Long-term Effectiveness and Cost of a Systematic Care Program for Bipolar Disorder

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Context: Despite the availability of efficacious treatments, the long-term course of bipolar disorder is often unfavorable.

Objective: To test the effectiveness of a multicomponent intervention program to improve the quality of care and long-term outcomes for persons with bipolar disorder.

Design: Randomized controlled trial with allocation concealment and blinded outcome assessment.

Setting: Mental health clinics of a group-model prepaid health plan.

Patients: Of 785 patients in treatment for bipolar disorder who were invited to participate, 509 attended an evaluation appointment, 450 were found eligible to participate, and 441 enrolled in the trial.

Interventions: Participants were randomly assigned to a multicomponent intervention program or to continued care as usual. Three nurse care managers provided a 2-year systematic intervention program, including the following: a structured group psychoeducational program, monthly telephone monitoring of mood symptoms and medication adherence, feedback to treating mental health providers, facilitation of appropriate follow-up care, and as-needed outreach and crisis intervention.

Main Outcome Measures: In-person blinded research interviews every 3 months assessed mood symptoms using the Longitudinal Interval Follow-up Examination. Health plan administrative records were used to assess the use and cost of mental health services.

Results: Intent-to-treat analyses demonstrated that the intervention significantly reduced the mean level of mania symptoms (z = 2.09, P = .04) and the time with significant mania symptoms (19.2 vs 24.7 weeks; F₁ = 6.0, P = .01). There was no significant intervention effect on mean level of depressive symptoms (z = 0.19, P = .85) or time with significant depressive symptoms (47.6 vs 50.7 weeks; F₁ = 0.56, P = .45). Benefits of the intervention were found only in a subgroup of 343 persons with clinically significant mood symptoms at the baseline assessment. The incremental cost (adjusted) of the intervention was $1251 (95% confidence interval, $55-$2446), including approximately $800 for the intervention program services and an approximate $500 increase in the costs of other mental health services.

Conclusions: Population-based systematic care programs can significantly reduce the frequency and severity of mania in bipolar disorder, and cost increases are modest considering the clinical gains. The incorporation of more specific cognitive and behavioral content or more effective medication regimens may be necessary to significantly reduce the symptoms of depression.

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Effective long-term treatment of bipolar disorder remains a difficult challenge for patients and clinicians. Despite the availability of effective pharmacotherapies,1-3 most persons with bipolar disorder experience frequent mood episodes,4 significant residual symptoms,5 and substantial disability.6,7 Accumulating evidence supports the efficacy of structured psychotherapy for bipolar disorder,8-10 but such treatments are rarely available outside of academic settings. Outcomes in everyday practice fall short of those seen in controlled clinical trials.10-12

Gaps in the treatment of bipolar disorder are similar to those in the treatment of other chronic medical conditions.13 Adherence to mood stabilizer treatment is often poor,12,13-16 and interruptions in treatment are the norm.15,17 Follow-up care is typically inconsistent.15

Systematic disease management programs have proved effective in the care of unipolar depression18,19 and other chronic conditions. Founded on the models for
chronic illness described by Wagner and Von Korff and their colleagues, these programs attempt to close the gaps between treatment efficacy and actual effectiveness. These population-based care programs typically include information systems to support population-based care, reorganization of practice to promote active follow-up, use of expert systems to apply evidence to practice, and support for patients’ self-management.

We report herein the results of a 2-year effectiveness trial evaluating a multicomponent care program for bipolar disorder. The interim results at 12 months, reported previously, indicated a significant effect on the severity of mania and suggested an increasing effect on the depressive symptoms over time. Data from the full 24-month study period are used herein to evaluate the effectiveness among a population-based sample of patients with bipolar disorder, including acceptability and uptake, effects on mood symptoms, effects on the use of conventional mental health services, and incremental cost compared with care as usual.

The study methods are described in detail in earlier publications. They are summarized briefly herein.

