Journal of Consulting and Clinical Psychology
2003, Vol. 71, No. 3, 482–492

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0022-006X/03/$12.00 DOI: 10.1037/0022-006X.71.3.482

Family-Focused Treatment Versus Individual Treatment for Bipolar Disorder: Results of a Randomized Clinical Trial

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Recently hospitalized bipolar, manic patients ($N = 53$) were randomly assigned to a 9-month, manual-based, family-focused psychoeducational therapy ($n = 28$) or to an individually focused patient treatment ($n = 25$). All patients received concurrent treatment with mood-stabilizing medications. Structured follow-up assessments were conducted at 3-month intervals for a 1-year period of active treatment and a 1-year period of posttreatment follow-up. Compared with patients in individual therapy, those in family-focused treatment were less likely to be rehospitalized during the 2-year study period. Patients in family treatment also experienced fewer mood disorder relapses over the 2 years, although they did not differ from patients in individual treatment in their likelihood of a first relapse. Results suggest that family psychoeducational treatment is a useful adjunct to pharmacotherapy in decreasing the risk of relapse and hospitalization frequently associated with bipolar disorder.

The quality of outpatient treatment for bipolar disorder advanced considerably with the introduction of lithium carbonate in the 1960s and the anticonvulsants in the 1980s. Whereas patients with bipolar disorder tended to follow deteriorating courses in the pre-pharmacological era (Cutler & Post, 1982), lithium- or anticonvulsant-treated patients remain out of the hospital for extended periods (Goodwin & Jamison, 1990). At least 60% of patients with bipolar disorder respond to lithium (Goodwin & Zis, 1979) and a comparable number respond to the anticonvulsants (McElroy & Keck, 2000). Moreover, lithium nonresponders frequently respond to the anticonvulsants (American Psychiatric Association, 1994; Bowden, 1996).

Nonetheless, there is increasing recognition that pharmacological treatment does not fully control the symptomatic fluctuations of bipolar illness. In a community follow-up, Gitlin, Swendsen, Heller, and Hammen (1995) found that 37% of bipolar patients relapsed in one year despite maintenance pharmacotherapy and 73% relapsed over 5 years. Gelenberg et al. (1989) reported a similar rate (40%) over 1 year among lithium-treated patients, even with drug compliance assured. Patients with bipolar disorder also experience considerable psychosocial and occupational deficits despite pharmacotherapy (Coryell et al., 1993; Dion, Tohen, Anthony, & Waternaux, 1988; Goldberg, Harrow, & Grossman, 1995). Further, studies suggest that as many as 75% of individuals with bipolar disorder experience inter-episode residual symptoms despite pharmacotherapy (Gitlin et al., 1995; Kalbag, Miklowitz, & Richards, 1999; Keller et al., 1986).

At least a part of this variability in illness course can be attributed to psychosocial stressors. Specifically, patients who return to a stressful family milieu after a hospitalization are more likely to relapse in 9-month to 1-year community follow-ups than those who return to less stressful family environments (Miklowitz, Goldstein, Nuechterlein, Snyder, & Mintz, 1988; O'Connell, Mayo, Flatow, Cuthbertson, & O'Brien, 1991; Priebe, Wildgrube, & Mueller-Oerlinghausen, 1989). Furthermore, episodes of bipolar disorder are often precipitated by significant life events, particularly those events that disrupt patients' sleep–wake cycles or that promote goal directedness (Ellicott, Hammen, Gitlin, Brown, & Jamison, 1990; Johnson & Roberts, 1995; Johnson et al., 2000; Malkoff-Schwartz et al., 1998).

The overall pattern of these findings suggests the possibility that pharmacotherapy can be augmented by psychosocial interventions

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Michael J. Goldstein died in March 1997. We gratefully acknowledge his essential contributions to this research.

This research was supported by National Institute of Mental Health (NIMH) Training Grant MH-14584, NIMH Grant MH-42556, and the University of California, Los Angeles, Clinical Research Center for the Study of Schizophrenia, NIMH Grant MH-30911.

Special thanks go to Emily Altman, Jeffrey Ball, Steven Erhardt, Jodie Halpern, Constance Hammen, Jennifer Christian-Herman, Robin Kissell, Robert Liberman, Sandra Malik, Keith Neuchterlein, Noosha Niv, Sumie Okazaki, Meg Racenstein, Irwin Rosenfarb, Angus Strachan, Joseph Ventura, Amy Weisman, Stephanie Woo, and Sibyl Zaden for their contributions.

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whose objectives include decreasing family stress and improving psychosocial functioning, compliance with medication, and the patients' ability to cope with environmental triggers (Miklowitz, 1996). Although promising results have been published, the psychosocial treatment literature for bipolar disorder is in its infancy (for reviews, see Craighead & Miklowitz, 2000; Huxley, Parikh, & Baldessarini, 2000; Miklowitz & Craighead, 2001). Studies of individual therapy have included a controlled trial by Cochran (1984), who demonstrated that bipolar outpatients who received lithium and brief cognitive therapy were more compliant with medications at a 6-month follow-up, and had fewer medication noncompliance-associated relapses of mood disorder, than patients who received only lithium. Perry, Tarrier, Morriss, McCarthy, and Limb (1999) found that medication administered with an individual cognitive–behavioral therapy aimed at early recognition of prodromal symptoms was more effective in delaying manic relapses over an 18-month follow-up than a medication-only intervention. Frank et al. (1997) demonstrated the positive benefits of individual–interpersonal and social rhythm therapy on patients' capacities to regulate their daily routines and sleep–wake cycles. Preliminary data also suggest that patients treated with maintenance interpersonal therapy and medication are more likely to maintain stable mood states than patients treated with an intensive clinical management intervention and medication (Frank, 1999).

Models of family-based interventions for bipolar disorder have been informed by the literature on psychoeducational treatments for schizophrenic disorders. Falloon et al. (1985) demonstrated the utility of a behavioral family intervention for schizophrenic patients over an individual supportive intervention, in terms of reductions in relapse rates and improvements in psychosocial functioning over 2 years. Hogarty et al. (1986, 1991) showed that a family psychoeducational treatment and pharmacotherapy had more lasting effects—in terms of community survivorship—than individual social skills training and pharmacotherapy in 1- and 2-year follow-ups of schizophrenic patients. Involving the family in the outpatient management of schizophrenia has received strong support from the empirical literature, although questions remain about which forms of family treatment are most effective (Goldstein & Miklowitz, 1995).

