators. Any clinician could recommend that a patient be removed from the study. If such a recommendation were made, the patient’s progress and assessment data would be discussed by the clinical team, who were blind to matched/mismatched assignment. A patient was declared a treatment failure based on a consensus judgment of the team that the patient was exhibiting a high suicide risk or clinical deterioration and that the current treatment was not adequately mitigating these risks.

“Dropouts” were defined as patients who left randomly assigned treatment for any other reason (were noncompliant, withdrew consent, moved away).

Treatment response—Treatment response was measured by scores on the Modified Hamilton Rating Scale for Depression, the Beck Depression Inventory, and the Modified Scale for Suicidal Ideation as assessed at hospital discharge, week 12, and week 24. In addition to continuous measures of symptom change, we also defined two treatment-response categories as follows: 1) remission was defined as a Modified Hamilton Rating Scale for Depression score <7 , a Beck Depression Inventory score <9 , and remaining in treatment, and 2) improvement was defined as $\geq 50\%$ improvement on both the Modified Hamilton Rating Scale for Depression and the Beck Depression Inventory and remaining in treatment.

Analyses—Hierarchical linear modeling (22,23) was used to analyze change in depressive symptoms and suicidal ideation. Hierarchical linear modeling is ideal for these analyses because it accommodates missing data among repeated measurements by using empirical Bayesian estimates. We first examined overall change for the entire group, not accounting for treatment group (i.e., null models). This allowed us to estimate overall symptom change and to determine whether change varied across individuals.

In a second set of analyses, we examined whether treatment assignment accounted for differential symptom change over time. For these analyses, total linear change (β_{11}) consists of three parameters: 1) linear change for individuals, with a treatment value of 0 (γ_{10}); 2) linear change for individuals, with a treatment value of 1 (γ_{11}); and 3) unexplained error (μ_1). Of importance, significance tests of γ_{11} indicate whether the average change for individuals with a treatment value of 1 is statistically different from the average change for individuals with a treatment value of 0. Because of space limitations, we report only tests of γ_{11} .

To extend these hierarchical linear modeling analyses, chi-square comparisons were also conducted to assess differences in categorical variables (noncompletion, treatment response). All statistical tests were conducted with a two-tailed alpha level of 0.05, with intent-to-treat groups. Effect sizes (Cohen’s d) were calculated on the basis of the hierarchical linear modeling t and chi-square values and degrees of freedom. It should be noted that different statistical

software packages calculate degrees of freedom differently; thus generalization of these effect size estimates of hierarchical linear modeling across studies should be done cautiously.

Results

Treatment Received

Overall, during the 24 weeks of the study, the patients received a mean of 8.4 clinical management sessions with a psychiatrist ($SD=4.3$). An “adequate” trial of medication was defined as a period of 4 weeks or longer of at least the minimum targeted dose of a medication (e.g., 150 mg/day of imipramine, 20 mg/day of fluoxetine) (24). With these criteria, 61 (80%) of the 76 patients received at least one adequate medication trial. Eight (11%) of the 76 patients dropped out of treatment before receiving an adequate trial. All of the remaining seven patients received between one and four trials of antidepressants, but because of side effects and/or noncompliance, they were not receiving the criterion dose for a 4-week period. Of the patients who received at least one adequate trial, 48% ($N=29$) received one trial, 25% ($N=15$) received two trials, and the remaining 27% ($N=17$) had three or more medication trials. There were no significant differences between any treatment groups in the proportion of patients who received an “adequate” medication trial. The patients in the combined cognitive therapy plus pharmacotherapy and the combined cognitive plus family therapy conditions received a mean of 13.0 cognitive therapy sessions ($SD=6.0$), whereas the patients in the combined family therapy plus pharmacotherapy and the combined cognitive plus family therapy conditions received a mean of 5.1 family therapy sessions ($SD=4.3$).