STUDY SAMPLE AND RECRUITMENT

Participants were identified in 1999-2000 using computerized visit and hospital discharge records at a group-model behavioral health clinic of a managed care organization in Washington State (Group Health Cooperative [GHC]). General medical and specialty mental health care is provided on a prepaid (capitated) basis. Specialty mental health staffing levels are similar to those at other group-model managed care organizations. The treated prevalence of bipolar disorder among the GHC population is approximately 0.4%. We systematically sampled health plan members 18 years and older having any diagnosis of bipolar spectrum disorder (bipolar disorder type I or type II, schizoaffective disorder, or cyclothymia) during the prior 12 months.

INITIAL BASELINE ASSESSMENT

Potentially eligible members were invited (by letter, followed up with a telephone call) to an in-person baseline assessment. Relevant modules of the Structured Clinical Interview for DSM-IV (SCID) (current and lifetime depression, current and lifetime mania or hypomania, alcohol abuse or dependence, drug abuse or dependence, and psychosis screening) were used to confirm a diagnosis of bipolar disorder type I or II. If the diagnosis could not be confirmed using the SCID, one of us (G.S.) consulted with the treating psychiatrist and reviewed the medical records to identify mood episodes undetected by the structured interview. All patients with confirmed diagnoses were invited to participate. The only exclusion criterion was cognitive impairment severe enough to preclude informed consent (as assessed by the treating physician). Medical or psychiatric comorbidity was not a reason for exclusion.

TREATMENT ASSIGNMENT

During the informed consent process, each participant was advised that he or she might be offered additional treatment services but that willingness to accept any specific treatment was not a condition for enrollment. Using a concealed table of computer-generated random numbers (without blocking or stratification), eligible and consenting participants were randomly assigned to continued usual care or to usual care plus a multicomponent intervention program.

USUAL CARE COMPARISON GROUP

Participants assigned to usual care received no additional services, but no services that are normally available (inside or outside of the GHC) were withheld. Usual care participants were advised to continue treatment with their current GHC mental health providers, but there was no additional study monitoring of follow-up visits or medication adherence. Treatment could include medication management visits, individual psychotherapy, or group psychotherapy, but no group program specifically for persons with bipolar disorder was available in usual care. No formal case management program was available. Although all participants had made at least 1 visit within the past 12 months (a requirement for eligibility), the level of engagement in or adherence to treatment varied widely.

INTERVENTION GROUP

Intervention Components

A multicomponent intervention was provided by 3 nurse care managers working in collaboration with the participants’ usual mental health providers. The 24-month program included the following 5 elements that were adapted from systematic care programs for unipolar depression or for bipolar disorder:

Assessment and Care Planning

First, the nurse care manager reviewed each patient’s treatment history and developed a collaborative treatment plan, including current medications, expected frequency of follow-up visits, early warning signs of mood episodes, coping strategies for responding to warning signs, and identification of a care partner (family member or significant other).

Structured Monthly Telephone Calls

Second, the nurse care managers called each patient monthly to complete structured clinician ratings of current symptoms (depression, mania, and psychosis), current medication use, and medication adverse effects. Nurse care managers also used the Internal State Scale by Bauer and colleagues to support patients’ ongoing self-monitoring.

Feedback to the Mental Health Treatment Team

Third, following each telephone contact, nurse care managers sent structured feedback to the treating mental health providers regarding mood symptoms, current medication use, adverse effects, and algorithm-based suggestions about medication adjustments, laboratory testing, and follow-up visits. Communication with the treating psychiatrists and psychotherapists was by printed reports, voice messages, electronic messages, live telephone calls, or in-person conversations, determined by the clinical urgency. Participants’ usual psychiatrists and psychotherapists received no special training other than general information about the intervention program and the role of the nurse care manager. An individual physician could have patients in both treatment condition groups.
Structured Group Psychoeducational Program

Fourth, implementation of the Life Goals Program by Bauer and McBride included 5 weekly group sessions (phase 1), followed by twice-monthly sessions for the duration of the intervention (phase 2), for a total of up to 48 sessions. Phase 1 included education on the nature of bipolar illness, triggers, early symptoms, and self-management strategies. Phase 2 used a structured problem-solving format to focus on accomplishment of specific life goals. Participants created and updated personalized self-management plans describing triggers, warning signs, and coping strategies.