Bipolar disorder shares many of the clinical characteristics of schizophrenia, including a relapse–remission course, significant psychosocial impairment, the need for maintenance medication and associated issues of noncompliance, and the negative impact of family stress on clinical outcomes. Thus, a natural step in examining psychosocial intervention for bipolar disorder is to test the efficacy of family-based treatments that have proven efficacious with schizophrenia. Clarkin, Carpenter, Hull, Wilner, and Glick (1998) showed that individuals with bipolar disorder who received a marital psychoeducational intervention in conjunction with pharmacotherapy had better medication adherence and global functioning scores over 1 year of treatment than those who had pharmacotherapy alone, despite no group differences in symptomatic outcome. Miklowitz and colleagues (Miklowitz et al., 2000; Simoneau, Miklowitz, Richards, Saleem, & George, 1999) reported the 1-year results of a University of Colorado trial comparing family-focused psychoeducational treatment (FFT; Miklowitz & Goldstein, 1997) and pharmacotherapy to a crisis management intervention, also with pharmacotherapy. Among bipolar patients followed over 1 year, family-focused treatment was associated with longer delays prior to mood disorder relapses, more dramatic improvements in depression symptoms, and higher levels of positive family communication than the crisis management intervention. The results remained robust even when individual differences in pharmacotherapy regimes, and compliance with those regimes, were statistically controlled.

The results of the Colorado trial, while encouraging, must be interpreted in light of the fact that the two psychosocial treatments were not matched on number of therapist contact hours. The family treatment consisted of 21 sessions over a 9-month period, whereas the crisis management intervention condition consisted of two family education sessions and crisis intervention sessions offered as needed, also over a 9-month period. Thus, it is possible that the superior outcomes of patients in the family treatment were in part a function of the greater attention they received from project clinicians. In addition, the effects of the family treatment could reflect the impact of intensive psychosocial treatment more generally, and not the influence of family intervention specifically.

The present study evaluated, in a randomized design, the effects of FFT and pharmacotherapy against a comparably paced, individually focused patient treatment, which included education, case management, and problem solving alongside standard pharmacotherapy. This trial, conducted at the University of California, Los Angeles (UCLA), matched the two psychosocial treatments on number of therapy contacts (21 sessions over 9 months). All patients ($N = 53$) were offered 12 months of study-based pharmacotherapy from study psychiatrists working in a specialty outpatient clinic. The impact of the two psychosocial interventions was compared in terms of the timing and rates of relapse and rehospitalization over a 1-year interval of active treatment and a 1-year posttreatment follow-up. We predicted that patients in FFT would experience fewer rehospitalizations and fewer symptom relapses, and demonstrate better compliance with medications, than patients in individual treatment.

Method

Participants

Participants were recruited from the inpatient services of three large hospitals in the Los Angeles area. Criteria for inclusion in the study were (a) a diagnosis of bipolar disorder, manic type; (b) between age 18 and 45; (c) competency to give written informed consent; (d) currently taking mood-regulating medications (lithium carbonate, divalproex sodium, carbamazepine, or a combination of these medications); and (e) availability of at least one close family member to participate with the patient. Subjects were excluded if they showed evidence of organic central nervous system disorder or chronic alcohol or substance abuse/dependence. All but one of the patients was approached by research staff members while hospitalized. If time permitted, the diagnostic interview was conducted with the patient prior to his or her discharge. At the initial patient contact, research staff obtained written permission to speak with relatives.

Of those patients approached and evaluated, 76 met the above criteria. However, 20 of these were not assigned to psychosocial treatment for the following reasons: The patient refused all follow-up care ($n = 11$), the family refused ($n = 3$), the patient reported transportation problems ($n = 5$), or the patient needed extended inpatient care ($n = 1$). Three additional participants were dropped from the study when further evaluation of the patients' symptoms revealed a change of the diagnosis to a schizophrenic or schizoaffective disorder. Thus, 53 families participated in the randomized trial.

The 53 patients ranged from 18 to 46 years of age ($M = 25.6$; $SD = 6.4$), and had, on average, 14.2 years ($SD = 2.2$) of education. Sixty percent were Caucasian ($n = 32$), 23% ($n = 12$) were African American, 9% ($n = 5$) were Asian American, and the remaining 9% ($n = 4$) were from other ethnic groups. The majority of the patients lived with their relatives at study entry ($n = 38$; 72%). Forty percent ($n = 21$) had experienced only one episode of mania, and 60% ($n = 32$) had a history of multiple episodes of mania. Sixty-six percent of the patients ($n = 35$) had only one relative who participated in the study, and 34% ($n = 18$) had multiple relatives (i.e., mother and father). Relatives ($n = 74$) included 29 mothers, 22 fathers, 1 stepfather, 9 spouses, 7 siblings, 1 grandmother, 1 uncle, and 4 aunts.

Procedure

Treatment protocol. All patients received individual medication management sessions with a staff research psychiatrist for 1 year. Patients were prescribed at least one of the major mood-regulating medications used in the treatment of bipolar disorder (lithium carbonate, carbamazepine, or divalproex sodium). Treatment was individually tailored to the patient's clinical state and at times included antipsychotics, anticholinergics, antidepressants, and anxiolytic agents. The two treatment groups did not differ in medication protocols at any point during the 1-year study period (see Table 1; for all comparisons, $p > .10$).

In addition to the medication management sessions, the patients were randomly assigned to either family-focused treatment ($n = 28$) or individually focused patient treatment ($n = 25$). Patients and relatives were informed of treatment assignments following the pretreatment baseline assessments described below. Contact with the psychiatrist and the psychosocial intervention team was more intensive in the early stages of the year-long treatment protocol and became less frequent as patients became increasingly stable. Thus, both medication management and psychosocial intervention (family or individual) sessions took place weekly for the first 3 months of participation, every other week for the second 3 months of the study, and monthly thereafter. In order to provide optimal care, psychiatrists conducting the medication management sessions and therapists conducting the psychosocial sessions communicated with each other on a weekly basis about all patients. Thus, psychiatrists were aware of patients' psychosocial treatment assignments.