Overall Group

Study results can be seen in Table 1. Twenty-one percent of the group ($N=16$) dropped out of treatment, and 24% ($N=18$) were removed from the study as “treatment failures.” There was a significant linear decrease in Modified Hamilton Rating Scale for Depression scores from discharge to week 24 ($\gamma_{10}=-2.96$, $t=-5.23$, $df=75$, $p<0.001$). Furthermore, there was moderate variability in Modified Hamilton Rating Scale for Depression change in score over time ($\mu_1=2.63$, $\chi^2=83.61$, $df=69$, $p=0.11$), suggesting differentiation in score change across individuals. A significant linear decrease in Beck Depression Inventory scores was also observed ($\gamma_{10}=-2.31$, $t=-2.97$, $df=75$, $p<0.01$). This decrease also had significant variability ($\mu_1=3.64$, $\chi^2=98.88$, $df=69$, $p<0.01$). Finally, scores on the Modified Scale for Suicidal Ideation did not significantly change over time ($\gamma_{10}=0.73$, $t=1.13$, $df=75$, $p=0.26$). Despite this overall stability, there was significant variance in linear change ($\mu_1=2.85$, $\chi^2=97.30$, $df=69$, $p<0.05$). This suggests that scores on the Modified Scale for Suicidal Ideation increased for some individuals and decreased for others, leading to relatively small change overall. Noncompleters reported higher levels of suicidal ideation during hospital admission than completers ($\gamma_{01}=-4.54$, $t=-5.51$, $df=74$, $p<0.05$). However, the completers and the noncompleters did not differ in their rates of change in suicidal ideation during the course of treatment ($\gamma_{11}=-0.13$, $t=-0.10$, $df=74$, n.s.). At the end of treatment, 29% of the group ($N=22$) met the criteria for improvement, and 16% ($N=12$) met the criteria for remission.

To summarize, substantial proportions of the patients did not complete the 6-month treatment. Depression scores significantly decreased over time. Not everyone changed similarly because change parameters had moderate variability. Suicidal ideation did not significantly change over time. However, there was significant variability in change in scores on the Modified Scale for Suicidal Ideation, indicating that suicidal ideation changed differently across individuals. Overall rates of improvement and remission were low. We next examined whether treatment allocation could account for individual differences in response over time.

Primary Hypothesis: Matched Treatment

Our primary set of analyses compared the matched and the mismatched subjects across all treatment conditions (cells 1, 3, 6, 8 against cells 2, 4, 5, 7; see Figure 1). As can be seen in Figure 1, these comparisons used the entire group, with the two conditions (matched and mismatched) taking equivalent proportions of each patient subgroup (high versus low cognitive dysfunction, high versus low family impairment) and type of treatment (cognitive therapy, family therapy, and pharmacotherapy alone).

There were no significant differences in Modified Hamilton Rating Scale for Depression scores, Beck Depression Inventory scores, or Modified Scale for Suicidal Ideation scores at discharge between the matched and mismatched groups. Similarly, there were no significant differences between the matched and the mismatched groups in the proportions of treatment failures or dropouts.

Matched treatment led to significantly greater change in score on the Modified Hamilton Rating Scale for Depression than mismatched treatment ($\gamma_{11}=-2.12$, $t=1.95$, $df=74$, $p=0.05$, $d=0.45$). However, treatment matching did not lead to significantly different change in Beck Depression Inventory scores compared to mismatched treatment ($\gamma_{11}=-2.10$, $t=-1.38$, $df=74$, $p=0.58$, $d=0.32$). Similarly, treatment matching did not produce greater change in scores on the Modified Scale for Suicidal Ideation compared to mismatched treatment ($\gamma_{11}=-1.06$, $t=-0.86$, $df=74$, $p=0.39$, $d=0.20$).

At the end of treatment, the matched condition had a significantly higher proportion of patients who improved ($\chi^2=3.9$, $df=1$, $p<0.05$, $d=0.47$), but there were no significant differences in the proportion whose illness remitted (Figure 2).

Secondary Hypotheses

The secondary hypotheses investigated the more specific efficacy of different treatment approaches by comparing the outcome of the patients who received 1) cognitive therapy versus no cognitive therapy (cells 1, 3, 5, 7 versus cells 2, 4, 6, 8) and 2) family therapy versus no family therapy (cells 1, 4, 6, 7 versus cells 2, 3, 5, 8). These comparisons also included the entire group, with each comparison (cognitive therapy versus no cognitive therapy; family therapy versus no family therapy) taking equivalent proportions of each patient subgroup and other types of treatments. We do not report analyses of specific treatment conditions—pharmacotherapy, combined cognitive therapy and pharmacotherapy, etc. Although the data are potentially interesting, these comparisons between individual treatment conditions either 1) are completely confounded with patient grouping and/or 2) are composed of only two of the four patient groups (Figure 1).

Family therapy—There were no significant differences in Modified Hamilton Rating Scale for Depression, Beck Depression Inventory, or Modified Scale for Suicidal Ideation scores at discharge between the groups with family therapy and no family therapy. The patients who received family therapy had a significantly lower proportion who were treatment failures ($\chi^2=5.8$, $df=1$, $p<0.05$, $d=0.57$) than those who did not. But the two groups did not differ in the proportion who were dropouts.