As-Needed Support, Education, and Care Coordination

Fifth, as clinically necessary, nurse care managers made additional telephone contacts to provide general support, encourage group participation, and facilitate in-person follow-up care. As appropriate, nurse care managers also provided education regarding medication adverse effects, crisis intervention, coordination with family members or significant others, and assistance with barriers to treatment.

Intervention Delivery

Care managers were registered nurses with at least 5 years of clinical psychiatric experience. Case loads averaged 95 patients per full-time equivalent. The training for the telephone monitoring program and group program is described elsewhere and included didactic instruction, demonstration or role playing, training in the techniques of motivational interviewing, observation of group sessions, and leadership of group sessions under supervision. Nurse care managers received 60 minutes of weekly supervision from one of us (G.E.S. or E.J.L.).

Telephone monitoring and care management were supported by a Web-based computer application integrating contact tracking, structured assessment, and standardized feedback reports to providers. Provider reports included graphic displays of mood symptoms over time, patient-reported medication use, ratings of medication adverse effects, and algorithm-based recommendations for medication adjustment. For example, a scenario of manic symptoms in a patient taking lithium with a current blood level of 0.3 mEq/L and no significant adverse effects would lead to a computer-generated recommendation to consider increasing the dosage of lithium. A similar scenario with no recorded lithium level in the past 6 months would lead to a recommendation for blood level testing. A combination of persistent manic symptoms, low lithium level, and moderate or severe adverse effects would lead to a recommendation to consider switching to or augmentation with a different mood stabilizer. The complete algorithm considered approximately 7000 clinical scenarios defined by symptom pattern, current medication dosage, blood levels (where applicable), and adverse effects. Additional details are available from the author. Each provider report included advice to consider algorithm-generated recommendations in light of each patient’s individual treatment history.

BLINDED OUTCOME ASSESSMENTS

In-person follow-up assessments were conducted every 3 months during the 2-year study period. Assessments included relevant modules of the SCID (current depression, current mania or hypomania, alcohol abuse or dependence, and drug abuse or dependence) and a weekly timeline follow-back rating of depressive and manic or hypomanic symptoms using the Longitudinal Interval Follow-up Evaluation. This assessment yielded separate ratings of mania and depression severity for each week of follow-up using the 6-point Psychiatric Status Rating (PSR) scale. Ratings of 1 or 2 on this scale represent remission or minimal symptoms, ratings of 3 or 4 represent clinically significant subthreshold symptoms, a rating of 5 represents a current episode of hypomania or moderate major depression, and a rating of 6 represents a current episode of mania or severe depression. Interviewers were mental health clinicians with at least 1 year of clinical experience in the assessment of mood disorders. Details of the interviewer training have been described previously. To maintain interviewer blinding, participants were repeatedly advised not to reveal their group assignment or details of treatment. A substudy using random telephone reappraisals at varying times during the recall period supported the validity of 3-month mood recall using the Longitudinal Interval Follow-up Evaluation method.

PROTECTION OF HUMAN SUBJECTS

All study procedures were approved by institutional review boards at the GHC and at the University of California, Los Angeles. Participants provided written informed consent at the following 3 stages: before the baseline assessment, before enrollment in the randomized controlled trial, and (for those in the intervention group) before the initial intervention visit.

PHARMACY, RESOURCE USE, AND COST DATA

Computerized pharmacy and visit registration data were used to examine the mental health visits and psychotropic drug prescription fills and refills throughout the follow-up period. Refill data were used to calculate the total days’ supply of individual drugs and drug classes used. Health plan cost accounting data were used to calculate the cost of mental health and general medical services. The costs of intervention services (telephone monitoring, group sessions, and supervision meetings) were calculated based on actual personnel time (including fringe benefits and overhead costs) for nurse care managers and for clinical supervisors.

