Long-Term Mental Health Resource Utilization and Cost of Care Following Group Psychoeducation or Unstructured Group Support for Bipolar Disorders: A Cost-Benefit Analysis

Jan Scott, M.D., Ph.D., F.R.C.Psych.; Francesc Colom, Psy.D., M.Sc., Ph.D.; Ekaterina Popova, M.D.; Antonio Benabarre, M.D., Ph.D.; Nuria Cruz, M.D., Ph.D.; Marc Valenti, M.D.; José M. Goikolea, M.D.; Jose Sánchez-Moreno, Psy.D.; Miguel A. Asenjo, M.D., Ph.D.; and Eduard Vieta, M.D., Ph.D.

Objective: To explore the short- and long-term mental health resource utilization and cost of care in a sample of 120 individuals with bipolar disorders who participated in a randomized controlled efficacy trial of group psychoeducation versus unstructured group support.

Method: Prospective, independent monitoring of DSM-IV bipolar disorder type I or II patients aged 18 to 65 years was conducted during the intervention phase (6 months) and follow-up phase (5-year postintervention) of a randomized controlled trial reporting clinical outcomes and inpatient and outpatient mental health service utilization, with estimation of cost of treatment per patient. The study was conducted from October 1997 through October 2006.

Results: Compared with individuals with bipolar disorder receiving the control intervention, psychoeducated patients had twice as many planned outpatient appointments, but the estimated mean cost of emergency consultation utilization was significantly less. There were trends for psychoeducated patients to opt for self-funded psychotherapy after completing group psychoeducation and to utilize more medications. However, inpatient care accounted for 40% estimated total cost in the control group but only about 15% in the psychoeducation group.

Conclusions: This study demonstrates the importance of taking a long-term overview of the cost versus benefits of adjunctive psychological therapy in bipolar disorders. If viewed only in the short-term, the psychoeducation group used more mental health care resources without clear additional health gain. However, extended follow-up demonstrated a long-term advantage for psychoeducated individuals, such that, compared to an unstructured support group intervention, group psychoeducation is less costly and more effective.

J Clin Psychiatry 2009;70(3):378–386

Received April 30, 2008; accepted July 30, 2008. *From the Royal Victoria Infirmary, University of Newcastle upon Tyne, and Institute of Psychiatry, London, United Kingdom (Dr. Scott); the Bipolar Disorders Program, Institute of Neuroscience, Hospital Clinic, IDIBAPS, CIBERSAM, Barcelona (Drs. Colom, Popova, Benabarre, Cruz, Valenti, Goikolea, Sánchez-Moreno, and Vieta); and Department of Preventive Medicine and Public Health, Hospital Clinic, IDIBAPS, University of Barcelona (Dr. Asenjo), Catalonia, Spain.*

The authors thank the support of the Spanish Ministry of Health, Instituto de Salud Carlos III, CIBERSAM, and the Stanley Medical Research Institute. This work was also partly supported by grants from the Spanish Ministry of Health, Instituto de Salud Carlos III (98/700 and PI050206), Fundació Marató TV3 (028/97), and RETICS RD06/011 (REM-TAP Network). Dr. Popova's participation was partly funded by an unrestricted grant from Janssen-Cilag.

Financial disclosure appears at the end of the article.

Corresponding author and reprints: Eduard Vieta, M.D., Ph.D., Bipolar Disorders Program, Hospital Clinic of Barcelona, Villarroel 170, 08036 Barcelona, Spain (e-mail: EVIETA@clinic.ub.es).

The World Health Organization's "Global Burden of Disease" report[1] identified bipolar disorder as 1 of the 10 leading causes of disability worldwide. The overall economic burden of bipolar disorder in the United States is about $45 billion per year in 1991 dollars.[2] In the United Kingdom, it is about £207 million per year[3]; £199 million is direct health care costs, of which 35% (£70 million) is accounted for by hospitalization costs. Naturalistic and cohort studies of health care resource utilization suggest that the costs of health care for bipolar disorder subjects show a 4-fold increase compared to age- and gender-matched, non–bipolar disorder populations,[4] while a 4-group comparison by Simon and Unutzer[5] reported that health care costs for individuals with bipolar spectrum disorders significantly exceeded those for depression, general medical conditions, and diabetes. Furthermore, individuals with bipolar depression use significantly more resources than individuals with unipolar depression.[6] To reduce the cost burden and morbidity of bipolar disorder, new treatments should reduce symptoms and restore interepisode functioning as well as prevent relapse or recurrence.[7] The latter is particularly important,

FOR CLINICAL USE

- Group psychodeucation is a useful tool for preventing relapses in patients with bipolar disorders.
- In the long term (5 years), group psychoeducation is less costly and more effective than unstructured group support.
- Group psychoeducation decreases the treatment costs associated with bipolar disorders mainly by preventing hospitalizations.

as it is the most likely reason for psychiatric hospital admission, which is the most costly component of mental health care services.

