Methods

Diagnostic Evaluation

Interviewers were trained to identify well-demarcated periods of hypomania or mania, lasting at least 4 or 7 days respectively, that represented a change from other mood states and caused impairment in multiple contexts. Discrepancies between parents' and adolescents' reports were resolved by interviewing the pair to make a consensus rating and/or obtaining ancillary information. Diagnostic evaluators (minimum MA-level or psychiatric nurse) completed K-SADS training prior to the trial, with bimonthly training and reliability teleconferences during the trial.

Pharmacotherapy Protocol

Pharmacotherapy consisted of a 2-hour initial evaluation with the adolescent and parents, a 1-hour follow-up visit within the next 2 weeks, and then approximately 30-minute visits every 2-4 weeks until the child achieved a stable mood. The visits were then tapered to once every month for the remainder of the 2 year study, with increased frequency of visits when clinically indicated. Based on clinical response or patient/family preferences, an antidepressant (selective serotonin reuptake inhibitor or bupropion) could be added for short-term treatment of anxiety. Selective serotonin reuptake inhibitors and psychostimulants for ADHD were permitted only after adequate mood stabilization occurred.

Family-Focused Treatment: Structure and Content

In *psychoeducation* (sessions 1-7), clinicians assisted adolescents and parents to (1) develop a common understanding of the symptoms, etiology, and course of pediatric bipolar disorder and risk factors for recurrences; (2) maintain adherence with pharmacotherapy; and (3) develop strategies to avert relapses when prodromal symptoms appeared. In the second phase (sessions 8-15), *communication enhancement training*, participants rehearsed skills for active listening, offering positive feedback or constructive criticism, or requesting changes in each others' behavior. In *problem-solving*, (sessions 16-21), participants learned to identify, generate solutions to, and implement solutions to problems in day-to-day life.

The nature of family-focused treatment was adjusted to the patient's clinical condition upon entry. When patients entered in a depressed state, clinicians administering family-focused treatment focused on education about factors that aggravate low mood (i.e., low social support) and introduced behavioral activation (i.e., pleasant life events) exercises. When patients entered in a hypomanic or manic state, clinicians emphasized identifying early warning signs of recurrence, keeping regular sleep/wake cycles, and managing emotional conflicts in the home environment.

The clinician's manual for family-focused treatment can be downloaded from http://www.semel.ucla.edu/champ/downloads-clinicians).

Results

Time to Recovery and Recurrence Based on a 4-Week Recovery Criterion

The present study and recent naturalistic studies of pediatric bipolar disorder (e.g., 4) have used a $\geq$ 8-week criterion for recovery, whereas earlier studies (including

our prior randomized trial with adolescents, 11) used a $\geq$ 4-week criterion. In our prior 2-year trial, 91.4% (53/58) of the participants met the $\geq$ 4 week recovery designation over an average of 19.8 weeks (SE = 3.3). In the present study, using the 4-week definition resulted in 91.0% (112 of 123) of the participants meeting recovery criteria in an average of 23.3 weeks (SE = 2.2).

Using the 4-week recovery criterion did not alter the results of the survival analyses comparing the treatment groups. In family-focused treatment, 49 of 57 (86.0%) participants recovered from the index episode in a median of 14 weeks (95% CI, 11-22); in enhanced care, 63 of 66 (95.5%) recovered in a median of 17 weeks (95% CI, 12-21) with no group differences (p = .89). Of the 112 who had a $\geq$ 4-week recovery, 72 had a recurrence over 2 years (Kaplan-Meier estimate of probability of recurrence, 67.3%). Of 49 participants in family-focused treatment who recovered, 35 (71.4%) had a recurrence (median 23 weeks, 95% CI, 19-51). Of 63 in enhanced care who recovered, 37 (58.7%) had a recurrence (median 21 weeks, 95% CI not calc.), a nonsignificant group difference (p = .69).

Site Differences

There were differences between the three sites in the study population. The Colorado sample was of higher socioeconomic status (overall test for site difference, $F[2,142]=23.87$, $p<.0001$). The Pittsburgh site had a higher proportion of bipolar II patients (65.9%) compared to Colorado (50%) or Cincinnati (25.5%) (overall $\chi^2[2]= 15.21$, $p<.0005$). Patients at the Colorado site participated in the study for 101.3$\pm$16.7 weeks, whereas patients at Pittsburgh participated for 78.5$\pm$35.8 weeks, and at Cincinnati, 62.1$\pm$ 36.4 weeks ($F[2,120]=18.68$, $p<0.0001$).

There were also differences between the sites in the number of therapy sessions ($F(1,141)=8.33$, $p < .005$). For the family-focused treatment condition, patients at Colorado (n = 26) received 19.0±9.4 sessions and patients at Pittsburgh (n = 23) received 15.1±14.8 sessions, whereas patients at Cincinnati (n = 23) received 7.9±7.9 sessions. For enhanced care , patients at Colorado (n=28) received 4.86± 4.2 sessions; at Pittsburgh (n=21), 4.1± 1.9 sessions; and at Cincinnati (n = 24), 3.1± 1.8 sessions. Post-hoc comparisons ($p < .05$) indicated that fewer family-focused treatment sessions were delivered at Cincinnati than at Colorado, although the number of enhanced care sessions was comparable.

Patients at Cincinnati had less time to any mood recurrence than patients at Colorado or Pittsburgh ($\chi^2[1]= 4.27$, $p=0.04$). However, computing the survival models without data from the Cincinnati site did not reveal a significant difference between the family-focused treatment and enhanced care conditions on time to recovery or recurrence.