DATA ANALYSIS

The primary analyses of clinical outcomes compared the intervention and usual care participants’ mean PSR scores across the 104-week follow-up period using a repeated-measures linear model with relevant baseline characteristics (age, sex, psychotic symptoms, substance abuse, and recent psychiatric hospitalization) included as the covariates. Each follow-up measure was included as the independent variable, while baseline mania and depression ratings were included as covariates. All analyses were based on original treatment assignment regardless of the treatment actually received. Each participant could contribute up to 104 weeks of follow-up data, but the analyses included all participants contributing any follow-up data. Test statistics were calculated using generalized estimating equations as implemented by the SAS version 8 software package (SAS Institute, Cary, NC). The use of generalized estimating equations is a semiparametric estimation approach based on the specification of the mean and covariance, but not the full distribution, of modeled outcomes. All models were estimated using an independence working correlation structure, with variance based on the empirical covariance matrix. Our primary hypothesis was that the intervention participants would have lower mean mania and depression scores across the full follow-up period (ie, the main effect of treatment assignment) after accounting for baseline severity. Secondary analyses compared the number of weeks in the follow-up period during which par-
Study Sample

Of 785 patients initially contacted, 509 (64.8%) attended a baseline assessment. Nonparticipants did not differ significantly in age, sex, or likelihood of psychiatric hospitalization or psychiatric emergency department use in the past year. Of 450 patients found eligible, 441 (98.0%) enrolled in the trial. The baseline characteristics of the participants are compared in Table 1. At baseline, 98 participants (22.2%) were in a threshold mood episode (current major depression, hypomania, or mania), and the remaining 160 participants (36.3%) had subthreshold mood symptoms.

Of 441 patients randomized, 414 (93.9%) completed at least one blinded outcome assessment and were included in the analyses of clinical outcomes. Three hundred eighty-one patients (86.4%) contributed at least 12 months of follow-up data, and 335 patients (76.0%) contributed the full 24 months of follow-up data. Compared with the patients contributing 24 months of follow-up data, the patients with fewer than 24 months of data were significantly younger (41 vs 45 years, P = .01) but did not differ significantly in baseline mania PSR scores (3.4 vs 3.6, P = .27) or in baseline depression PSR scores (3.8 vs 3.5, P = .48). Of 441 patients randomized, 331 (75.1%) remained enrolled in the GHC health plan for the full 24 months and were included in the resource use and cost analyses. Compared with the patients who remained enrolled in the study, the patients disenrolling were younger (39 vs 46 years, P < .001), had higher baseline mania PSR scores (3.4 vs 2.6, P < .001), and had higher baseline depression PSR scores (3.8 vs 3.4, P < .02). Figure 1 shows the progress of participants through the trial.

Participation in the Intervention Program

Of 212 participants assigned to the intervention group, 203 (95.8%) completed at least one telephone monitoring contact, and 180 (84.9%) completed 12 or more telephone contacts. One hundred thirty-seven (64.6%) attended at least 1 group session, 125 (59.0%) continued group participation for 12 months or longer. Neither participation in telephone monitoring nor participation in the group program was significantly associated with the severity of mood symptoms at baseline.

Effects on Clinical Outcomes

As shown in Figure 2, the mean mania severity ratings were lower in the intervention group throughout the 24-month follow-up period. In a repeated-measures linear