Health economic analyses on new treatments or service modifications for bipolar disorder lag behind clinical outcome research; most of the available studies of the relative cost-effectiveness of different treatments focus on the short-term (3 months) or medium-term (12–18 months) cost-effectiveness of older medications compared to newer ones or they make direct comparisons between newer medications.[8,9] This is unfortunate, as medication usually accounts for about 20% of the direct health service treatment costs.[10] An exception to this trend is the study by Kashner et al.,[11] which, although it explored cost over only a 1-year period, provided a comprehensive estimate of all health care utilization and the benefits of participation in the Texas Medication Algorithm Project for individuals with bipolar disorder, unipolar disorder, and schizophrenic disorders.[12] They demonstrated that, for individuals with bipolar disorder, a disease management program was both less costly and achieved better symptomatic outcomes than usual care. However, the cost per symptom advantage declined over each 3-month time period. As bipolar disorder is a chronic disorder, it is valid to explore longer-term costs and benefits of medications and other service utilization in order to demonstrate reliable differences and also to explore benefits in terms of the cost of relapse avoidance.

The next level of intervention after medication guideline implementation involves either service-based approaches or adjunctive psychological therapies. Service-based interventions usually combine brief (6–10 sessions) group or individual psychoeducation with enhanced access to and response from service providers,[13] while the model of adjunctive psychological therapy usually offers ≥ 20 sessions of individual therapy (such as cognitive-behavior therapy [CBT] or interpersonal social rhythms therapy), family-focused therapy, or group psychoeducation. Overall, service-oriented approaches show significant effects on mania but only weak effects on bipolar depression while extended therapies are highly likely to impact on depression, with varying levels of impact on manic symptoms or relapses.[14] Two recent randomized controlled trials (RCTs) reported on the cost and/or cost effectiveness of these different types of intervention.[13,15,16] Lam and colleagues[15] explored the costs of relapse prevention in the national health service in the United Kingdom for 103 euthymic bipolar disorder patients who were randomly allocated to CBT plus usual treatment compared to usual treatment alone and were followed up for 30 months. In the United States, Simon and colleagues[13] reported on the additional costs of providing a systematic service-based intervention over 24 months for over 400 patients from a typical group-model prepaid mental health plan. Thus, the data available so far give some indication of the cost and benefits of individual therapy or a service-based initiative (which incorporated some group work), the former in a public health system, the later in a managed-care organization.

The economic analysis reported here fits usefully into the spectrum of data currently available. It explores mental health service resource utilization and direct costs of these services for 120 individuals recruited to an efficacy RCT of up to 21 sessions of either group psychoeducation or a control group therapy (nonspecific support) provided over 6 months. The study was based in Barcelona, Spain, where the health system has parallels with the Veterans Affairs (VA) system in the United States and is similar to that in the United Kingdom in terms of provision of core health services, but (apart from research therapy interventions) psychotherapy is usually regarded as an additional service that individuals elect to purchase. Thus, the experimental psychological intervention and the system of mental health care delivery are hybrid models of the therapies and systems explored in the previously published health economic analyses of RCTs. Furthermore, this study explored direct mental health care costs during the intervention phase (6 months) and then for an extended follow-up period of 5 years. This offers an important opportunity to explore the durability of any effects on costs and outcomes that may be achieved with adjunctive therapies.

METHOD

Study Design

The methodology of the RCT has been described in detail elsewhere.[17] Essentially, the clinical study com-

© COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC.

prised a parallel 2-group randomized, single-blind trial carried out in the Bipolar Disorders Program of the Hospital Clinic of Barcelona (Catalonia, Spain), whose research and ethics committee approved the study. There were 2 research phases: the intervention phase comprised 6 months of randomized treatment in which all patients received standard psychiatric care and pharmacologic treatments, and the experimental group received 21 sessions of group psychoeducation (each session was 1.5 hours' long, with 8–12 participants per group, and run by 2 psychologists), while the control group had similar, but unstructured, group meetings with the therapists. The follow-up phase comprised 5 years during which time patients continued to receive psychiatric care and treatment but without the research intervention.[18] The study was conducted from October 1997 through October 2006.

Subjects

One hundred twenty participants fulfilling DSM-IV criteria for bipolar disorder type I or II, aged 18 to 65 years, were recruited from patients enrolled at the Bipolar Disorders Program. Inclusion criteria were a lifetime diagnosis of bipolar disorder type I or II elicited by a trained psychiatrist, at least 6 consecutive months of euthymia prior to commencing the study, and written informed consent to participate. Exclusion criteria were DSM-IV Axis I comorbidity and evidence of organic brain damage, mental impairment (intelligence quotient < 70), or deafness. Also excluded were patients currently receiving any kind of psychotherapy or enrolled in any other pharmacologic trial.

Assessments

During the acute phase, all subjects were assessed monthly by study psychiatrists who were blind to treatment. During the follow-up phase, assessment of relapses, symptom fluctuations, and treatment was performed every 2 months. Plasma levels of mood stabilizers (and any other required associated laboratory studies) were completed at least every 6 months during the first 2 years of the study[17] and then at 3- to 6- month intervals for the rest of the follow-up phase. Computerized clinic data and registers of appointments were also used to explore the number and types of clinical appointments (planned or emergency) and the number and duration of hospitalizations. Psychiatric medication and treatment changes were recorded. As described in previous publications,[19] treatment adherence was assessed by the combination of a "medication compliance–focused interview" with the patient and with a first-degree relative or a partner as well as by plasma levels of mood stabilizers.