Psychosocial intervention sessions were scheduled for a total of 9 months (21 sessions), and medication management sessions continued for the remainder of the 3 months of the 1-year active treatment period. Patients in family treatment had two cotherapists, whereas those in individual patient treatment had one therapist. At the end of the study year, participants were referred to treatment providers in the community, and considerable effort was made to assist in this transition. As might be anticipated, the intensity of this continuation treatment varied from patient to patient. However, the two treatment groups were equal with regard to the proportion of patients who pursued psychiatric treatment after the 12-month active treatment phase. At a 24-month follow-up, 71% (12 of 17) of the individual treatment patients, and 71% (15 of 21) of the family treatment patients, had pursued and had become engaged in continuing psychiatric care.

The research staff contacted patients approximately 1 year following the active study treatment period to obtain follow-up data on clinical and psychosocial outcomes. Data from this evaluation will be referred to as the posttreatment follow-up. Typically, patients received this final follow-up interview at 24 months after entry into the study. However, several patients could not be contacted for follow-up interviews at that point. Patients in the two treatment groups did not differ in the length of the follow-up interval, FFT group: $M = 128.7$ weeks, $SD = 34.5$; individual group, $M = 123.2$ weeks, $SD = 31.6$; $t(37) = 0.52$, $p > .10$. Furthermore, an approximately equal proportion of patients in the family-focused treatment (16 of 28, or 57%) and in the individually focused treatment (13 of 25, or 52%) were contacted and interviewed after the 24-month point. Given that survival modeling is ideally suited for data in which follow-up times vary, we have included in survival analyses all outcome data for patients in the sample regardless of their length of follow-up.

Patients were informed at the outset of the study that they would not be able to continue in the psychosocial protocol if they chose to discontinue

Table 1
Medication Protocols During Study Treatment

Follow-up period	Medication protocol: Mood regulator only *n* (%)	Mood regulator plus antidepressant *n* (%)	Mood regulator plus antipsychotic *n* (%)	Mood regulator, antipsychotic, and antidepressant *n* (%)	χ^2
3 month					
FFT	16 (59)	2 (8)	7 (26)	2 (7)	5.09
IPM	7 (29)	3 (12)	9 (38)	5 (21)	
6 month					
FFT	16 (67)	2 (8)	6 (25)	0 (0)	1.13
IPM	12 (57)	4 (19)	5 (24)	0 (0)	
9 month					
FFT	14 (64)	2 (9)	5 (23)	1 (4)	2.01
IPM	10 (50)	5 (25)	4 (20)	1 (5)	
12 month					
FFT	13 (65)	2 (10)	5 (25)	0 (0)	2.86
IPM	7 (42)	5 (29)	5 (29)	0 (0)	
24 month					
FFT	6 (40)	3 (20)	4[a] (27)	2 (13)	1.87
IPM	2 (17)	3 (25)	5 (41)	2 (17)	

Note. Medication protocols did not differ across the two treatment groups ($p > .10$) at any of the evaluation points. FFT = family-focused treatment; IPT = individually focused patient treatment.
[a] One patient in this cell was receiving antipsychotic medication alone.

their medications. Patients who did discontinue medications were assisted in obtaining psychiatric care outside of the study. Forty-two of the 53 patients (79%) completed the full 9-month psychosocial treatment protocol. Of those who did not complete treatment, 6 participated in the family-focused intervention and 5 in the case management condition—a nonsignificant difference in rates of attrition, $\chi^2(1, N = 53) = 0.02$, $p > .10$. Of the 11 who did not complete treatment, 7 dropped out during the first 3 months of treatment (3 patients moved out of the area, 2 families refused further involvement, 1 patient refused all further psychosocial sessions and pharmacotherapy, and 1 required long-term inpatient care), and 4 dropped out during the second 6 months (2 refused all treatment, 1 chose to see a private psychiatrist, and 1 refused further family involvement).

Follow-up data, including symptom, psychosocial, and medication regimen–compliance ratings, were obtained on 9 of the 11 patients who did not complete 9 months of psychosocial treatment. Of these 9 individuals, one patient had 9 months of follow-up data, 3 had 6 months of data, and 5 patients had 3 months of data. Consistent with the intent-to-treat design of the study, data from all patients were included in the survival analyses regardless of whether they completed the treatment protocol.

Family-focused treatment. The FFT was modeled after the original structure of Falloon, Boyd, and McGill (1984) behavioral family management for patients with schizophrenia but substantially modified by Miklowitz and Goldstein (1997) for individuals with bipolar disorder and their families. The 21 sessions were an hour in length and included three primary components: psychoeducation about bipolar disorder, communication enhancement training, and problem-solving skills training. Allocation of time to each component was dependent on the individual family's needs and preparation, given their prior knowledge of bipolar disorder, current family difficulties, and the patient's clinical status. The psychoeducation component included information about the symptoms, course, causes, and treatment of bipolar disorder. Information was presented within a vulnerability–stress framework, with careful attention paid to risk factors (e.g., drug use, poor sleep patterns) and protective factors (e.g., medication compliance, social support) in the course of bipolar disorder. Second, family members were taught communication skills, including active listening, giving one another structured positive and negative feedback, and making positive requests for changes in one another's behavior. Communication training included in-session role playing and homework assignments that required between-session rehearsal. Third, family members learned problem-solving techniques, including identification of specific problems, brainstorming of solutions, evaluating the advantages and disadvantages of each proposed solution, and implementing self-selected solutions. Although topics in the problem-solving component were geared toward each family's specific concerns, all families completed a "relapse drill," in which problem-solving focused on planning a family-wide response should the patient's symptoms return. Finally, crisis intervention was available to families on an as-needed basis (see Miklowitz & Goldstein, 1997).

Therapists were trained in conducting FFT in three ways. First, all new therapists reviewed an initial version of the Miklowitz and Goldstein (1997) treatment manual and studied case examples in detail. Second, they viewed a set of training tapes outlining the steps for conducting FFT. Third, all new therapists were apprenticed to a senior FFT therapist. Only after successfully conducting therapy with two families could the new FFT therapist be considered senior and able to train new therapists. To ensure that treatment delivery was uniform and adhered to the manualized protocol, an experienced family therapist, the first author, viewed all treatment sessions either live or on videotape and provided regular supervision. In addition, all therapists and psychiatrists met in weekly group supervision sessions in which cases were reviewed.