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Table 1. Baseline Characteristics Among 441 Patients in the Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention Group (n = 212)</th>
<th>Usual Care Group (n = 229)</th>
<th>Test Statistic</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>44.1 ± 13.4</td>
<td>44.3 ± 12.9</td>
<td>t = 0.10</td>
<td>.92</td>
</tr>
<tr>
<td>Female sex</td>
<td>144 (67.9)</td>
<td>157 (68.6)</td>
<td>χ² = 0.02</td>
<td>.89</td>
</tr>
<tr>
<td>White race</td>
<td>184 (86.8)</td>
<td>206 (90.0)</td>
<td>χ² = 1.07</td>
<td>.30</td>
</tr>
<tr>
<td>Currently employed</td>
<td>138 (65.1)</td>
<td>142 (62.0)</td>
<td>χ² = 0.45</td>
<td>.50</td>
</tr>
<tr>
<td>Type I bipolar disorder</td>
<td>165 (77.8)</td>
<td>171 (74.7)</td>
<td>χ² = 0.60</td>
<td>.44</td>
</tr>
<tr>
<td>Psychiatric Status Rating scale baseline score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression score</td>
<td>3.44 ± 1.48</td>
<td>3.54 ± 1.45</td>
<td>t = 0.73</td>
<td>.46</td>
</tr>
<tr>
<td>≥3</td>
<td>158 (74.5)</td>
<td>167 (72.9)</td>
<td>χ² = 0.15</td>
<td>.70</td>
</tr>
<tr>
<td>≥5</td>
<td>71 (33.5)</td>
<td>83 (36.2)</td>
<td>χ² = 0.37</td>
<td>.54</td>
</tr>
<tr>
<td>Mania score</td>
<td>2.77 ± 1.72</td>
<td>2.78 ± 1.60</td>
<td>t = 0.02</td>
<td>.98</td>
</tr>
<tr>
<td>≥3</td>
<td>101 (47.6)</td>
<td>116 (50.7)</td>
<td>χ² = 0.40</td>
<td>.53</td>
</tr>
<tr>
<td>≥5</td>
<td>33 (15.6)</td>
<td>35 (15.3)</td>
<td>χ² = 0.01</td>
<td>.94</td>
</tr>
<tr>
<td>Current psychotic symptoms†</td>
<td>33 (15.6)</td>
<td>30 (13.1)</td>
<td>χ² = 0.55</td>
<td>.46</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>8 (3.8)</td>
<td>7 (3.1)</td>
<td>χ² = 0.17</td>
<td>.68</td>
</tr>
<tr>
<td>Lifetime</td>
<td>81 (38.2)</td>
<td>96 (41.9)</td>
<td>χ² = 0.63</td>
<td>.43</td>
</tr>
<tr>
<td>Drug abuse or dependence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>9 (4.2)</td>
<td>7 (3.1)</td>
<td>χ² = 0.45</td>
<td>.50</td>
</tr>
<tr>
<td>Lifetime</td>
<td>51 (24.1)</td>
<td>59 (25.8)</td>
<td>χ² = 0.17</td>
<td>.68</td>
</tr>
<tr>
<td>Psychiatric hospitalization in the past year</td>
<td>17 (8.0)</td>
<td>28 (12.2)</td>
<td>χ² = 2.13</td>
<td>.14</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD or as number (percentage) unless otherwise indicated.
†Rating of “definite” for any item of the Structured Clinical Interview for DSM-IV or psychiatric screen module.
model adjusting for baseline mood symptoms, baseline psychotic symptoms, and baseline substance use comorbidity, the mean mania PSR scores were significantly lower in the intervention group ($z=2.09$, $P=.04$).

As shown in Figure 3, the mean depression severity ratings seemed to be higher in the intervention group in the first quarter and slightly lower from the third quarter onward. Averaged across the full follow-up period, there was no significant difference in the depression ratings between the 2 treatment groups ($z=0.19$, $P=.85$). Post hoc analyses limited to the second year of follow-up also demonstrated no difference in the mean depression ratings ($z=0.64$, $P=.52$).

Figure 4 shows the distribution of weekly mood ratings classified as remissions (PSR score, 1-2), clinically significant subthreshold symptoms (PSR score, 3-4), and full mood episodes (PSR score, 5-6). Across both treatment groups, the mania ratings were in the remission range for approximately 75% of the follow-up period. A secondary analysis (defined a priori) examined the number of weeks during which patients had mania PSR scores of 3 or higher. The mean±SD number of weeks during which patients had clinically significant mania symptoms was 19.2±20.2 in the intervention group, compared with 24.7±24.3 in the usual care group. In a linear model adjusting for the covariates of age, sex, and likelihood of psychiatric hospitalization or psychiatric emergency department use in the past year, the number of weeks during which patients had significant mania symptoms was significantly lower in the intervention group ($F_{1}=6.0$, $P=.01$). Across both groups, the depression ratings were in the remission range for approximately 45% of the follow-up period. The mean±SD number of weeks during which patients had depression PSR scores of 3 or higher was 47.6±29.7 in the intervention group, compared with 50.7±31.9 in usual care group ($F_{1}=0.56$, $P=.45$). Data from the SCID interviews at each follow-up assessment showed a similar pattern. The overall probability of manic episodes across the 8 quarterly assessments was lower in the intervention group ($\chi^{2}=6.4$, $P=.04$), but the probability of depressive episodes did not differ significantly between the 2 groups ($\chi^{2}=2.6$, $P=.26$).