Main Outcome Measures

Individual and group outcomes. Three types of outcome were recorded in this study: number of individuals experiencing a relapse or hospitalization, group differences in the mean number of relapses and emergency visits, and group differences in number of days in episode and of days hospitalized.[17,18]

While relapse and admission rates were key outcome measures, Lam and colleagues[15] point out that simply analyzing cost compared with number of individuals experiencing such an event is not the most sensitive measure, as length of hospital stay or length of episode shows considerable interindividual variability. Also, over a 5-year follow-up period, the natural history of bipolar disorder indicates that, even with intensive treatment, relapse is the rule rather than the exception for most individuals.[14] For this reason, we focused more on group differences in mean number of days spent in relapse or hospitalized. The latter is relevant as use of inpatient services is a major contributor to direct health care cost in all health care systems.[10] However, it is usually the least frequent event, so we focused on hospital bed-days occupied rather than simply the mean number of admissions. A similar view was taken of emergency visits in which number of visits rather than simply number of individuals using the service can be regarded as a more sensitive measure of the frequency of crises in each group.

Resource utilization. We report use of outpatient, crisis, and inpatient services; number and type of medications prescribed; and use of group therapies in the intervention phase (when it was provided as part of the RCT) and then any reported elective use of individual therapy during the postintervention follow-up phase. Direct health care cost was derived using activity data and applying the appropriate unit cost to each consultation or service use recorded. Cost accounting data from the Hospital Clinic of Barcelona were used to estimate the cost for direct mental health care in Euros (€): estimated costs for 1 day in an acute psychiatric ward, an emergency consultation, and a planned outpatient appointment were €303, €200, and €129, respectively. Costs for group therapy were calculated based on actual personnel time involved in delivering the groups; the cost per group participant took into account actual group attendance rates (i.e., if there were dropouts in groups, the actual cost per attendee was higher for these groups than for others). Medication costs were calculated from the price per milligram and took into account both psychotropic medications prescribed and estimated adherence patterns.[10] Costs for medication over the course of the study also incorporate costs of laboratory tests associated with monitoring (e.g., costs of plasma level monitoring plus any other appropriate tests of renal functioning). The use of individual therapy during the follow-up phase is estimated, as in Spain patients usually seek therapy independent of directly provided state health care services. Although it was identified which individuals sought further therapy, the therapists were nearly all in private practice, so the exact number of

sessions was not recorded in all hospital records. Rather than exclude this service item, costs were calculated for an approximate number of sessions attended for individuals reported to have received therapy, and a range of costs were used for therapists who allowed for the different levels of fees charged. The final cost figures were adjusted appropriately for patient variables (age, gender, illness severity, and duration).

Data Analysis

The resource utilization data demonstrated skewed distributions due to a number of "high-cost outliers" for some services and a number of individuals never using certain other services (e.g., emergency visits or inpatient facilities), as such comparisons predominantly employed Mann-Whitney U tests, with χ^2 tests for categorical variables. The results of the cost analysis are reported as mean values with SDs and as mean differences between groups with 95% confidence intervals (CIs). Statistical significance was set at $p \leq .05$ with 2-tailed testing.

The unit cost estimates for each service were combined with resource utilization data to obtain a net cost per patient over the entire study period. As cost was nonnormally distributed, the comparison of differences was tested using nonparametric bootstrapping methods.[10] The analysis initially compared cost per item of service and then estimated differences in cost by group and took into account the potential confounding effects of missing data. During the intervention phase, 16 of 60 patients (26.7%) in the experimental and 7 (12%) in the control condition dropped out of the group interventions or met criteria for a relapse. However, these patients continued with psychiatrist visits and the follow-up phase procedures, so most resource utilization data were available. During the postintervention phase, 21 patients (17.5%) were lost to follow-up at different time points over the 5 years: 11 from the control and 10 from the psychoeducation group. Although this meant that resource utilization data were available on at least 82% of subjects in each group, there were missing items of data from these 21 subjects plus occasional, random, single missing items of data in 0% to 53% of the psychoeducated and 0% to 41% of the control subjects. To compensate for this, we repeated the base-case analysis twice, first using mean imputation (where missing cost values were replaced with predicted mean estimates for the relevant group and assessment period) and, secondly, after imputing missing assessments, using last value carried forward. As the results of these alternative approaches did not differ significantly from each other, we have reported only the findings from the analyses using mean imputation, as this allows the economic analyses to incorporate all the subjects whose clinical outcomes were known.

As well as overall cost per patient, we explored incremental cost-effectiveness by relating the differential cost for patients receiving either the control or the experimental intervention to the differential effectiveness of each treatment over the entire study period. To enable differences in types of outpatient service utilization to be fully explored, we excluded hospitalization costs from the preliminary cost analyses and estimated the outpatient cost for directly provided services and then for all services (i.e., including private psychotherapy).

Table 1. Baseline Characteristics of Sample and Key Outcomes of Patients With Bipolar Disorder Who Were Treated With Group Psychoeducation or Unstructured Group Support

Characteristic	Control Group (N = 60)	Psychoeducation Group (N = 60)
Male gender, N (%)	22 (36.7)	22 (36.7)
Age, mean (SD), y	34.26 (7.80)	34.03 (9.32)
Bipolar I subtype, N (%)	48 (80.0)	52 (86.7)
No. of previous episodes, mean (SD)	8.81 (6.60)	10.31 (10.55)
No. of previous hospitalizations, mean (SD)	2.01 (2.12)	1.81 (1.78)
Comorbid Axis II disorder, N (%)	22 (36.7)	15 (25.0)
Group therapy dropouts for any reason, N (%)	7 (11.7)[a]	16 (26.7)[a]
Poor overall level of medication adherence, N (%)	17 (28.3)	23 (38.3)
Hospitalized during intervention phase, N (%)	9 (15.0)	8 (13.3)
Relapsed or lost to follow-up during study period, N (%)	57 (95.0)	51 (85.0)
No. of relapses during study period, mean (SD)	8.37 (6.02)[b]	3.86 (4.18)[b]
≥ 1 Admission to hospital during study period, N (%)	24 (40.0)	17 (28.3)
≥ 1 Emergency department visit during study period, N (%)	25 (41.6)	21 (35.0)

[a] $\chi^2 = 4.36$, $p < .05$.
[b] Mann-Whitney U test: $Z = 2.01$, $p = .04$.