The therapists' competence with and adherence to the FFT treatment manual were evaluated by a separate group of raters who viewed the videotaped sessions and applied ratings using the 13 Likert-type Therapist Competency/Adherence Scales (see Weisman et al., 1998). These scales measure treatment fidelity in five domains: providing psychoeducation, implementing communication training, teaching problem-solving skills, general therapeutic skills, and therapist cooperation. Ratings for the study therapists averaged 5.61 ($SD = 0.73$) across the 13 scales, each of which could range from 1 (*low*) to 7 (*high*), indicating that, on average, therapists delivered the FFT manual with skill and consistency.

Individually focused patient treatment. In the individually focused patient treatment condition, patients met with a therapist for 30-min sessions, also titrated over 9 months (12 weekly, 6 biweekly, 3 monthly). The treatment was supportive, problem-focused, and educational. The goals were to educate the patient about the illness, monitor and increase the patient's awareness of symptoms, conduct crisis intervention, and reduce ongoing life stress. In the initial phase of treatment (Sessions 1–8) the patient and therapist reviewed the symptoms of the index episode and the precipitating life circumstances. Therapists acquainted patients with the importance of regular sleep patterns, medication effects and side effects, and the role of alcohol or street drugs in precipitating symptom exacerbations. In the middle phases of treatment (Sessions 9–18), sessions focused on problem solving concerning ongoing life stressors, establishing realistic short-term goals, and exploring feelings about the illness and its stigma. The final sessions focused on problem solving about likely future stressors and disposition plans for the period immediately following completion of the study.

The individual therapists were trained in the goals of the intervention prior to conducting the treatment. Group supervision for therapists was conducted weekly, and audiotapes of sessions were monitored regularly. No standardized measures of treatment adherence were used to evaluate the individually focused treatment. However, the same therapists conducted both the family-focused and individually focused interventions and were supervised in both modalities by the same experienced clinicians. As a result, levels of therapist training and experience with bipolar patients were standardized across conditions.

Diagnosis. Shortly after referral to the study, the patient's diagnosis according to the *Diagnostic and Statistical Manual of Mental Disorders*—Third Edition, Revised (*DSM–III–R*; American Psychiatric Association, 1987) was confirmed by use of the Present State Examination (PSE; Wing, Cooper, & Sartorius, 1974) with supplementary mania items from the Structured Clinical Interview for the *DSM–III–R* (SCID; Spitzer, Williams, Gibbon, & First, 1990). Any additional information needed for diagnostic purposes was obtained through chart reviews and/or information from the relatives. Interviewers who were trained by the Diagnostic and Psychopathology Unit of the University of California, Los Angeles Intervention Research Center for Major Mental Disorders conducted all diagnostic assessments. Training consisted of (a) scoring videotapes of diagnostic interviews with accompanying ratings; (b) conducting diagnostic interviews while an expert diagnostician co-rated the interviews; and (c) participating in biannual fidelity checks to prevent rater drift (Ventura, Liberman, Green, Shaner, & Mintz, 1998).

Two interrater reliability statistics were calculated to measure diagnostic agreement. First, kappa statistics compared agreement on the presence or absence of each critical PSE/SCID item. All interviewers met the minimum standards of acceptable symptom agreement, with an overall kappa of .75, a specificity of .75, and a sensitivity of .75. Second, the study interviewers achieved high interrater reliability in the differential diagnosis of mood disorder versus schizophrenia and schizoaffective disorder, with an overall kappa of .88, a sensitivity of .88, and a specificity of .88.

To determine whether participants in the two treatment conditions were from comparable clinical populations, a number of demographic and clinical variables were assessed on entry into the study. These included gender, age, years of education, current marital status, employment, and socioeconomic status (SES; based on the Amherst Modification of the Hollingshead–Redlich Scale; Watt, 1976). Clinical variables included age at illness onset, presence–absence of previous episodes of mania, total duration of illness, and premorbid social adjustment. The latter was mea-

sured with the UCLA Social Attainment Scale (SAS; Goldstein, 1978), a seven-item face-to-face interview that assesses social and sexual adjustment during adolescence (ages 16–20 years).

Assessment of patients' outcomes. Patients' outcomes were measured in three domains: symptomatic functioning, rehospitalization, and medication compliance. All measures were administered at the outset of treatment and every 3 months throughout the patients' participation in the 1-year active treatment phase of the study. Further, patients and relatives were contacted for a final follow-up interview at least 2 years after entering the study. Project staff members assessed patients' symptoms using the Brief Psychiatric Rating Scale (BPRS; Lukoff, Nuechterlein, & Ventura, 1986) and supplementary items from the Schedule for Affective Disorders and Schizophrenia—Change Version (SADS-C; Endicott & Spitzer, 1978), which provides more detailed assessments of changes (both major and subclinical) in levels of depression and mania. The supplementary SADS-C items included neurovegetative symptoms (i.e., lack of energy, poor appetite, weight loss, increased activity, increased energy, and less sleep), affective symptoms (loss of interest), and cognitive symptoms (discouragement, negative self-evaluation).

Raters who were blind to patients' psychosocial treatment conditions conducted the BPRS/SADS-C interviews. In addition to rigorous training in BPRS administration and scoring, all raters attended yearly group and individual quality assurance sessions to maximize their consistency with the BPRS scoring manual. These methods have been shown to greatly improve rater reliability and decrease rater drift (Ventura, Green, Shaner, & Liberman, 1993). Intraclass correlation coefficients across all BPRS items were computed between each rater and a criterion rater on a minimum of nine interviews and ranged from .83 to .93 (for all, $p < .01$). In making BPRS/SADS-C ratings covering the interval from the end of active treatment (12 months) to the final posttreatment follow-up, interviewers followed the manual-based instructions to use all sources of information, including data from patients, family members, and, where possible, medical records (Ventura et al., 1993).

For each 3-month follow-up period, participants were placed in one of the following clinical outcome categories: (a) *relapse*, defined as a rating of 6 or 7 on the BPRS/SADS-C core symptoms of depression (depressed mood, loss of interest), mania (hostility, elevated mood, grandiosity), or psychosis (unusual thought content, suspiciousness, hallucinations, conceptual disorganization) and at least two ancillary symptoms (suicidality, guilt, sleep disturbance, appetite disturbance, lack of energy, negative evaluation, discouragement, increased energy–activity), or (b) *nonrelapse*, defined as a score of 5 or below on all relevant BPRS/SADS-C core symptoms during the 3-month interval. For each relapse, approximate dates of symptom onset and resolution were noted. In addition to relapse, rehospitalization was an important outcome variable for the study. Data on rehospitalization were collected at each time point using patients' and relatives' reports. Inpatient medical records were consulted, where possible, to verify that rehospitalizations had occurred.