Linear change in Modified Hamilton Rating Scale for Depression scores was significantly greater for family therapy than for no family therapy ($\gamma_{11}=-2.19$, $t=-2.05$, $df=74$, $p=0.04$, $d=0.48$). Family therapy also produced a significantly greater decrease in scores on the Modified Scale for Suicidal Ideation across time compared to no family therapy ($\gamma_{11}=-2.70$, $t=-2.36$, $df=74$, $p=0.02$, $d=0.55$). However, inclusion of family therapy produced only a

nonsignificant tendency for change in Beck Depression Inventory scores ($\gamma_{11}=-2.58$, $t=-1.71$, $df=74$, $p=0.09$, $d=0.40$).

At the end of treatment, the patients receiving family therapy had significantly higher proportions of patients who improved ($\chi^2=10.1$, $df=1$, $p<0.01$, $d=0.78$) and showed a nonsignificant tendency to have higher proportions whose illness remitted ($\chi^2=2.7$, $df=1$, $p=0.10$, $d=0.38$) (Figure 2).

Cognitive therapy—There were no significant differences in Modified Hamilton Rating Scale for Depression, Beck Depression Inventory, or Modified Scale for Suicidal Ideation scores at discharge between groups with and without cognitive therapy. The patients receiving cognitive therapy had significantly fewer members who were treatment failures than the patients who did not receive cognitive therapy ($\chi^2=7.5$, $df=1$, $p<0.05$, $d=0.66$). There were no significant differences in proportions of dropouts. Hierarchical linear modeling analyses indicated no significant differences between cognitive and noncognitive treatments on scores on the Modified Hamilton Rating Scale for Depression, the Beck Depression Inventory, and the Modified Scale for Suicidal Ideation. Similarly, there were no significant differences in the proportion of patients who improved or whose illness remitted (Figure 2).

Discussion

Our study found inconsistent evidence for the effects of matching patients to type of treatment. Although the matching procedure did result in a higher proportion of patients who improved and a faster decrease in interviewer-rated depression scores, we found no differences in self-reported depression, suicidal ideation, or the percentage of patients whose illness remitted. Thus, matching patients to treatments on the basis of their types of deficits produced a moderate gain in overall treatment efficacy.

Further analyses indicated that the patients who received additional family therapy had significantly better outcomes than those who did not. The patients receiving family therapy had a significantly faster decrease in depressive symptoms and suicidal ideation, significantly higher rates of improvement, a nonsignificant tendency toward lower self-reported depression, and a greater proportion of patients whose illness remitted. This overall pattern of results suggests that adding family therapy to pharmacotherapy substantially improves the outcome of severely depressed patients. These results mirror studies of other major psychiatric disorders (bipolar disorder, schizophrenia) that also have found evidence for significant benefits of additional family therapy (25–27). They are also congruent with previous studies suggesting that family or marital treatments may be effective as stand-alone treatments for depression (5–7). It is particularly noteworthy that the results of this study were obtained with relatively few family therapy sessions (mean=5). Thus, our results suggest that inclusion of a brief family therapy intervention as part of a treatment package for severely depressed patients may have significant benefits.

Our results do not provide strong support for the efficacy of the addition of individual cognitive therapy. Although the patients receiving additional cognitive therapy did have lower rates of treatment failures (the patients were removed because of suicide risk), we found less support for the efficacy of additional cognitive therapy in producing better depression outcomes. These results are contrary to previous research (including our own studies) that has suggested that combined pharmacotherapy plus individual cognitive therapy is more effective than pharmacotherapy alone for severely depressed patients (28–30).

There are several possibilities why the addition of cognitive therapy was not efficacious in this study. First, in one of our previous studies (29), cognitive therapy began while the patients

were in the hospital, and the patients received an average of 10 inpatient sessions. With changes in the health care system, the hospital stay was reduced to the extent that beginning therapy in the hospital was not logistically feasible. It is possible that beginning cognitive therapy while in the hospital is more beneficial than delaying initiation until discharge.