RESULTS

Clinical Outcomes

As reported previously,[17,18] the sample comprised 120 euthymic patients who primarily met criteria for bipolar I disorder (> 80%). Their mean age was about 34 years, two thirds were female, and they had about 9 previous bipolar disorder episodes. During the intervention phase, significantly more patients in the psychoeducation compared with the control group dropped out or experienced a relapse (16 vs. 7; $\chi^2 = 4.36$, $p < .05$), but the number of individuals hospitalized (psychoeducation, N = 8 vs. control, N = 9) was about the same. Over the course of the study, about 30% of subjects in each group were assessed as poorly adherent to medication.

As shown in Table 1, at 5 years' postintervention, 57 control subjects (95%) and 51 psychoeducation subjects (85%) had experienced at least 1 relapse. However, the mean number of relapses was significantly lower in the psychoeducation group compared with control group

Table 2. Resource Utilization by Group During Intervention Phase and Follow-Up Phase

	Resource Use, 6-Month Intervention Phase			Resource Use, 5-Year Follow-Up Phase		
Variable	Mean	SD	Range	Mean	SD	Range
Therapy sessions						
Control group	17.25	2.87	0–21	12.63[a]	4.91	0–42
Psychoeducation group	17.62	3.61	0–21	17.92[a]	7.23	0–54
Outpatient visits						
Control group	2.48	2.31	1–10	8.59[b]	8.99	0–41
Psychoeducation group	3.13	3.35	1–14	17.27[b]	17.02	1–68
Emergency visits						
Control group	0.59	1.24	0–4	2.89	4.90	0–21
Psychoeducation group	0.40	0.63	0–2	1.47	2.23	0–8
Number of psychotropic medications						
Control group	2.88	1.01	0–5	3.11	1.51	2–5
Psychoeducation group	3.07	0.96	2–5	3.30	1.18	2–5
Total days hospitalized						
Control group	1.9	6.62	0–12	25.62[c]	29.41	0–73
Psychoeducation group	1.3	8.35	0–7	8.17[c]	17.45	0–49

[a]Mann-Whitney U test: Z = 2.09, p = .04.
[b]Mann-Whitney U test: Z = 4.97, p = .01.
[c]Mann-Whitney U test: Z = 3.98, p = .02.

(3.86 vs. 8.37; Z = 2.01, p = .04), and there was a trend toward more control subjects than psychoeducated subjects being admitted to a hospital (24 vs. 17) or having emergency department visits (25 vs. 21). Overall, patients in the psychoeducation group had a mean of 0.24 (SD = 0.52) admissions compared with 0.59 (SD = 0.96) in the control group (Z = 2.01, p = .05). The mean number of inpatient days per hospitalized patient was significantly higher (Z = 2.37, p = .02) in the control group (N = 24; mean = 68.26, SD = 65.13) compared with the psychoeducation group (N = 17; mean = 31.66, SD = 16.40). The mean number of days in relapse was about 4 times less in the psychoeducation compared to the control group (153.73 vs. 586.45; Z = 7.31, p = .01), with significantly fewer days spent in depression (93.28 vs. 398.55) or in other types of episodes (manic, hypomanic, or mixed episodes, combined) (60.44 vs. 187.91). The mean between-group differences were estimated for days in any relapse (432.0; 95% CI = 317.67 to 546.33), depressive relapse (305.27; 95% CI = 230.73 to 379.81), other types of relapse (127.47; 95% CI = 58.63 to 196.31), and days in hospital (17.45; 95% CI = 8.71 to 26.91).

The effects of the interventions on the resource and medication use are given in Tables 2 through 4. As noted in Table 2, statistically significant between-group differences in use of mental health services were only apparent during the postintervention phase: patients in the psychoeducation group compared with the control group attended twice as many outpatient appointments (mean 17.27 vs. 8.59; Z = 4.97, p = .01) and were more likely to elect to attend further therapy sessions during the follow-up phase (17.92 vs. 12.63; Z = 2.09, p = .04). The mean number of days hospitalized was 3 times higher in the control group than in the psychoeducation group (25.62 vs. 8.17; Z = 3.98, p = .02). However, a small number of patients (7 in the control and 4 in the psychoeducation group) accounted for about 70% of the days hospitalized; so further analyses were undertaken. These demonstrated that only 1 individual in the control group (who had 12 separate admissions) was a true outlier, and the repeated analyses confirmed the robustness of the between-group differences.