Medication compliance. Medication compliance was rated every 3 months by the patient's psychiatrist, using a standardized form which included detailed information about the current medication regimen and associated blood serum levels as well as any changes in the medication protocol since the last visit. The psychiatrist made ratings of compliance on a 7-point Likert scale ranging from *full compliance* (1) to *discontinued medication against medical advice* (7), using all available compliance information, including patients' reports, psychiatrists' observations, and medication blood levels. Although interrater reliability evaluations of the psychiatrists' medication compliance ratings were not undertaken for this study, past research conducted with this scale has demonstrated a high level of rater agreement (Miklowitz et al., 1988). In that study, medication compliance was evaluated longitudinally among 23 bipolar patients who originated from the same inpatient hospital as the patients in the present study. The Pearson correlation coefficient between two independent raters using this 7-point scale was .97.

Results

In examining patient outcomes, two central questions were addressed. First, were there differences between the treatment groups in the probability of symptom relapse and rehospitalization during the 1-year active treatment period and the posttreatment interval? We predicted that, compared with the individual-focused patient treatment, FFT would be associated with a lower risk of relapse and rehospitalization. Second, does participation in family, as opposed to individual, treatment improve compliance with medications?

Preliminary Analyses

Prior to examining the outcome data, preliminary analyses were conducted to determine how successful the randomization had been in yielding equivalent groups on demographic characteristics (age, ethnicity, gender, marital status, employment status, SES, education) and clinical variables (age of onset, premorbid adjustment, and history of prior episodes). Student's *t* tests were used to examine group differences on continuous variables, and likelihood ratio chi-square analyses were used to examine group differences on categorical variables. As Table 2 indicates, there were no differences between the treatment groups on any variable except age at illness onset and premorbid adjustment.

Table 2
Treatment Group Differences on Demographic and Clinical Variables

Variable	Individual treatment ($n = 25$)	Family-focused treatment ($n = 28$)
Gender		
Male	40%	46%
Female	60%	54%
Ethnicity		
Caucasian	56%	64%
African American	16%	29%
Other	28%	7%
Marital status		
Single	84%	68%
Married	4%	25%
Divorced	12%	7%
First manic episode	52%	29%
Employment	44%	61%
Age		
M	24.6	26.5
SD	5.80	6.86
Age at onset		
M	21.2[a]	23.5[a]
SD	3.68	4.51
Premorbid adjustment		
M	24.50[a]	27.48[a]
SD	6.12	4.64
SES (Hollingshead-Redlich)		
M	2.6	2.6
SD	1.20	0.90
Education		
M	14.08	14.32
SD	2.31	2.04

Note. SES = socioeconomic status.
[a] The groups were significantly different at $p < .05$.

Despite the randomization, patients in individual treatment had a significantly younger age of illness onset and poorer premorbid adjustment than patients in family-focused treatment (for both, $p < .05$). However, age of illness onset was not significantly associated with premorbid adjustment (Pearson's $r = .10$, $p > .10$). Given the difference between the treatment groups on these clinical variables, subsequent analyses were conducted controlling for each separately.

Description of Clinical Outcomes

During the 1-year active treatment period, 26 of the 53 (49%) participants experienced a total of 32 relapses. Nine of the participants experienced an episode of depression, 12 experienced a single episode of mania, 2 had two episodes of mania, 2 had one episode of mania and one episode of depression, and 1 had three episodes of mania. During the posttreatment follow-up interval, 19 of the 39 available individuals (49%) experienced a total of 24 relapses. Eight had a single episode of mania, 6 had a single episode of depression, 3 had two episodes of mania and 2 had episodes of both depression and mania. To ascertain the degree to which the measure of relapse had clinical significance, we examined the association between relapse and rehospitalization. Of those 26 patients experiencing relapses during the active treatment year, 18 (69%) were rehospitalized for a total of 20 rehospitalizations. Twelve individuals had a single rehospitalization for mania, 4 were rehospitalized for depression, and 2 experienced two separate rehospitalizations for mania. Of those 19 patients who experienced a relapse during the posttreatment follow-up period, 16 (84%) were rehospitalized for a total of 19 rehospitalizations. Ten had a single rehospitalization for mania, 3 had a single rehospitalization for depression, 2 individuals were rehospitalized twice for mania, and 1 had separate rehospitalizations for mania and depression. Although there was a significant association between having had a relapse and having been hospitalized during the 1-year active treatment period, $\chi^2(1, N = 53) = 28.3$, $p < .01$, and during the posttreatment follow-up interval, $\chi^2(1, N = 39) = 23.0$, $p < .01$, a proportion of the patients (31% during the intervention and 16% in the follow-up period) were not rehospitalized despite a symptom relapse. Thus, relapse and rehospitalization represented overlapping but different categorical outcomes and were examined separately.

Treatment Group and Clinical Outcome

Survival analyses examined the relationships between treatment group, relapse, and rehospitalization. First, we used survival curves based on the Kaplan–Meier method (Kalbfleisch & Prentice, 1980) to estimate the risk of relapse–rehospitalization (time to first relapse or rehospitalization) in each of the treatment groups, and log-rank chi-square tests were conducted to evaluate the equivalence of the resultant survival curves. Second, because we continued to follow and treat patients after they relapsed, participants could (and did) have multiple relapses and rehospitalizations during the 1-year active treatment period and the posttreatment follow-up period. These multiple events were analyzed with the Andersen and Gill (1982) counting process approach, a method of proportional hazard survival regression analysis that permits entry of multiple events of the same type. Participants were included in the analysis regardless of whether they completed the full year of psychosocial treatment. For all analyses, two-tailed tests were used.

Relapse

Figure 1 demonstrates the cumulative probability of symptom relapse during the entire 1-year treatment period and posttreatment follow-up interval together. Calculated with the Kaplan–Meier method, the probability of having an episode of mood disorder did not differ between the FFT and individually focused patient treatment groups, $\chi^2(1, N = 53) = 0.50$, $p > .10$. However, when multiple relapses were examined with the Andersen–Gill model, results indicated a treatment group effect. Those in FFT had fewer relapses during the entire follow-up interval (intervention year and posttreatment follow-up together) than did those in individual treatment, $\chi^2(1) = 5.04$, $p < .05$.