Second, despite the fact that our protocol specified 20–24 sessions of cognitive therapy, the actual mean number of therapy sessions received was substantially fewer (mean=13) than in both our previous study and in usual cognitive therapy protocols. The major reason for this reduced number of sessions was patient compliance. A substantial proportion of the patients assigned to cognitive therapy missed a number of scheduled sessions. As noted previously, because of the typical history of treatment non-compliance, we did not remove patients for noncompliance, except under extreme circumstances. Thus, the patients assigned to the cognitive therapy condition were not removed from treatment if they attended a minimal number of sessions and/or were compliant with other assigned treatments. It may be that the reduced number of cognitive therapy sessions adversely affected treatment efficacy. However, although the correlation between the number of cognitive therapy sessions and Modified Hamilton Rating Scale for Depression scores at the end of treatment was significant ($r=0.45$, $p<0.05$), these correlations were positive, suggesting that a greater number of cognitive therapy sessions was associated with a greater level of depressive symptoms. Although a complete analysis and description of these effects are beyond the scope of the current article, it appears as if the patients who were doing relatively well choose not to attend as many therapy sessions.

In summary, although the matching hypotheses of the study received modest support, the secondary analyses strongly suggested that a treatment approach that includes family therapy was more efficacious than one that did not. These results emphasize the importance of operationalizing the biopsychosocial model when providing treatment to this severely impaired population of depressed patients.

Acknowledgements

The authors thank the following for their help: G. Alberts, Ph.D., J. Alves, M.S.W., D. Bishop, M.D., S. Bishop, Ph.D., R. Brown, Ph.D., E. Costello, Ph.D., L. Cronan, B.A., L. Drury, M.S.W., N. Epstein, M.D., M. Furman, M.D., A. Heru, M.D., J. Kelley, B.A., S. Luczak, B.A., W. Norman, Ph.D., R. Stout, Ph.D., C. Wagner, M.A., and M. Weishaar, Ph.D.

References

1. Jacobson NS, Hollon SD. Cognitive-behavior therapy versus pharmacotherapy: now that the jury's returned its verdict, it's time to present the rest of the evidence. *J Consult Clin Psychol* 1996;64:74–80. [PubMed: 8907086]
2. Friedman MA, Detweiler-Bedell JB, Leventhal HE, Thorne R, Keitner GI, Miller IW. Combined psychotherapy and pharmacotherapy for the treatment of major depressive disorder. *Clin Psychol* 2004;11:47–68.
3. Keitner GI, Miller IW. Family functioning in major depression: an overview. *Am J Psychiatry* 1990;147:1128–1137. [PubMed: 2201221]
4. Clarkin J, Glick I, Haas G, Spencer J, Lewis A, Peyser J, DeMane N, Ellis M, Harris E, Lestelle V. A randomized trial of inpatient family intervention, V: results for affective disorders. *J Affect Disord* 1990;18:17–28. [PubMed: 2136866]
5. Jacobson N, Dobson K, Fruzzetti A, Schmaling K, Salusky S. Marital therapy as a treatment for depression. *J Consult Clin Psychol* 1991;59:547–557. [PubMed: 1918559]
6. Beach S, O'Leary D. The treatment of depression occurring in the context of marital discord. *Behav Ther* 1986;17:43–49.
7. Leff J, Vearnals S, Brewin C, Wolff G, Alexander B, Asen E, Dayson D, Jones E, Chisholm D, Everitt B. The London Depression Intervention Trial. *Br J Psychiatry* 2000;177:95–100. [PubMed: 11026946]