An additional secondary analysis (defined a priori) stratified the participants into a group of 98 patients with...
mania and depression PSR scores lower than 3 (in remission) at baseline and a group of 343 patients with mania and depression PSR scores of 3 or higher (not in remission) at baseline. The results are shown in Figure 5, with the mean PSR scores collapsed across all time points. For the group in remission at baseline, repeated-measures models adjusting for the covariates of age, sex, and likelihood of psychiatric hospitalization or psychiatric emergency department use in the past year found no effect of the intervention program on the follow-up mania scores ($z=0.23, P=.81$) or depression scores ($z=1.26, P=.21$). For patients with substantial symptoms at baseline, the intervention program had a significant effect on the mean mania scores ($z=2.27, P=.02$) but not on the mean depression scores ($z=0.64, P=.52$).

Additional post hoc analyses examined the intervention effects according to the specific bipolar diagnosis (type I vs type II) and the presence or absence of substance use disorder at baseline. We found no indication of different intervention effects between these subgroups (details are available from the author).

**EFFECTS ON RESOURCE USE AND COST**

The effects of the intervention on the resource use and cost of health services are given in Table 2. The patients in the intervention group had more medication management visits and consumed more atypical antipsychotic medications than the usual care group, but neither of these differences was statistically significant at the 5% level. The direct costs of the intervention program were approximately $500 during the first year and $300 during the second year. The total costs (unadjusted) of mental health treatment (including the intervention program costs) were $1302 higher in the intervention group. After adjustment for the baseline covariates of age, sex, and likelihood of psychiatric hospitalization or psychiatric emergency department use in the past year, the 2-year mental health treatment costs in the intervention group were $1251 (95% confidence interval, $55–$2446) higher than those in the usual care group.

**POTENTIAL MEDIATORS OF THE INTERVENTION EFFECT**

Because the number of medication management visits and the use of atypical antipsychotic medications were greater in the intervention group, these were examined as potential mediators of the effect of the intervention on the mania scores. Neither the number of medication management visits nor the use of atypical antipsychotic medications was significantly associated with lower mania ratings during the follow-up period.

**COMMENT**

A systematic management program proved to be feasible and generally acceptable among a population-based sample of outpatients treated for bipolar disorder. Almost all participants assigned to the intervention group engaged in the telephone care management program, and almost 60% completed the initial phase of the group program. These participation rates are notable given the nature of our sample. We attempted to enroll all patients with any treatment contact in the past year and did not require that participants agree to accept any particular treatment. Almost two thirds of the GHC members with bipolar disorder enrolled in the trial, and nonparticipants did not differ significantly from the patients who enrolled. These high rates of participation in the intervention program were achieved through vigorous and persistent outreach.

The complete follow-up data confirm the preliminary finding that this systematic care management program reduced the frequency and severity of manic symptoms. The mean mania ratings decreased in both treatment groups over time, but the mania ratings were lower in the intervention group throughout the 2-year follow-up period. The number of weeks during which patients had significant manic symptoms was approximately 25% lower in patients assigned to the intervention program.

Although we cannot determine the specific mechanism by which the intervention program reduced the symptoms of mania, we can observe how the program affected the use of conventional mental health services. During 12 months, the intervention group patients had more medication management visits and more frequently used atypical antipsychotic drugs, but these differences were not statistically significant in the 24-month analysis. Neither the number of medication management visits nor the use of atypical antipsychotic drugs was significantly associated with improved clinical outcomes, so neither can be considered an important mediator of the intervention effect. The treatment groups did not differ in the use of mood stabilizer medications or other outpatient services.

