Effectiveness of Electroconvulsive Therapy in Community Settings

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Background: *Clinical trials indicate that electroconvulsive therapy (ECT) is the most effective treatment for major depression, but its effectiveness in community settings has not been examined.*

Methods: *In a prospective, naturalistic study involving 347 patients at seven hospitals, clinical outcomes immediately after ECT and over a 24-week follow-up period were examined in relation to patient characteristics and treatment variables.*

Results: *The sites differed markedly in patient features and ECT administration but did not differ in clinical outcomes. In contrast to the 70%–90% remission rates expected with ECT, remission rates, depending on criteria, were 30.3%–46.7%. Longer episode duration, comorbid personality disorder, and schizoaffective disorder were associated with poorer outcome. Among remitters, the relapse rate during follow-up was 64.3%. Relapse was more frequent in patients with psychotic depression or comorbid Axis I or Axis II disorders. Only 23.4% of ECT nonremitters had sustained remission during follow-up.*

Conclusions: *The remission rate with ECT in community settings is substantially less than that in clinical trials. Providers frequently end the ECT course with the view that patients have benefited fully, yet formal assessment shows significant residual symptoms. Patients who do not remit with ECT have a poor prognosis; this underscores the need to achieve maximal improvement with this modality.*

Key Words: Electroconvulsive therapy, efficacy, effectiveness, relapse, major depression, outcome prediction

Medical treatments frequently do not perform as well in routine practice as in controlled clinical trials (Hewitt et al 1999; Hoekstra et al 2002; U.S. Institute of Medicine 2001). In a variety of contexts, the effectiveness of pharmacologic and psychological treatments of psychiatric disorders delivered in community settings also falls below that achieved in controlled research (Dixon et al 1995; Schoenbaum et al 2001; Unutzer et al 1999; Weersing and Weisz 2002). This gap between patient outcomes in clinical trials and routine practice poses a central challenge to programs seeking to improve the quality of mental health care (National Advisory Mental Health Council 1999; U.S. Department of Health and Human Services 1999).

In the acute treatment of major depression, a vast literature has documented the efficacy of antidepressant medications (Nelson 1999; Thase and Ninan 2002) and some forms of psychotherapy (Casacalenda et al 2002; Markowitz 1999). Electroconvulsive therapy (ECT) is a vital treatment for this disorder. Patients who receive this modality are typically more severely ill, with more chronic and treatment-resistant conditions, than patients who receive other antidepressant treatments (Abrams 2002; American Psychiatric Association 2000, 2001; U.S. Department of Health and Human Services 1999). Nonetheless, controlled comparisons with antidepressant medications generally find superior clinical outcome with ECT (Folkerts et al 1997; Gangadhar et al 1982; Janicak et al 1985; Medical Research Council 1965). Largely on the basis of results from controlled clinical trials, it is estimated that the remission rate after ECT is on the order of 70%–90% and substantially exceeds that of any other form of antidepressant treatment (American Psychiatric Association 2000, 2001; Petrides et al 2001; Sackeim et al 1993, 2000).

In community practice, patients who receive ECT, like those treated with other modalities, vary in demographic features, comorbid psychiatric and medical conditions, cognitive status, treatment history, and other clinical characteristics (Hermann et al 1995; Olfson et al 1998). Multiple dimensions impact on ECT referral (e.g., treatment resistance, chronicity, illness severity, suicidality, and medication intolerance. Thus variability in patient features might be particularly pronounced in ECT community samples. Although some patient characteristics, such as comorbid substance abuse and personality disorders, are widely believed to predict poor acute clinical outcome with ECT (Black et al 1988; DeBattista and Mueller 2001), there is limited empirical support for these impressions. At the same time, ECT administration in the community varies in important technical characteristics, including electrical waveform, dosing strategy, and number and frequency of treatments (Pippard 1992; Prudic et al 2001). These technical features are readily identifiable and have been shown in controlled research to have marked impact on short-term efficacy and the magnitude of cognitive side effects (McCall et al 2000b; Sackeim et al 1987, 1993, 2000; Shapira et al 1998).