8. Spitzer, RL.; Williams, JBW. Structured Clinical Interview for DSM-III-R—Patient Version (SCID-P). New York: New York State Psychiatric Institute, Biometrics Research; 1985.
9. Miller IW, Bishop S, Norman WH, Maddever H. The Modified Hamilton Rating Scale for Depression: reliability and validity. *Psychiatry Res* 1985;14:131–142. [PubMed: 3857653]
10. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–571. [PubMed: 13688369]
11. Miller I, Norman W, Keitner G. Treatment response of “high cognitive dysfunction” depressed inpatients. *Compr Psychiatry* 1991;30:62–71.
12. Norman W, Miller I. Characteristics of depressed patients with elevated levels of dysfunctional cognitions. *Cognit Ther Res* 1988;12:39–52.
13. Weissman, AN.; Beck, AT. Development and validation of the Dysfunctional Attitude Scale; paper presented at the 1978 meeting of the American Educational Research Association; Washington, DC, AERA. 1978.
14. Krantz S, Hammen C. The assessment of cognitive bias in depression. *J Abnorm Psychol* 1979;88:611–619. [PubMed: 512187]
15. Epstein, N.; Baldwin, L.; Bishop, D. McMaster Clinical Rating Scale. Providence, RI: Brown University Family Research Program; 1982.
16. Miller I, Kabacoff R, Bishop D, Epstein N, Keitner G. The development of the McMaster Clinical Rating Scale. *Fam Process* 1994;33:53–69. [PubMed: 8039568]
17. Fawcett, J.; Epstein, P.; Fiester, S.; Elkin, I.; Autry, J. Clinical Management: Imipramine-Placebo Administration Manual. Rockville, Md: National Institute of Mental Health Psychotherapy of Depression Collaborative Research Program; 1980.
18. Beck, A.; Rush, A.; Shaw, B.; Emery, G. Cognitive Therapy for Depression. New York: Guilford; 1979.
19. Epstein, N.; Bishop, D. Problem centered systems therapy of the family, in *Handbook of Family Therapy*. Gurman, A.; Kniskern, D., editors. New York: Brunner/Mazel; 1981. p. 444–482.
20. Wei I. Application of an urn model to the design of sequential controlled clinical trials. *J Am Stat Assoc* 1978;73:559–563.
21. Miller I, Bishop S, Norman W, Dow M. The Modified Scale for Suicidal Ideation: reliability and validity. *J Consult Clin Psychol* 1986;54:724–725. [PubMed: 3771893]
22. Byrk, A.; Raudenbush, S. Hierarchical Linear Models: Applications and Data Analysis Methods. Newbury Park, Calif: Sage Publications; 1992.
23. Byrk, A.; Raudenbush, S.; Cheong, Y.; Congdon, R. HLM 5: Hierarchical Linear and Nonlinear Modeling. Chicago: Scientific Software; 2001.
24. Crison M, Trivedi M, Pigott T, Rush A, Hirshfeld R, Kahn D, De-Battista C, Nelson C, Nierenberg A, Sackheim H, Thase M. The Texas Medication Algorithm Project: report of the Texas Consensus Conference Panel of Medication Treatment of Major Depressive Disorder. *J Clin Psychiatry* 1999;60:142–156. [PubMed: 10192589]
25. Falloon IR, Boyd JL, McGill CW, Williamson M, Razani J, Moss HB, Gilderman AM, Simpson GM. Family management in the prevention of morbidity of schizophrenia. *Arch Gen Psychiatry* 1985;42:887–896. [PubMed: 2864032]
26. Hogarty GE, Anderson CM, Reiss DJ, Kornblith SJ, Greenwald DP, Ulrich RE, Carter M. (Environmental-Personal Indicators in the Course of Schizophrenia [EPICS] Research Group): Family psychoeducation, social skills training, and maintenance chemotherapy in the aftercare treatment of schizophrenia, II: two-year effects of a controlled study on relapse and adjustment. *Arch Gen Psychiatry* 1991;48:340–347. [PubMed: 1672589]
27. Miklowitz D, Simoneau T, George E, Richards J, Kalbag A, Sachs-Ericsson Suddath R. Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. *Biol Psychiatry* 2000;48:582–592. [PubMed: 11018229]
28. Bowers W. Treatment of depressed inpatients: cognitive therapy plus medication, relaxation plus medication and medication alone. *Br J Psychiatry* 1990;156:73–78. [PubMed: 2404539]
29. Miller IW, Norman WH, Keitner GI. Cognitive-behavioral treatment of depressed inpatients: six- and twelve-month follow-up. *Am J Psychiatry* 1989;146:1274–1279. [PubMed: 2782470]

30. Miller I, Norman W, Keitner G, Bishop S, Dow M. Cognitive-behavioral treatment of depressed inpatients. *Behav Ther* 1989;20:25–47.

Patient Group		Treatment			
Cognitive distortion	Family impairment	Pharmacotherapy, cognitive therapy, and family therapy	Pharmacotherapy and cognitive therapy	Pharmacotherapy and family therapy	Pharmacotherapy
High	High	1. Match	—	—	2. Mismatch
High	Low	—	3. Match	4. Mismatch	—
Low	High	—	5. Mismatch	6. Match	—
Low	Low	7. Mismatch	—	—	8. Match

FIGURE 1.
Treatment Matching Study Design for Recently Discharged Patients With Major Depression

FIGURE 2.
Proportion of a Group of 76 Recently Discharged Patients Who Improved or Whose Depression Remitted After 24 Weeks

TABLE 1

Baseline, Discharge, and Week-24 Demographic and Clinical Characteristics of Recently Discharged Patients With Major Depression