We did not observe significant effects of the intervention program on the frequency or severity of depression. Preliminary analyses suggested a trend toward increasing intervention effects on depression during the first 12 months. The complete data seemed to demonstrate lower depression ratings in the intervention group beginning with the third quarter of follow-up. However, this
difference did not approach statistical significance, even in a post hoc analysis limited to the second year of follow-up. This finding is disappointing given that depression accounts for most of the long-term morbidity among persons with bipolar disorder.41

There are 2 possible explanations for the discrepancy between the intervention effects on mania and the intervention effects on depression. First, the group psychoeducational program emphasized early recognition and early intervention for mood episodes. Such an approach might have a greater effect on preventing or shortening episodic mania than on relieving more chronic depression. Second, available pharmacotherapies are generally more successful for acute treatment of manic episodes than for acute treatment of depression.42 Consequently, our attempts to improve the quality of pharmacotherapy might be expected to have stronger effects on the symptoms of mania.

Several previous efficacy trials have evaluated psychoeducational and structured psychotherapies for bipolar disorder. Perry and colleagues43 found that a 7- to 12-session psychoeducational program that focused on early symptom recognition significantly reduced the risk of manic relapse. Colom et al44 found that a 21-session group psychoeducational program emphasizing early recognition and building self-management skills significantly reduced the risk of subsequent mania or depression. Lam and colleagues45 reported that a 14- to 20-session individual cognitive behavior therapy program significantly reduced the frequency of manic and depressive episodes. Miklowitz and coworkers46 found that a 21-session family-focused psychoeducational program significantly reduced the patients’ mood disorder symptoms and reduced the risk of relapse. In all cases, psychoeducation or structured psychotherapeutic interventions were added to ongoing pharmacotherapy. Interventions that are focused on self-monitoring and on early recognition of mood episodes43 may be sufficient to reduce the risk of manic episodes. Reducing the frequency and severity of depression may require more intensive interventions, including development of specific depression management skills.44,45

The incremental costs of the intervention program were modest compared with the overall costs of treatment for bipolar disorder. The direct costs of the intervention services were approximately $800 during 2 years, and the costs of other mental health treatments were approximately $500 higher for the intervention patients. The added cost (adjusted) of $1251 per year accounted for approximately one sixth of the mental health treatment costs for the intervention patients. Although there is no generally accepted metric to assess the cost-effectiveness of interventions for bipolar disorder, the incremental cost of $1251 can be balanced against a benefit of 5.5 additional weeks that are free of significant manic symptoms.

The costs of psychotropic medications accounted for approximately half of all mental health treatment costs. Among a 1995 sample from the Group Health Cooperative,47 prescriptions accounted for approximately 20% of mental health treatment expenditures. This change probably reflects the increasing use of anticonvulsant agents and atypical antipsychotic medications and a shift toward more expensive antidepressant drugs.

The benefits of the intervention program were limited to patients with significant mood symptoms at baseline. The subgroup in remission at the baseline assessment had overall mean mania and depression scores in the remission range throughout the follow-up period. This subgroup may include patients with less severe disorder and those whose illness is well controlled by usual care. Our results do not support the benefit of more intensive management programs among patients who fare well with usual care.

Both treatment groups showed significant improvement in mood symptoms over time. Although we did not select participants who were at treatment stages during