The extent to which variation in patient characteristics and ECT technique influence outcomes in community settings is unknown. Early investigators remarked that virtually all patients with major depression remit with ECT (Kalinowsky and Hoch 1946), but these claims were impressionistic. Subsequent investigation of community practice has involved self-report surveys (Farah and McCall 1993; Prudic et al 2001) and audits examining variation in treatment technique (Halliday and Johnson 1995; Latey and Fahy 1985; O'Dea et al 1991; Pippard 1992; Pippard and Ellam 1981). Despite 65 years of use, there has been no systematic documentation of the effectiveness of ECT in community practice.

A high rate of relapse has been observed in recent studies of patients who remit with ECT (Grunhaus et al 2001; Sackeim et al 1990, 1993, 2000, 2001). The extent to which this occurs in community settings is also unknown. Furthermore, regardless of setting, there has never been a prospective follow-up of a substantial number of patients who do not remit when treated

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with ECT. Determining longer-term clinical outcome in ECT nonremitters is important, especially because ECT is most commonly given to patients who have not benefited from pharmacotherapy (American Psychiatric Association 2000, 2001; Prudic et al 1990).

Here we report the results of a prospective, naturalistic study of a large sample of patients treated for major depression with ECT in diverse community settings. We determined the overall clinical effectiveness of ECT and assessed the effects of variation in patient and practice characteristics on short-term clinical outcome. The sample was followed for 24 weeks after ECT, and long-term outcome was examined in all patients, both those who were remitters and those who were nonremitters immediately after ECT. Patient and practice features associated with risk of relapse were also examined.

Methods and Materials

Study Sites and Study Participation

The study was conducted at seven hospitals in the New York City metropolitan area. The sites included two private psychiatric hospitals, three community general hospitals, and two hospitals at university medical centers. A clinical outcomes evaluator was assigned to each hospital and collected all the research information. These evaluators conducted clinical and neuropsychological research assessments and obtained data on clinical and treatment history. They had no involvement or impact on the care patients received because the goal was to document patient outcomes at each facility with minimal influence on the outcomes. The study was directed by investigators at the New York State Psychiatric Institute (NYSPI), but patients at this facility did not participate. The study was approved by the institutional review board at NYSPI and each of the seven hospitals.

Participants were recruited from those referred for ECT at each hospital who had a provisional psychiatric diagnosis of a depressive disorder. Over a 26-month period, 751 patients were so referred (Figure 1). To be included, patients had to meet DSM-IV criteria (American Psychiatric Association 1994) for a major depressive episode (unipolar or bipolar) or schizoaffective disorder, depressed, on the basis of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P; First et al 1996a). Patients were excluded if they had received ECT in the past 2 months, had a Mini-Mental State Examination (MMSE) (Folstein et al 1975) score of less than 15, spoke neither English nor Spanish, or had previously participated in the study (Figure 1). Patients were at least 18 years of age and provided informed consent.

Study Measures

Patients who consented to study participation were administered a battery of assessments to evaluate clinical status and treatment history. The primary instrument to assess severity of depressive symptoms was the 24-item Hamilton Rating Scale for Depression (HRSD; Hamilton 1967). Self-reports of depressive symptoms were also assessed with the Beck Depression Inventory-II (BDI; Beck et al 1996). The Global Assessment of Functioning (GAF) was used to estimate global impairment (American Psychiatric Association 1994). Comorbid DSM-IV psychiatric Axis I disorders, including substance abuse or dependence, were determined from administration of the full SCID-I/P interview. Medical comorbidity was assessed with the Cumulative Illness Rating Scale (Miller et al 1992). Global cognitive status was assessed with the MMSE (Folstein et al 1975).