Variable	Total Group (N=76)			Matched Patients (N=45)			Mismatched Patients (N=31)			Patients Who Received Cognitive Therapy (N=34)			Patients Who Did Not Receive Cognitive Therapy (N=42)			Patients Who Received Family Therapy (N=40)			Patients Who Did Not Receive Family Therapy (N=36)		
	N	%	SD	N	%	SD	N	%	SD	N	%	SD	N	%	SD	N	%	SD	N	%	SD
Baseline status																					
Female gender	62	82		37	82		25	81		26	77		36	86		31	78		31	86	
≥3 Previous episodes	41	54		24	53		17	55		17	50		24	57		21	53		20	56	
Married	51	67		30	67		21	68		18	53		33	79		27	68		24	67	
Caucasian race	71	93		42	93		29	93		32	94		39	93		38	95		33	92	
	Mean		SD	Mean		SD	Mean		SD	Mean		SD	Mean		SD	Mean		SD	Mean		SD
Baseline measures																					
Age (years)	37.6	11.7		39.1	11.9		35.6	11.4		35.2	12.3		39.6	11.0		37.7	10.3		37.6	13.3	
Education (years)	12.9	2.5		13.0	2.5		12.7	2.5		12.7	2.7		13.1	2.3		13.3	2.4		12.6	2.5	
Age at illness onset (years)	26.0	12.9		28.0	13.6		23.1	11.5		22.9	11.3		28.5	13.8		27.1	12.7		24.8	13.2	
17-item Modified Hamilton Rating Scale for Depression score	25.5	4.3		25.4	4.2		25.7	4.4		24.9	4.1		26.0	4.4		25.6	4.4		25.4	4.1	
Beck Depression Inventory score	35.2	8.7		34.0	8.5		36.9	8.9		34.3	8.1		36.0	9.2		34.0	8.7		36.5	8.7	
Modified Scale for Suicidal Ideation score	21.2	12.7		19.7	12.4		23.5	13.0		22.7	10.8		26.0	14.1		19.0	12.0		23.7	13.2	
Dysfunctional Attitude Scale score	167.9	42.2		162.0	38.5		176.5	46.3		168	33.7		168	48.4		161	36.6		175	47.0	
Cognitive Bias Questionnaire score	3.9	3.1		3.3	2.5		4.7	3.7		3.5	2.6		3.9	3.6		3.2	2.6		4.6	3.5	
McMaster Clinical Rating Scale score	2.8	1.0		2.9	0.9		2.7	1.0		2.9	1.0		2.8	1.0		2.8	0.8		2.9	1.1	
Length of stay (days)	13.7	8.8		14.7	7.9		12.3	1.0		14.3	9.8		13.2	8.0		14.6	10.4		12.8	6.7	
Discharge scores																					
17-item Modified Hamilton Rating Scale for Depression	18.3	6.0		17.8	5.9		18.9	6.2		17.4	6.2		19.0	5.8		17.8	5.9		18.9	6.2	
Beck Depression Inventory Modified Scale for Suicidal Ideation	22.8	10.8		20.8	9.1		25.7	12.4		21.7	9.3		23.7	11.9		20.6	10.2		25.3	11.1	
Week-24 status	5.6	13.7		5.3	15.8		6.1	10.1		3.8	7.7		7.1	17.1		5.0	16.6		6.3	9.7	
Adequate medication trial ^d	61	80		38	84		23	74		29	85		32	76		33	83		28	78	
Treatment failures	18	24		8	18		10	32		3	9		15	36		5	13		13	36	
Dropouts	16	21		8	18		8	26		4	12		12	28		8	20		8	22	
Patients with remitted depression	12	16		9	20		3	10		6	18		6	15		9	23		3	9	
Patients with improved depression	22	29		17	38		5	17		11	32		11	27		18	45		4	11	
Week-24 scores																					
17-item Modified Hamilton Rating Scale for Depression	13.0	8.9		11.4	8.7		15.4	8.7		11.6	7.1		14.3	10.1		11.0	8.6		15.4	8.8	

Variable	Total Group (N=76)	Matched Patients (N=45)	Mismatched Patients (N=31)	Patients Who			Patients Who Did Not Receive Family Therapy (N=40)	Patients Who Did Not Receive Family Therapy (N=36)
				Received Cognitive Therapy (N=34)	Did Not Receive Cognitive Therapy (N=42)	Received Family Therapy (N=40)		
Beck Depression Inventory	17.9	15.7	21.4	17.7	18.1	15.8	14.9	25.7
Modified Scale for Suicidal Ideation	5.5	3.8	8.0	4.4	6.5	10.2	2.9	8.5
				11.1			8.1	10.6

^aFour weeks or longer of taking at least the minimum targeted dose of a medication.