The median number of psychotropic medications prescribed was 3 in both groups. As shown in Table 3, there were some differences in medication use at baseline, with fewer patients in the control group than in the psychoeducation group receiving a recognized mood stabilizer (50 vs. 60; $\chi^2 = 9.9$, $p < .01$) but more patients in the control group receiving antidepressants (23 vs. 11; $\chi^2 = 8.1$, $p < .01$). These differences largely disappeared over the time both groups were treated at the Hospital Clinic, although it is noteworthy that by the end of the follow-up, psychoeducated individuals were significantly more likely than control subjects to be prescribed an antipsychotic (40 vs. 24; $\chi^2 = 6.2$, $p < .05$). (The additional use of antipsychotics may relate to their increasing use as mood stabilizers—a topic covered in the psychoeducation sessions—and/or the provision of such medications to allow self-management of early symptoms of manic relapse.) There were no significant differences in mean dosages of the medications prescribed, so the costs (in Euros) for mean dosages of the most commonly prescribed medications in each medication class are provided in Table 4.

The direct mental health care costs over the entire study are detailed in Table 5. As shown, the mean cost differences for group therapy (€513; 95% CI = 4 to 1108) and outpatient visits (€699; 95% CI = 12 to 1386) favor the psychoeducation group, while the mean cost differences for emergency visits (€–311; 95% CI = –604 to –17) and days in hospital (€–5494; 95% CI = –7854 to

Table 3. Brief Overview of Prescribed Medications at the Beginning and End of the Study

Variable	Control Group (N = 60)	Psychoeducation Group (N = 60)	Statistic
No. of psychotropic medications, median	3	3	NS
Proportion of individuals prescribed any mood stabilizer, N (%)			
Beginning of study	50 (83.3)	60 (100.0)	$\chi^2 = 9.9$, $p < .01$
End of study	56 (93.3)	58 (96.6)	NS
Proportion of individuals prescribed any antipsychotic, N (%)			
Beginning of study	22 (36.6)	27 (45.0)	NS
End of study	24 (40.0)	40 (66.6)	$\chi^2 = 6.2$, $p < .05$
Proportion of individuals prescribed any antidepressant, N (%)			
Beginning of study	23 (38.3)	11 (18.3)	$\chi^2 = 8.1$, $p < .01$
End of study	18 (30.0)	11 (18.3)	NS
Proportion of individuals prescribed any benzodiazepine, N (%)			
Beginning of study	23 (38.3)	21 (35.0)	NS
End of study	24 (40.0)	24 (40.0)	NS

Abbreviation: NS = not significant.

Table 4. Data on Commonly Prescribed Psychotropic Medications and Estimated Cost per Day in Euros of Mean Prescribed Dosages of Each Medication

		Dosage of Prescribed Medication, mg				Medication Costs in Euros	
Medication	Number of Individuals	Mean Dose	SD	Minimum	Maximum	Cost per mg	Cost per Day for Mean Dosage
Lithium	91	1074.73	264.40	600.0	1600.0	0.00015	0.16
Valproate	14	1020.00	319.37	600.0	1500.0	0.00058	0.59
Carbamazepine	33	634.38	229.45	300.0	1200.0	0.00175	1.11
Lamotrigine	8	187.50	25.00	150.0	200.0	0.00394	0.74
Olanzapine	17	9.42	6.52	2.5	25.0	0.50866	4.79
Risperidone	31	2.91	2.38	1.0	9.0	0.81940	2.38
Quetiapine	10	350.00	304.18	150.0	700.0	0.02891	10.12
Fluoxetine	8	26.67	11.54	20.0	40.0	0.00360	0.09
Venlafaxine	12	193.75	133.63	75.0	450.0	0.01626	3.15
Diazepam	7	7.50	3.53	5.0	10.0	0.03179	0.24
Lorazepam	14	2.85	2.64	0.5	6.0	0.31287	0.89

–3256) favor the control group. The total mean cost for all outpatient services was lower in the control as compared to the psychoeducation group (€12,636 vs. €14,865), but this scenario changes considerably when the cost of hospitalization is included, with the control group mean cost exceeding that of the psychoeducation group by over €3300 (€20,909 vs. €17,582). Hospitalization accounted for about 40% of the health care cost in the control group but only about 15% in the psychoeducation group. As there was considerable interindividual variability in resource utilization in both groups, the overall mean adjusted cost differences and 95% CIs suggested the cost of services for each group could not be entirely separated. However, the overall pattern of outcomes and cost suggests that psychoeducation dominates the control group intervention as it is more effective clinically and less costly (or at least no more costly) than the control treatment.

Analysis of Cost Versus Benefit

The mean cost differences adjusted for baseline variables for outpatient services was €2219 (95% CI = –1739 to 4921) in favor of the psychoeducation group and for all costs (including hospitalization) was €3341 (95% CI = –2013 to 4961), favoring the control group. As total costs were greater in the control group, we did not explore any other aspects of cost-effectiveness using this mean cost difference. However, to give an indication of incremental cost-effectiveness ratios, we used mean outpatient cost differences to undertake a calculation of the cost per additional relapse or emergency visit avoided and the cost per additional relapse-free day and the cost per additional inpatient day avoided. We justify this as, in many health care systems, outpatient and inpatient providers operate separately, and, in addition, hospital admission (and its associated costs) can be considered as an outcome or consequence of failure to prevent relapse.[20] However, as the following analyses do not include all direct mental health care costs and involve no other non–mental health care or indirect cost, we give these estimates as an indication only of potential cost offsets. The estimated mean additional cost of outpatient services per year for each additional relapse-free person in the psychoeducation group was €4035 (95% CI = –1795 to 10,621) and, for each