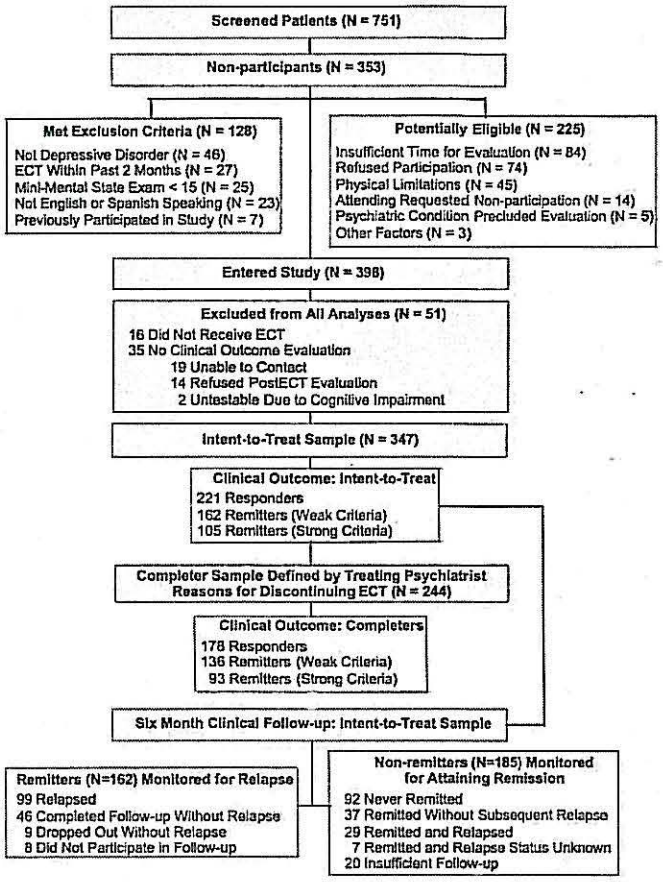

Figure 1. Participant flow through the study. ECT, electroconvulsive therapy.

Consent was obtained to contact previous health care providers to gather information on the psychiatric treatments received during the current depressive episode, including dosage and duration of psychotropic medications. This information, coupled with patient interviews and medical records review, was used to complete the Antidepressant Treatment History Form (ATHF) (Prudic et al 1990; Sackeim 2001; Sackeim et al 1990). The ATHF quantifies the adequacy of antidepressant treatments by evaluating the adequacy of each treatment trial in episode with respect to dose and duration. Demographic information was collected on all patients, including socioeconomic status of the household (Hollingshead 1975). At pre-ECT baseline, immediately after the ECT course, and at 24-month follow-up, an extensive neuropsychological battery was administered. The findings regarding cognitive outcomes will be the subject of a separate report.

The outcomes evaluators attended ECT treatments and documented the type and doses of medications administered before anesthesia induction, agents used for anesthesia and their doses, type of physiologic and seizure monitoring, and the ECT device model, electrical waveform, electrode placement, stimulus dosing strategy, and the specific parameters used for stimulation. The duration of the motor convulsion and, when monitored, the electroencephalogram (EEG) seizure were also recorded. Complications during the procedure and in the immediate postictal period were documented, as well as any additional medications administered after each treatment.

When the treating psychiatrist indicated that the acute course of ECT treatment was completed, the post-ECT assessment was

conducted. The HRSD and BDI were repeated. The Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First et al 1996b) was administered to derive DSM-IV diagnoses of personality disorders. The treating psychiatrist documented the reason for terminating the ECT course. The choices included "full response," "nonresponder and additional ECT not expected to benefit clinically," and a variety of other reasons related to premature termination, including withdrawal of consent, intercurrent illness, medical complication, excessive cognitive impairment, and medical insurance limitations.

Classification of Clinical Outcomes

Patients were classified as having met response or remission criteria immediately after the ECT course. Responders had a reduction in HRSD scores at post-ECT relative to pre-ECT baseline of 50% or greater. Although this dichotomization is commonly used to characterize outcome in pharmacotherapy trials (Frank et al 1991), it is rarely applied to ECT. This is partly because the high baseline symptom severity of ECT patients often makes a 50% reduction an inadequate clinical end point. Moreover, because persistent depressive symptoms are associated with continued functional impairment and a high rate of relapse, the standard in the treatment of depression has moved from achieving response to achieving remission (Paykel 2002; Thase and Ninan 2002). In this study, remission was defined according to both moderate and strict criteria. The moderate criteria ($remitter_{10}$), commonly used in ECT trials, required a minimum 60% reduction in HRSD scores and a post-ECT score of 10 or less (Petrides et al 2001; Sackeim et al 2000, 2001). The strict criteria ($remitter_7$) were identical to the $remitter_{10}$ criteria but required a post-ECT score of 7 or less. Some have argued that because an HRSD threshold of 10 might allow for significant residual symptoms, a HRSD score of 7 or less corresponds to full remission (Frank et al 1991; McIntyre et al 2002; Thase and Ninan 2002).

Patients who met $remitter_{10}$ criteria were monitored for relapse during follow-up. To be considered provisionally relapsed, patients had to have at least a 10-point increase in their HRSD score at a follow-up interview relative to the score immediately after ECT and a minimum score of 16. Patients who met these criteria were re-interviewed 1 week later; they were considered relapsed if they continued to meet these criteria. Relapse was also declared whenever patients were hospitalized for treatment of depression, received another acute course of ECT, attempted suicide, or manifested psychotic symptoms.