Why should an analytic strategy that includes multiple events reveal differences between the treatment groups, whereas an analysis that considers only the time until a first incident does not reveal such differences? Given that the majority of the second events occurred in the posttreatment interval, separate survival models examined the 1-year active treatment and the posttreatment follow-up intervals independently. During the active treatment year, there were no differences between the treatment groups in risk of relapse according to either survival method: Kaplan–Meier, $\chi^2(1, N = 53) = 0.47$, $p > .10$; Andersen–Gill, $\chi^2(1) = 0.85$, $p > .10$. Forty-six percent of patients in FFT and 52% of patients in individual treatment experienced at least one relapse during the active treatment year, $\chi^2(1, N = 53) = 0.16$, $p > .10$; $h = 0.11$. However, patients who had participated in FFT were much less likely to relapse in the posttreatment follow-up period than were patients in individual treatment: Kaplan–Meier, $\chi^2(1, N = 39) = 4.05$, $p < .05$; Andersen–Gill, $\chi^2(1) = 5.13$, $p < .05$. During the posttreatment follow-up period, 28% of patients in FFT experienced at least one relapse compared with 60% of patients in individual treatment, $\chi^2(1, N = 39) = 4.66$, $p < .05$; $h = 0.66$.

Given the pretreatment group differences on premorbid adjustment scores and age at illness onset, separate analyses were conducted, controlling for each. First, we examined whether premorbid adjustment could account for the relationships observed between treatment group and time to relapse. Premorbid adjust-

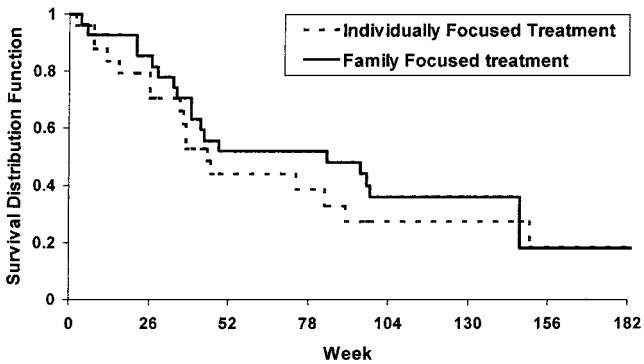

Figure 1. Cumulative probability of symptom relapse over 1-year treatment period and follow-up interval.

ment, treatment group, and their interaction term were entered into Cox proportional hazards regression models for each of the two study periods (the 1-year active treatment year and the posttreatment follow-up interval). The regression model for the year of study treatment revealed a significant interaction of treatment group and premorbid adjustment in predicting relapse, $\chi^2(1, N = 51) = 4.73$, $p < .05$. To further examine this interaction, subjects were placed into high and low premorbid groups with a median split on the UCLA Social Attainment Scale, and separate survival models were tested for both premorbid groups (good vs. poor premorbid adjustment). Whereas patients with good premorbid adjustment were equally likely to relapse during the first year whether in family or individual treatment, $\chi^2(1, N = 31) = 1.68$, $p > .10$, being in family treatment decreased the odds of relapse threefold among poorer premorbid patients, in comparison with the individual treatment, $\chi^2(1, N = 20) = 3.56$, $p = .06$. The gender of the patient was not associated with relapse, $\chi^2(1, N = 53) = 0.20$, $p > .10$, nor did its inclusion in the model improve prediction of relapse.

During the posttreatment follow-up period, there was no interaction between treatment group and premorbid adjustment and no significant effect of premorbid adjustment on relapse risk. However, inclusion of premorbid adjustment, $\chi^2(1, N = 39) = 0.80$, $p > .10$, in the regression model reduced the predictive significance of treatment group, $\chi^2(1, N = 39) = 2.46$, $p < .12$, during the posttreatment interval.

Second, in parallel analyses we examined whether age of illness onset could account for the relationships observed between treatment group and time to relapse. Age of illness onset was not associated with relapse risk during either the 1-year active treatment period or the posttreatment follow-up interval, and its inclusion in multiple regression models did not reduce the predictive significance of treatment group.

Rehospitalization

The cumulative probability of rehospitalization for the two treatment groups during the entire study period (active treatment and follow-up) is depicted in Figure 2. Kaplan–Meier survival analysis revealed that individuals who participated in FFT were less likely to be hospitalized over the entire study interval than were individuals who participated in individual treatment, $\chi^2(1, N = 53) = 3.87$, $p < .05$. When multiple rehospitalizations were considered in an Andersen–Gill survival model, these treatment group differences were equally evident, $\chi^2(1) = 4.21$, $p < .05$. Next, Kaplan–Meier survival analyses separately examined rehospitalizations for the year-long treatment period and the posttreatment follow-up. No effect of treatment group was observed during the 1-year active treatment period, $\chi^2(1, N = 53) = 1.38$, $p > .10$. Twenty-nine percent of patients in FFT and 40% of patients in individual treatment were rehospitalized during the active treatment year, $\chi^2(1, N = 53) = 0.76$, $p > .10$; $h = .24$. Nonetheless, those patients who received FFT had a much lower risk of rehospitalization during the posttreatment follow-up period than those patients who received individual treatment, paralleling the findings for relapse, $\chi^2(1, N = 39) = 10.32$, $p = .01$. Indeed, during the posttreatment follow-up period, 12% of patients in FFT were rehospitalized compared with 60% of patients in individual treatment, $\chi^2(1, N = 39) = 11.52$, $p < .01$; $h = 1.06$.

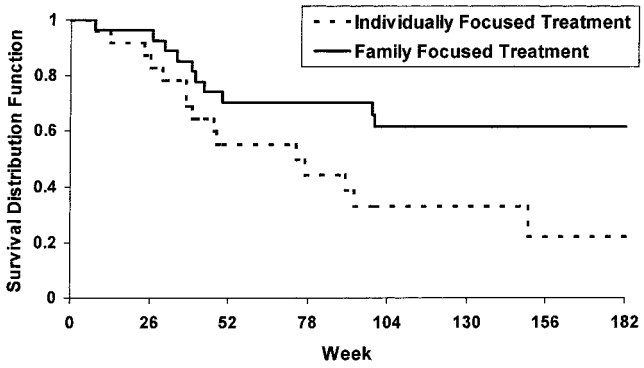

Figure 2. Cumulative probability of hospitilization over 1-year treatment period and follow-up interval.