Table 5. Mean Costs for Services Used Throughout Study Period and Differences in Costs Between Groups[a]

Variable	Control Group (N = 60) Mean	Control Group (N = 60) SD	Psychoeducation Group (N = 60) Mean	Psychoeducation Group (N = 60) SD	Cost Difference in Euros: Psychoeducation-Control, Mean (95% CI)
Group therapy (intervention phase)	2,716	1,268	3,229	1,745	513 (4 to 1,108)
Outpatient visit	1,060	1,278	1,759	2,363	699 (12 to 1,386)
Emergency visit	691	1,032	379	504	–311 (–604 to –17)
Prescribed medication[b]	6,297	8,481	6,745	7,946	449.26 (–2,357 to 1,467)
Inpatient service	8,274	8,980	2,718	1,408	–5,494 (–7,854 to –3,256)
Individual therapy (follow-up phase)	1,872	1,601	2,751	2,276	676 (–3,069 to 4,378)
Total outpatient cost (ie, excluding hospitalization)	12,636	10,657	14,865	11,389	2,228 (–1,756 to 6,213)
Total cost	20,909	17,392	17,582	16,395	–3,327 (–9,779 to 3,124)

[a]Costs are rounded to whole Euros; hence, mean differences or totals may not exactly tally.
[b]Including laboratory costs of medication monitoring.

additional hospitalization-free person, €3478 (95% CI = –1072 to 9321). However, when actual numbers of inpatient bed-days and emergency visits were explored for each group, the mean cost for each additional inpatient bed-day avoided was €128 (95% CI = 11 to 486), and the mean cost for each additional emergency visit avoided was about €253 (95% CI = –101 to 461). The simple, easy-to-recall estimate from these analyses is that the mean cost across the study period was about €5 per day for each additional day free of any relapse symptoms, which worked out at about €7 per day for each additional depression-free day and €17 per day for each additional day free of mania, hypomania, or mixed symptoms.

DISCUSSION

It is acknowledged that the treatment of individuals with bipolar disorder is rarely medication alone, and it is increasingly likely that medication will be combined with some form of psychological support to maximize outcomes and improve quality of life.[7] Having established that clinical benefits accrue from adjunctive therapy or systematic service interventions, it is also important to estimate the costs associated with such interventions. Estimating their relative cost-effectiveness or any cost offsets in the short and longer term allows informed choices to be made between these different types of intervention. In this study, we showed that, when adjunctive therapy (in this case, group psychoeducation) is assessed over a short-term intervention phase (6 months), individuals often utilize more mental health care resources with no additional health gain compared with the control intervention (usual treatment plus an unstructured support group). However, when cost and benefits were explored over an extended 5-year postintervention period, it was demonstrated that, compared to an unstructured support group intervention, psychoeducation was dominant (i.e., less costly and more effective). Importantly, although the cost of scheduled outpatient appointments was significantly higher in psychoeducated individuals, this was offset by significantly lower costs associated with emergency visits and a striking difference in the cost of inpatient services. It is noteworthy that inpatient care accounted for 40% of total cost in the control group but only about 15% in the psychoeducation group.

The findings of the current study can be contrasted with the only other RCTs of psychological therapy in bipolar disorder that have explored costs and benefits.[15–18] The RCT by Lam and colleagues[15] explored the costs of relapse prevention over a 30-month period for U.K. patients randomly allocated to either CBT plus usual treatment or usual treatment alone. Even if the estimated cost of 20 sessions of individual CBT was varied between £863 and £1295, it was found that the cost per person in the CBT group was £1300 less than for those in the usual treatment group (mean total cost: £10,352 vs. £11,724). As such, CBT showed dominance; again most of the additional resource use in the treatment-as-usual group was a result of inpatient admissions. However, unlike the present study, the clinical advantage of the CBT group was predominantly for depressive symptoms and was not sustained at 24 months postintervention. Thus, if this approach were commissioned in day-to-day practice, consideration would need to be given to the potential cost of further booster sessions or an extended course of CBT that might be required in order to maintain the initial additional clinical benefit of CBT. The provision of further therapy may erode some of the apparent cost benefit reported at this follow-up. In contrast, Simon and colleagues[13] reported on the additional cost to patients (N > 400) of a systematic service-based intervention over a period of 24 months compared with usual treatment. The experimental intervention showed a significant impact on overall severity of manic symptoms and duration

of manic symptoms (mean, 19.2 vs. 24.7 weeks). The additional cost of the intervention was $1251 (total cost: $8046 vs. $6743), of which $500 was the cost associated with increased mental health service utilization by the research intervention group. Interestingly, most of this additional resource use was accounted for by more frequent clinic visits for medication management rather than for inpatient services. However, the intervention did not demonstrate any significant impact on depressive symptoms (the most significant symptom burden in bipolar disorder), nor were any differences reported in overall relapse rates. Bauer et al.[16] used an intervention package that has a number of parallels to the Simon et al.[13] model but located their effectiveness RCT in 11 VA service sites across the United States. Interestingly, they also found that, compared with usual care in a staff-model health maintenance organization, their collaborative chronic-care package demonstrated significant effects on mania but not depression at an incremental cost of about $1250. Bauer and colleagues[16] concluded that the new intervention was overall at least cost neutral while achieving a net reduction of 6.2 weeks in affective episode. These factors would again need to be considered when deciding whether this program demonstrates the optimal balance of benefits versus cost.