Follow-up Procedures

Patients were clinically monitored for a period of 24 weeks after the end of the acute ECT course. They were administered the HRSD at 4-week intervals and interviewed regarding the treatments received since last contact. The adequacy of these treatments was scored according to ATHF criteria (Sackeim 2001), except that a minimal trial duration was not required. Nonremitters at post-ECT were classified into three groups on the basis of subsequent course: not meeting $remit_{10}$ criteria at any time during follow-up; meeting $remit_{10}$ criteria on only one occasion; meeting these criteria on two or more consecutive occasions. At the final follow-up visit, all patients were classified by reapplication of the response and $remit_{10}$ criteria.

Clinical Outcomes Evaluators

The clinical outcome evaluators were hired expressly for this project and were principally masters-level technicians who had prior experience working in clinical and/or research settings with psychiatric patients. The evaluators participated in a 6–10-week training program that involved didactics, observation of clinical interview videotapes, observation of expert evaluators assessing patients at NYSPI, and expert observation and critique of assessments conducted by each of the evaluators. The bulk of the training was provided by three of the authors (JP, MO, and HAS), although other faculty at the New York State Psychiatric Institute also participated. Throughout the study, supervision occurred at least weekly. Before collecting data, evaluators met reliability criteria for HRSD ratings. Each of the 10 evaluators rated 35 videotapes of HRSD interviews conducted in patients referred for ECT. The intraclass correlation coefficient for these ratings was .97.

Statistical Methods

The intent-to-treat sample comprised all patients who consented to study participation and participated in at least one post-ECT assessment of symptom status. The completer sample comprised the subset in which the treating psychiatrist indicated that a complete course of ECT had been given. These were patients for whom the reason for ending ECT was that full improvement had been achieved or that improvement was incomplete but additional treatments were not expected to produce further benefit. Patients for whom the treating psychiatrist considered the ECT course to be prematurely terminated, whatever the reason, were not included in the completer sample. The complete set of statistical analyses was conducted in both the intent-to-treat and completer samples.

The sites were compared with regard to patient demographic and clinical features and treatment methods by one-way analyses of variance (ANOVAs) on continuous measures and χ^2 tests on categoric measures. For all analyses, the criterion for statistical significance (α) was .05, except for the post hoc comparisons of site differences, for which α was reduced to .01, given the number of possible pair-wise comparisons. Post hoc Tukey-Kramer comparisons identified pair-wise differences among the sites. Information regarding the adequacy of antidepressant treatments during the index episode was not available for 24.5% of the sample. Therefore, the influence of treatment history was not examined in this report.

The primary clinical outcome measures were the rates of remission ($remit_{10}$ and $remit_7$) and the percentage change in HRSD scores over the ECT course. Secondary outcome measures were rates of response, absolute post-ECT scores on the HRSD and BDI, and the percentage change in BDI scores.

To compare the sites in clinical outcome after ECT, logistic regressions were performed on response and remission rates, with site as a between-subjects factor and the interval between last treatment and outcome assessment as a covariate. Analyses of covariance (ANCOVAs) were conducted on the absolute symptom scores (HRSD and BDI-II) after treatment, with site as the between-subjects factor and the baseline symptom score and interval to assessment as covariates. In ANCOVAs on percentage change in symptom scores from baseline to after ECT the same ANCOVA model was used but without the baseline symptom score as a covariate.

An a priori set of patient features was tested for associations with the primary clinical outcomes. These variables served as predictors in a simultaneous linear regression analysis on the percentage change in HRSD scores and in logistic regression analyses on $remit_{10}$ and $remit_7$ rates. The significant relationships in these multivariate analyses were retested for bivariate associ-

ations with t tests and χ^2 analyses. Similar analyses were conducted to examine the relationship to clinical outcome of an a priori set of predictor variables characterizing ECT treatment parameters. These variables included electrical waveform (brief pulse vs. sine wave), electrode placement (right unilateral [RUL] only, bilateral [BL] only, RUL and BL, and other), stimulus dosing strategy (individually titrated electrical dose vs. fixed arbitrary dose), the interaction of electrode placement and dosing strategy, electrical dosage (percent of maximal device output, averaged across all treatments), and number of treatments in the ECT course.