Separate Cox proportional hazards regression models were conducted to control for premorbid adjustment and age of illness onset. Neither premorbid adjustment, treatment group, nor their interaction predicted the likelihood of rehospitalization during the treatment year. However, both premorbid adjustment, $\chi^2(1, N = 39) = 4.65$, $p < .03$, and treatment group, $\chi^2(1, N = 39) = 4.90$, $p < .03$, were separate and statistically reliable predictors of rehospitalization during the posttreatment follow-up interval. As expected, good premorbid patients were less likely to be rehospitalized during the posttreatment interval than poor premorbid patients.

As in our analyses of relapse, age of illness onset was not associated with rehospitalization for either study interval. Furthermore, its inclusion in regression models did not attenuate the effects of treatment group on rehospitalization.

The above findings suggested that the impact of the family intervention was stronger for rehospitalization than for symptomatic relapse. To further understand the relationship between treatment, relapse, and rehospitalization, we divided the participants into those who had not been rehospitalized when they relapsed versus those who were rehospitalized at least once during a relapse, when considering the entire follow-up period (study year and follow-up together). A chi-square test revealed that patients in the family treatment were significantly less likely to be hospitalized at the time of relapse than patients in the individual treatment (55% vs. 88%, respectively), $\chi^2(1, N = 35) = 4.57$, $p < .03$; $h = .76$. These findings suggest that the family intervention had its greatest impact on assisting patients and their families to avoid the need for rehospitalization during a period of symptomatic deterioration.

Medication Compliance

The findings indicate that patients who participated in family treatment had a lower risk of rehospitalization and relapse than those in individual patient treatment during the posttreatment follow-up interval, but not during the treatment itself. Could these results be accounted for by the patients' utilization of mood-stabilizing medications, either their specific regimens or compliance with these regimens? As indicated earlier, medication regimens for the two groups were comparable at each individual assessment point (for all, $p > .10$; Table 1). We next examined the

7-point Likert-type physician's ratings on medication compliance across the treatment year using repeated measures analyses of variance (ANOVAs) and found no main effect for treatment group, $F(1, 49) = 0.98$, $p > .10$, no effect of time, $F(3, 117) = 0.76$, $p > .10$, and no Treatment Group × Time interaction, $F(3, 117) = 0.09$, $p > .10$. Means for the two treatment groups at each follow-up point are displayed in Table 3.

A Student's *t* test compared the treatment groups on medication compliance during the posttreatment follow-up interval (a single assessment) and found no differences, $t(34) = 0.25$, $p > .10$. On the whole, the participants were quite compliant with their medication, with at least 78% of the patients scoring within the compliant range at each assessment point.

Discussion

This study examined the efficacy of psychosocial treatment as an adjunct to standard pharmacological maintenance in preventing relapses of bipolar disorder. The findings indicate that an outpatient family-based treatment can lead to a reduced risk of relapse and rehospitalization, as compared with a comparably paced individual therapy program. Group differences were particularly apparent in the year following participation in the treatment program when 28% of those who had received family-based intervention relapsed, as opposed to 60% of those in individually based treatment. Results for rehospitalization during the posttreatment follow-up period were even more striking: Twelve percent of patients in family-based treatment were rehospitalized, compared with 60% in individually based treatment.

The findings add to the growing literature suggesting that psychoeducational treatment of the family plays an important role in the comprehensive outpatient management of bipolar disorder (Miklowitz & Craighead, 2001). Specifically, the findings are consistent with the Miklowitz et al. (2000) trial, which found that, over a 1-year active treatment and follow-up period, FFT and medication led to longer delays prior to relapse than a comparison group that received medication, two sessions of family education, and crisis support as needed.

Interestingly, in this study, the impact of FFT was strongest after completion of the treatment protocol but did not appear during the year of active intervention. The differential impact of the two treatment conditions in the first study year may have been diluted in several ways. First, unlike the study by Miklowitz et al. (2000), the FFT and the individual comparison treatments were matched on amount of therapist–patient contacts. Thus, a high level of intervention was available for both psychosocial treatment groups, including intensive medication management, frequent monitoring of emergent symptoms, family education, 24-hr staff availability to family members and patients, and thorough medical and psychosocial follow-up of missed appointments. Second, there were high rates of compliance to medication and psychotherapy in both treatment groups during the first study year. These rates of compliance are in contrast to the poor compliance often associated with bipolar disorder (Cochran, 1986). Although there was not a pharmacotherapy-only contrast group in this study, the finding of high compliance in both psychosocial treatment groups may suggest that a relatively intensive psychosocial intervention, either family- or individually based, may help assure consistency with drug regimens among bipolar patients. Alternatively, the study may have inadvertently sampled patients who were more medically compliant. In summary, a high intensity of psychosocial intervention and medication management may have led to comparable rates of relapse and rehospitalization in both psychosocial treatment groups during the 12-month active treatment phase.

Table 3
Physicians' Medication Compliance Ratings

	Family-focused treatment		Individual patient management	
Follow-up period	*M*	*SD*	*M*	*SD*
3 month	6.26	1.61	5.95	1.40
6 month	6.33	1.40	6.10	1.51
9 month	6.10	1.55	6.00	1.26
12 month	6.15	1.46	5.58	1.87
24 month	3.90	2.66	4.13	2.70

Note. Physicians' ratings of medication compliance did not differ across the two treatment groups ($p > .10$) at any of the evaluation points.

If treatment with FFT did not lead to better medical adherence among patients than individually focused patient treatment, then what might account for the better clinical status of FFT-treated patients over the 2-year course of the study? Possibly, the skills that patients and family members develop through participation in FFT, including a greater knowledge of bipolar disorder and effective communication and problem-solving skills, may be brought to bear in managing the illness. This possibility is supported by the finding that the impact of the family intervention was greatest after the year-long participation in the study, a point at which family members no longer had regular contact with the study's clinical team and had to rely on the tools they developed in family treatment, such as early symptom identification, appropriate use of mental health resources, and problem solving. Although the patients in individual treatment were taught skills for better illness management, family members were not brought into treatment as sources of support. For example, participants in the family treatment were encouraged to engage in anticipatory planning for future symptom recurrences, including developing a written contract regarding how a relapse could be handled. Bipolar patients may benefit from the assistance of a knowledgeable social system when their own coping strategies are compromised by their clinical state. The notion that family support leads to improved management of the disorder is underscored by the finding that, even in the face of symptomatic relapse, just over half of the patients in family treatment were rehospitalized, whereas almost 90% of patients in individual treatment were rehospitalized.