### Table 2. Treatment During 24 Months Among 331 Patients Who Remained Enrolled in the Group Health Cooperative*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intervention Group (n = 156)</th>
<th>Usual Care Group (n = 175)</th>
<th>Test Statistic†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient mental health visit, No.</td>
<td>14.0 ± 13.0</td>
<td>11.5 ± 9.0</td>
<td>z = 1.93</td>
<td>.05</td>
</tr>
<tr>
<td>Medication management</td>
<td>6.1 ± 10.6</td>
<td>6.7 ± 11.5</td>
<td>z = 0.8</td>
<td>.45</td>
</tr>
<tr>
<td>Individual psychotherapy</td>
<td>1.1 ± 3.8</td>
<td>1.4 ± 5.0</td>
<td>z = 0.11</td>
<td>.91</td>
</tr>
<tr>
<td>Psychiatric hospitalization, d</td>
<td>556 ± 279</td>
<td>522 ± 272</td>
<td>z = 0.54</td>
<td>.59</td>
</tr>
<tr>
<td>Mood stabilizer</td>
<td>379 ± 316</td>
<td>374 ± 310</td>
<td>z = 0.19</td>
<td>.85</td>
</tr>
<tr>
<td>Antidepressant§</td>
<td>163 ± 272</td>
<td>116 ± 232</td>
<td>z = 1.18</td>
<td>.23</td>
</tr>
<tr>
<td>Cost, $</td>
<td>2828 ± 2597</td>
<td>2651 ± 2456</td>
<td>t = 0.63</td>
<td>.53</td>
</tr>
<tr>
<td>Outpatient mental health visit</td>
<td>403 ± 1592</td>
<td>799 ± 3999</td>
<td>z = 0.96</td>
<td>.34</td>
</tr>
<tr>
<td>Psychiatric hospitalization</td>
<td>4008 ± 4057</td>
<td>3292 ± 3291</td>
<td>t = 1.77</td>
<td>.08</td>
</tr>
<tr>
<td>Psychotropic drug prescription</td>
<td>805 ± 239</td>
<td>0</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Intervention service</td>
<td>8046 ± 5974</td>
<td>6743 ± 6695</td>
<td>t = 1.86</td>
<td>.06</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD unless otherwise indicated. Contacts with nurse care managers were excluded.
†Statistics from the Mann-Whitney nonparametric test.
‡Includes lithium, divalproex sodium, carbamazepine, topiramate, lamotrigine, and gabapentin.
§Includes olanzapine, risperidone, quetiapine fumarate, ziprasidone hydrochloride, and clozapine.
||All values are rounded to whole dollars, so the rounded total does not equal the total of the rounded components.
which they manifested particularly severe symptoms (eg, after hospitalization), we required some treatment contact in the past year. The general trend to improvement may reflect the benefits of treatment and the tendency to seek treatment when symptoms are more severe. In addition, the therapeutic effects of 9 in-person interviews with research staff during 2 years may have influenced patient improvement.

The rates of treatment in the usual care group were higher than would be predicted from earlier research among patients in the Group Health Cooperative. The participants who were assigned to usual care made a mean of 15 individual visits to mental health providers during 2 years, and almost 60% made 12 or more visits. The usual care patients averaged at least 15 months of mood stabilizer use during the 24-month study period, and approximately 50% filled prescriptions for at least 18 months. These high rates of usual care treatment may reflect the process of selection into a randomized trial or the effects of increased attention associated with repeated contacts with the research staff. Even in a population-based study such as this one, the patients who are least likely to continue in treatment may also be those who are least likely to enroll in research.

There are some important limitations in the interpretation of our results. First, approximately 35% of patients invited to participate could not be reached or declined to attend the baseline assessment. How the acceptability or effectiveness of the intervention would generalize to non-participants is unknown. Second, the intervention program, especially the group component, was designed for delivery in mental health group practices, including community mental health centers and Veterans Affairs clinics. Implementation would be difficult in rural areas or in solo practices serving small numbers of patients. Third, a significant proportion of patients contributed only partial outcome data (24.0% with <24 months and 13.6% with <12 months of data). However, follow-up participation was not related to the severity of illness or to the treatment assignment. Fourth, despite the large sample size, the confidence limits for the cost estimates were wide, ranging from almost equal costs to a incremental cost for the intervention program as high as $2446. Fifth, participating physicians treated patients in both treatment groups, and experience with the intervention could have affected the treatment of the usual care patients. Although this crossover effect could obscure the results of the intervention (ie, conservative bias), previous studies of similar interventions to depression demonstrate no evidence of such an effect.

These findings build on a series of trials demonstrating the cost-effectiveness of systematic care programs for unipolar depression. The essential elements of those depression care programs included aggressive outreach to ensure appropriate follow-up care, systematic application of evidence-based guidelines, and psychoeducational or structured psychotherapy programs to support patient self-management. The present study extends earlier efforts to apply these principles to the management of bipolar disorder. The specific program tested herein proved to be acceptable to patients and significantly reduced the frequency and the severity of manic symptoms. Achieving similar improvements in the control of depressive symptoms may require a greater focus on the structured behavioral and cognitive interventions that have been shown to be effective in treating unipolar depression.

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REFERENCES