Site differences in relapse over the 24-week follow-up were examined with nonparametric estimates of the survival distribution function, by the Kaplan-Meier product-limit method and the log-rank test. A parametric simultaneous regression model was fit to the relapse-time data with use of the Weibull distribution (Sackeim et al 1990, 2001). Covariates in the regression model were site, patient age, post-ECT HRSD score, duration of the depressive episode, presence or absence at study intake of psychotic depression, comorbid Axis I disorder, comorbid Axis II disorder, number of treatments in the acute ECT phase, receipt of continuation ECT (before relapse or completion of follow-up), strength of continuation pharmacotherapy (at point of relapse or completion of follow-up), and the interaction between these last two variables. The regression parameters were estimated with the partial likelihood method. Scores on the HRSD from all time points were submitted to a longitudinal mixed-model analysis, with post-ECT $remit_{10}$ status as a fixed between-subjects factor and time point as a fixed repeated-measures factor. On the basis of actual 24-week scores (n = 263), or where missing (n = 83) on those predicted by the mixed model, percentage improvement at the 24-week end point was determined for the groups who did or did not meet post-ECT $remit_{10}$ criteria.

Results

Of the 751 patients scheduled to receive ECT at the 7 sites, 398 (53.0%) consented to study participation (Figure 1). Of the 353 patients who did not enter the study, 128 (36.3%) patients met one or more exclusion criteria, with a psychiatric diagnosis other than a depressive disorder being the most common (n = 46, 13.0%). Of the remaining 225 patients who might have been eligible, the most common reasons for nonparticipation were insufficient time before the first ECT treatment to conduct the baseline evaluation (n = 84, 37.3%) and patients declining to enroll (n = 74, 32.9%). There was no evidence that the 225 potentially eligible nonparticipants differed from the 398 participants in demographic features, such as age, gender, or race. Of the 398 patients who completed the baseline evaluation, 51 patients (12.8%) did not contribute to analyses of outcomes. This included patients who did not receive ECT (n = 16, 4.0%) and a larger number who did not participate in any post-ECT assessment owing to loss to follow-up (n = 19, 4.8%) or refusal of further participation (n = 14, 3.5%). Only 2 (.5%) of the 398 patients who entered the study had a level of cognitive impairment during the week after ECT that precluded the post-ECT outcome evaluation. Thus, the intent-to-treat sample comprised 347 (46.2%) of the 751 patients referred for ECT and screened for the study.

Site Differences in Patient Features and Treatment Administration

There were statistically significant differences among the sites in patient age, education, estimated verbal intelligence quotient, familial socioeconomic status, duration of current episode, age-at-onset of mood disorder, severity of cumulative medical burden, comorbid Axis I disorders, and the percentage treated as inpatients (Table 1).

The sites also varied markedly in methods of ECT administration (Table 2). Sine wave stimulation was in use at two sites, and 15.3% of the total intent-to-treat sample was treated with this waveform, with all other patients receiving constant-current, brief-pulse, bidirectional stimulation. Three sites mainly used BL electrode placement, two sites mainly treated with RUL ECT, and two sites used a mixture of electrode placements. Titration of electrical dosage to the individual patient's seizure threshold was used to determine subsequent stimulus dosing in 48.1% of patients; an arbitrary fixed dosage was used in the remaining 51.9% of patients. There were marked differences among the sites in the intensity of the electrical stimulus, and at two sites nearly all patients were treated at the maximal device output. The sites differed in the average number of treatments patients received, which ranged from 5.4 to 8.6. There were also substantial site differences in the medications administered at ECT before anesthesia, especially the use of anticholinergic and β-blocking agents, and in seizure monitoring (data not shown). Two sites used neither the "cuff" technique to block the distribution of the muscle relaxant to aid the timing of the motor convulsion (American Psychiatric Association 2001) nor EEG seizure monitoring [$\chi^2(6) = 431.9$, $p < .0001$].

Clinical Outcome Immediately after ECT: Intent-to-Treat Sample

Despite the differences among the sites in patient characteristics and treatment and monitoring methods, there were no differences in any of the primary or secondary observer-rated measures of short-term clinical outcome (Table 3). There was a small but significant difference among the sites in the change in patient ratings of symptoms on the BDI, but none of the pair-wise comparisons were significant. Across the intent-to-treat sample, 162 patients (46.7%) met $remission_{10}$ and 105 patients (30.3%) met $remission_7$ criteria. Most patients had substantial clinical improvement, with 221 (63.7%) patients classified as responders.