An unanticipated finding was that premorbid social adjustment—an established predictor of outcome in schizophrenic and other disorders (e.g., Houlihan, 1977)—interacted with treatment group in predicting patients' outcomes during the year of participation in the study-based treatment. During this period, poor premorbid patients were protected from relapse in the family treatment group but not in the individual therapy group. The gender of the patient did not moderate this interaction. In the 1-year period following the conclusion of the intervention, however, treatment group and premorbid adjustment were independent predictors of rehospitalization. Good premorbid patients had lower rates of rehospitalization following the study regardless of treat-

ment condition. In an early study of family crisis-oriented treatment for schizophrenia, Goldstein, Rodnick, Evans, May, and Steinberg (1978) found interactions between type of psychosocial treatment, premorbid adjustment, and gender. Premorbid adjustment was unrelated to relapse rates among females with schizophrenia. In contrast to the present findings, good premorbid males with schizophrenia had lower rates of relapse than poor premorbid males when treated with family therapy and phenothiazine medication.

Few studies have examined the relationship between premorbid adjustment and outcome in bipolar disorder. Glick, Clarkin, Haas, and Spencer (1993) examined prehospital functioning, a variable conceptually similar to premorbid adjustment, in evaluating the effects of a six-session family-based treatment for hospitalized individuals with schizophrenia and affective disorders. Among patients with affective disorders, positive benefits of family treatment were generally limited to female patients but did not vary with prehospital functioning. Results among patients with schizophrenia were somewhat different. At hospital discharge, those with good prehospital functioning appeared to benefit most from family treatment. However, results at 18 months after hospital discharge were similar to the present findings in that family treatment appeared to have its greatest impact on those with poor prehospital functioning. Taken as a whole, these studies underscore the complex relationships between type of treatment, diagnosis, and premorbid functioning. Future studies of the psychosocial treatment of bipolar disorder should examine premorbid psychosocial adjustment as a moderator of the impact of interventions during periods of active treatment and follow-up.

There are several limitations to the current study. First, the design did not allow for control over medication regimens. Standard drug treatments for bipolar disorder often consist of complex combinations of mood stabilizers, antipsychotics, and antidepressants. Medication regimens were clinically determined for individual patients, leading to a wide range of drug combinations and dosing patterns. Furthermore, it was not possible to keep physicians unaware of patients' psychosocial treatment assignments. This design precludes the analysis of potential interactions between specific types of medications or dosing protocols and psychosocial intervention strategies.

Second, although the study compared two treatments of equal duration (9 months) and number of sessions (21), there were nonetheless systematic differences between the treatments. Specifically, patients in the family-focused treatment had two therapists and attended 60-min sessions, whereas those in individually focused treatment had one therapist and attended 30-min sessions. Indeed, the individual treatment had more limited goals, and did not include a focus on the quality of family interactions or the coping styles of caregiving family members. Possibly, a more rigorous test of the difference between these two treatments would occur in a study in which both interventions were delivered by single providers and matched on the length of the treatment sessions.

Third, although therapists' adherence to the family-focused treatment was evaluated and revealed consistent fidelity to the treatment manual, similar measures of adherence were not obtained for therapists administering the individually focused treatment. The same therapists administered both treatments and received equally frequent supervision from the same, experienced clinicians. Nonetheless, it was not possible to determine whether the treatments were conducted with the same degree of skill or enthusiasm. Future randomized studies of bipolar disorder and psychosocial treatment need to document equivalence of therapists' fidelity and skill in delivering all study-based experimental treatments.

Fourth, this study was restricted to those patients who were willing to take mood stabilizers. The impact of the family intervention on unmedicated patients cannot be determined. Fifth, the findings are only applicable to patients who had families willing to be involved in treatment. Although this inclusionary criterion may have led to overselection of better prognosis bipolar patients with high levels of social support, rates of relapse over the first year (49%) were comparable to rates observed in other longitudinal or randomized treatment studies of bipolar patients (e.g., 37%, Gitlin et al., 1995; 44%, Miklowitz et al., 2000). Finally, this study included only patients whose index study episode was manic and, in all cases but one, hospitalized. Thus, the applicability of the findings to bipolar, depressed, mixed, rapid cycling, or bipolar II patients is less clear.

The current study lends strong support to the nascent literature on the role of psychosocial treatment generally, and family treatment specifically, in the comprehensive outpatient management of bipolar disorder. However, a number of challenges remain. First, the mechanisms underlying the impact of these treatments require further study. Prior studies have shown positive effects of individual or family psychosocial interventions on the stability of sleep–wake schedules and social routines (Frank et al., 1997), medication adherence (Cochran, 1984), and the efficiency of family communication and problem-solving behavior among patients with bipolar disorder (Simoneau, Miklowitz, Richards, Saleem, & George, 1999). Yet, we know little about how changes in these mediating variables alter a patient's vulnerability to episodes of mood disorder. Second, although a number of psychosocial interventions for bipolar disorder exist, it is not clear which subgroups of patients (e.g., depressed versus manic patients, medically noncompliant versus compliant, good versus poor premorbid) respond best to each and at which stages of their disorder.

Third, research needs to consider the barriers to implementing family or other psychosocial interventions for bipolar patients in community settings. Studies of patients with schizophrenia suggest the importance of including family interventions in comprehensive outpatient management protocols (Schooler et al., 1997). Family interventions, however, have rarely been implemented in community settings in the United States, due in part to the costs of such programs. The strongest finding of the current study was the notable group differences in rehospitalization rates, perhaps the most costly of treatment options. Possibly, the cost of a family-based treatment may be offset by the decreased rehospitalization risk conferred by the treatment over time. The cost-effectiveness of family-focused and other psychosocial treatments in a variety of community settings serving different patient populations—as is being done in the Systematic Treatment Enhancement Program for Bipolar Disorder (Sachs, in press)—should provide more comprehensive answers to these questions.

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Received June 19, 2001
Revision received May 6, 2002
Accepted May 7, 2002 ■

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