The current study used a therapy intervention that parallels that of Simon et al.[13] and Bauer et al.[16] in its use of group psychoeducation, but, like Lam et al.,[15] employs an extended (30 hours) course of therapy targeted at euthymic subjects who are not currently misusing drugs or alcohol. The group therapy in this study is associated with the utilization of fewer inpatient services (like Lam et al.[15] and Bauer et al.[16]) but more outpatient appointments and slightly higher medication costs (like Simon et al.[13]). For all participants in our RCT, medication accounted for a higher proportion, 30% to 40%, of the total cost in this long-term follow-up than in some shorter-term studies. However, it is not clear if this is more typical of resource distribution when an extended time period is studied or is a consequence of the fact that only direct mental health service costs were considered. It should also be noted that although the proportion of the total cost attributed to outpatient service use was similar to other recent studies, patients in this study had fewer outpatient encounters per year than in the U.S. or U.K. systems. This again may be related to the nature of the interventions, but it may be explained by the fact that in Europe the average number of outpatient appointments is about 2 to 3 per year,[21] compared to the United States, where the average number of office visits (for all types of intervention) is about 8 to 12 per year.[22] Furthermore, in Spain, therapy is usually provided (and paid for by the patient) separately from the mainstream health care system.

There are limitations in the current study that need to be borne in mind. First, it only explored direct mental health care costs. While this can be justified as they are most pertinent to an audience of mental health practitioners and service providers and we could access reliable and valid data about this resource utilization, these cost data may be only 20% to 30% of total resource utilization in bipolar disorder.[22] Furthermore, individuals with bipolar disorder are often frequent users of medical services and, to a lesser extent, of other agencies.[23] Our study does not allow us to explore whether, for example, the additional use of outpatient resources by psychoeducated patients might be associated with less or more use of other medical services, but such considerations are important when trying to estimate costs of all health services. The latter might occur if psychoeducation also raises awareness of physical health issues or consequences associated with bipolar disorder. Second, the cost of therapy in the postintervention phase was estimated from the limited specific data available. Although appropriate statistical techniques were utilized to take this into account,[24] it is a potential source of inaccuracies, and the estimates should be treated with caution—given this item influences the overall estimated outpatient and total costs, it is important to try to estimate this aspect of care more systematically in the future. A similar, but less likely source of error was the fact that the study was dependent on computerized outpatient records or clinical case notes for recordings of outpatient service utilization, prescribing, and medication adherence data, rather than individual interviews. All the data monitoring systems we employed are fallible, and many economic studies benefit from prospective assessment of resource utilization via face-to-face patient interviews with collateral information from other sources.[10] Having acknowledged these potential problems, it should be noted that the estimated mean cost of outpatient clinic attendance is far outweighed by the cost of inpatient service utilization (the most reliable dataset available to us); as such, the estimated cost of outpatient services and medication would need to be inaccurate to a degree that is hard to contemplate to dramatically change the trends reported.

CONCLUSIONS

The obvious strengths of this study are the systematic prospective monitoring of a cohort of 120 subjects over a 5.5-year period. There was limited loss of information due to dropouts or failure to track patients, and missing data were within an acceptable range for such a study.[10,13,15,16,24] The clinical information collated allowed cost data to be contrasted with a number of currently accepted measures of outcome, such as rates of admission and bipolar disorder relapse by group. Furthermore, our findings are entirely compatible with those reported previously in efficacy and effectiveness RCTs. Obviously, the methodological constraints affecting RCTs mean that our patient sample may not represent all the social, clinical, and

comorbid problems experienced by individuals with bipolar disorders seen in day-to-day practice. However, in a study modeling the cost-effectiveness of clinical interventions for reducing the global burden of bipolar disorders, Chisholm et al.[25] estimated that community-based treatment with a mood stabilizer (specifically lithium) and adjunctive psychosocial interventions was the most cost-effective approach. Our findings, derived from a clinical trial population, support this theoretical model as group psychoeducation plus usual care demonstrated greater efficacy and lower costs than an unstructured support group with usual care.

Drug names: carbamazepine (Carbatrol, Equetro, and others), diazepam (Valium and others), fluoxetine (Prozac and others), lamotrigine (Lamictal and others), lithium (Eskalith, Lithobid, and others), lorazepam (Ativan and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), venlafaxine (Effexor and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

Financial disclosure: **Dr. Scott** has received grant/research support from Janssen-Cilag and AstraZeneca UK and is a member of the speakers/advisory boards for AstraZeneca, Janssen-Cilag, Sanofi-Aventis, Eli Lilly, GlaxoSmithKline, and Otsuka. **Dr. Colom** is a member of the speakers boards for Bristol-Myers Squibb, Otsuka, Eli Lilly, AstraZeneca, GlaxoSmithKline, Pfizer, Sanofi-Aventis, and Tecnifar and has served as a consultant for Shire and AstraZeneca. **Dr. Benabarre** is a member of the speakers/advisory boards for AstraZeneca, Eli Lilly, Juste, Janssen-Cilag, Novartis, and Pfizer. **Dr. Goikolea** is a member of the speakers/advisory boards for AstraZeneca, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, Novartis, Pfizer, and Sanofi-Aventis. **Dr. Vieta** is a consultant for AstraZeneca, Bial, Bristol-Myers Squibb, Eli Lilly, Forest, GlaxoSmithKline, Janssen-Cilag, Jazz, Lundbeck, Merck-Sharp and Dohme, Novartis, Organon, Otsuka, Pfizer, Sanofi-Aventis, Servier, and United Biosource Corporation and has received grant/research support from CIBERSAM. **Drs. Popova**, **Cruz**, **Valenti**, **Sánchez-Moreno**, and **Asenjo** have no additional personal affiliations or financial relationships with any commercial interest to disclose relative to the article.