In the analyses examining potential site differences, the interval between final treatment and the assessment of post-ECT outcome was strongly associated with the percentage change from baseline in depression scores [HRSD: $F(1,339) = 56.6$, $p < .0001$; BDI: $F(1,310) = 14.0$, $p = .0002$] and rate of response [$\chi^2(1) = 31.6$, $p < .0001$], $remission_{10}$ [$\chi^2(1) = 27.2$, $p < .0001$], and $remission_7$ [$\chi^2(1) = 14.6$, $p = .0007$]. The median assessment took place 3 days after ECT (mean = 4.6 days; SD = 4.3), with 318 of 347 patients (91.6%) evaluated within 10 days. A longer interval to assessment was associated with less improvement and lower rates of response and remission. When the sample was restricted to patients assessed within 10 days of ECT termination, a regression analysis on the percentage change in HRSD scores indicated that with each day since the end of ECT until assessment there was a decrease of 4.0% (SE = .62) in the percentage of symptomatic improvement. Thus, this analysis suggested that, on average, 10 days after ECT, patients had lost 40% of the improvement that accrued over the ECT course.

Several patient features and the interval between last treatment and the assessment of clinical outcome were associated with the extent of improvement and remission rates (Table 4). The presence of a comorbid personality disorder, longer duration of current episode of mood disorder, diagnosis of schizoaf-

Demographic and Clinical Characteristics for the Intent-to-Treat Sample by Site[a]

	Total ($n = 347$)	Site I ($n = 92$)	Site II ($n = 62$)	Site III ($n = 48$)	Site IV ($n = 47$)	Site V ($n = 41$)	Site VI ($n = 35$)	Site VII ($n = 22$)	F^b or χ^{2c}
ıs Variables									
ars)	56.7 (17.6)	54.5 (17.6)†	57.1 (17.4)*,†	54.5 (16.8)†	51.5 (14.9)†	68.5 (15.8)*	55.3 (18.5)*,†	60.5 (18.3)*,†	4.61
on (years)	13.9 (3.2)	13.7 (2.3)*,†	13.7 (3.1)*,†	15.1 (3.3)*	14.3 (2.9)*	11.9 (3.9)†	15.0 (2.8)*	13.4 (3.7)*,†	5.58
ed verbal IQ	103.0 (12.1)	100.6 (10.7)*,†	102.9 (13.6)*,†	106.8 (11.4)*,†	107.3 (11.9)*	98.3 (11.8)†	103.4 (12.7)*,†	104.7 (11.2)*,†	3.64
onomic status	2.4 (1.2)	2.6 (1.0)*,†,‡	2.7 (1.3)*,†	2.0 (1.0)‡	2.0 (1.0)†,‡	2.9 (1.4)*	2.0 (1.0)†,‡	2.7 (1.3)*,†,‡	6.19
ın Rating Scale for ession	31.3 (6.9)	31.2 (6.0)	31.4 (8.4)	31.4 (6.8)	31.0 (6.5)	30.4 (7.0)	33.3 (8.1)	30.0 (5.0)	.77
epression Inventory	35.4 (11.7)	36.9 (11.9)	35.1 (11.1)	35.1 (12.6)	34.2 (11.7)	34.1 (10.3)	37.0 (12.4)	32.8 (13.1)	.64
Assessment Scale	31.0 (9.2)	28.7 (6.1)†	35.4 (9.3)*	29.1 (10.6)†	31.5 (8.5)*,†	30.2 (10.2)*,†	29.0 (11.3)*,†	34.6 (7.1)*,†	4.93
ıtive medical burden	2.7 (2.3)	1.8 (1.6)‡	1.6 (1.6)‡	3.4 (2.4)*,†	2.6 (2.2)†,‡	4.1 (1.9)*,†	4.9 (3.1)*	2.3 (2.2)†,‡	15.79
duration, median (wk)	24.0	23.1†	24.9*,†	30.3*,†	17.0†	43.9*	24.0*,†	15.4†	5.94
ıedication trials during ıde	4.7 (2.9)	4.7 (2.3)	4.3 (3.0)	5.3 (3.7)	5.0 (3.4)	5.1 (2.9)	4.8 (2.7)	2.9 (1.4)	2.15
dequate medication trials	1.2 (1.3)	1.3 (.9)	1.4 (1.7)	1.4 (1.3)	1.2 (1.4)	1.0 (1.1)	1.2 (1.2)	.8 (.7)	.87
ıg episode									
ɔnset (years)	36.3 (19.4)	35.5 (19.7)†	31.8 (14.6)†	34.8 (20.4)†	29.8 (16.4)†	49.1 (17.4)*	39.2 (22.9)*,†	40.7 (20.9)*,†	5.13
revious episodes	2.7 (3.3)	3.2 (3.2)	2.3 (3.2)	2.5 (3.3)	2.2 (3.4)	2.3 (3.1)	2.9 (3.1)	3.4 (3.9)	1.09
revious psychiatric italizations	1.8 (1.6)	1.7 (1.7)	2.2 (1.7)	1.5 (1.6)	1.9 (1.6)	1.5 (1.4)	1.6 (1.5)	2.2 (1.8)	1.55
Variables									
ı	63.1	67.4	62.9	70.8	53.2	73.2	57.1	40.9	10.80
hite	85.9	90.2	85.5	87.5	89.4	80.5	77.1	81.8	5.28
lisorder diagnostic subtype									
ɔlar nonpsychotic	59.9	64.1	62.9	52.1	59.6	68.3	54.3	45.5	5.69
ɔlar psychotic	20.5	18.5	19.4	16.7	10.6	29.3	31.4	27.3	8.65
ar nonpsychotic	11.8	7.6	11.3	20.8	17.0	2.4	14.3	13.6	11.21
ar psychotic	3.8	5.4	1.6	4.2	8.5	.0	.0	4.6	9.69
ɔaffective	4.0	4.4	4.8	6.3	4.3	.0	.0	9.1	7.99
bid psychiatric diagnosis									
l	42.1	43.5	40.3	29.2	48.9	29.3	65.7	40.9	15.28
2	28.5	33.7	30.7	25.0	31.9	14.6	28.6	27.3	6.30
ıt	85.0	88.0*	59.7†	100.0*	87.2*	85.4*	100.0*	81.8*	51.32
tion resistant	64.6	73.9	61.3	72.9	59.6	48.8	65.7	54.6	11.22
of previous ECT	43.5	44.6	48.4	39.6	40.4	41.5	40.0	50.0	1.75