REFERENCES

1. Murray C, Lopez A. The Global Burden of Disease: A Comprehensive Assessment of Morbidity and Disability from Diseases, Injuries and Risk Factors in 1990 and Projected to 2020. Cambridge, Mass: Harvard University Press; 1996
2. Wyatt RJ, Henter I. An economic evaluation of manic-depressive illness–1991. Soc Psychiatry Psychiatr Epidemiol 1995;30:213–219
3. Das GR, Guest JF. Annual cost of bipolar disorder to UK society. Br J Psychiatry 2002;180:227–233
4. Bryant-Comstock L, Stender M, Devercelli G. Health care utilization and costs among privately insured patients with bipolar I disorder. Bipolar Disord 2002;4:398–405
5. Simon GE, Unutzer J. Health care utilization and costs among patients treated for bipolar disorder in an insured population. Psychiatr Serv 1999; 50:1303–1308
6. Frye MA, Calabrese JR, Reed ML, et al. Healthcare resource utilization in bipolar depression compared with unipolar depression: results of a United States population-based study. CNS Spectr 2006;11:704–710
7. Scott J, Colom F. Psychosocial treatments for bipolar disorders. Psychiatr Clin North Am 2005;28:371–384
8. Gianfrancesco F, Pesa J, Wang RH. Comparison of mental health resources used by patients with bipolar disorder treated with risperidone, olanzapine, or quetiapine. J Manag Care Pharm 2005;11:220–230
9. Calvert NW, Burch SP, Fu AZ, et al. The cost-effectiveness of lamotrigine in the maintenance treatment of adults with bipolar I disorder. J Manag Care Pharm 2006;12:322–330
10. Scott J, Palmer S, Paykel E, et al. Use of cognitive therapy for relapse prevention in chronic depression: cost-effectiveness study. Br J Psychiatry 2003;182:221–227
11. Kashner TM, Rush AJ, Crismon ML, et al. An empirical analysis of cost outcomes of the Texas Medication Algorithm Project. Psychiatr Serv 2006;57:648–659
12. Suppes T, Rush AJ, Dennehy EB, et al. Texas Medication Algorithm Project, phase 3 (TMAP-3): clinical results for patients with a history of mania. J Clin Psychiatry 2003;64:370–382
13. Simon GE, Ludman EJ, Bauer MS, et al. Long-term effectiveness and cost of a systematic care program for bipolar disorder. Arch Gen Psychiatry 2006;63:500–508
14. Scott J, Colom F, Vieta E. A meta-analysis of relapse rates with adjunctive psychological therapies compared to usual psychiatric treatment for bipolar disorders. Int J Neuropsychopharmacol 2007;10:123–129
15. Lam DH, McCrone P, Wright K, et al. Cost-effectiveness of relapse-prevention cognitive therapy for bipolar disorder: 30-month study. Br J Psychiatry 2005;186:500–506
16. Bauer MS, McBride L, Williford WO, et al. Collaborative care for bipolar disorder, pt 2: impact on clinical outcome, function, and costs. Psychiatr Serv 2006;57:937–945
17. Colom F, Vieta E, Martinez-Aran A, et al. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. Arch Gen Psychiatry 2003;60:402–407
18. Colom F, Vieta E, Sánchez-Moreno J, et al. Group psychoeducation for stabilised bipolar patients: five-year outcome of a randomised clinical trial. Br J Psychiatry 2009;194:259–264
19. Colom F, Vieta E, Sánchez-Moreno J, et al. Stabilizing the stabilizer: group psychoeducation enhances the stability of serum lithium levels. Bipolar Disord 2005;7(suppl 5):32–36
20. Scott J, Paykel E, Morriss R, et al. Cognitive-behavioural therapy for severe and recurrent bipolar disorders: randomised controlled trial. Br J Psychiatry 2006;188:313–320
21. Montoya A, Gilaberte I, Costi M, et al. [Bipolar disorder in Spain: functional status and resource use on the basis of the Spanish sample of the observational, Pan European EMBLEM study]. Vertex 2007;18(71): 13–19
22. Stensland MD, Jacobson JG, Nyhuis A. Service utilization and associated direct costs for bipolar disorder in 2004: an analysis in managed care. J Affect Disord 2007;101:187–193
23. Stender M, Bryant-Comstock L, Phillips S. Medical resource use among patients treated for bipolar disorder: a retrospective, cross-sectional, descriptive analysis. Clin Ther 2002;24:1668–1676
24. Davison A, Hinkley D. Bootstrap Methods and Their Applications. Cambridge, UK: Cambridge University Press; 1997
25. Chisholm D, van Ommeren M, Ayuso-Mateos JL, et al. Cost-effectiveness of clinical interventions for reducing the global burden of bipolar disorder. Br J Psychiatry 2005;187:559–567

For the CME Posttest for this article, see pages 438–440.