ıuous variables are expressed as mean (SD) unless otherwise noted; categoric variables are expressed as %.

elligence quotient; ECT, electroconvulsive therapy.

/ sites with different superscript symbols above the mean or percentage values differed significantly in post hoc comparisons, whereas study sites sharing one or more superscript For example, for the mean age of patients, only Site V had the superscript "*", indicating that patients were oldest at this site. Sites I, III and IV had the superscript "†", indicating that s differed significantly from single site with superscript "*". In contrast, Sites II, VI, and VII had superscript "*,†". Each of these three sites did not differ in the age of patients from any e each of the other sites were specified by "*" or "†".

l p values refer to the effect of study site in one-way analyses of variance conducted on each continuous variable (df = 6, 340).

:he effect of study site in χ^2 analyses conducted on each categoric measure, and the p value is the significance level from the Likelihood Ratio test (df = 6).

Table 2. Characteristics of ECT Administration in the Intent-to-Treat Sample by Site[a]

Variables	Total Sample (n = 347)	Site I (n = 92)	Site II (n = 62)	Site III (n = 48)	Site IV (n = 47)	Site V (n = 41)	Site VI (n = 35)	Site VII (n = 22)	χ^{2b} or F^c	p
Electrical Waveform									191.9	<.0001
Brief pulse only	84.4	100.0*	24.2†	100.0*	85.1*	100.0*	100.0*	100.0*		
Any sine wave	15.6	.0	75.8	.0	14.9	.0	.0	.0		
Electrode Placement									324.9	<.0001
Bitemporal only	39.5	10.9†	87.1*	4.2†	65.9*	26.8‡	80.0*	4.6†		
Unilateral only	35.4	38.0†	1.6‡	87.5*	12.8‡	46.3†	5.7‡	81.8*		
Unilateral and bitemporal	13.3	6.5*	11.3*	8.3*	21.3*	26.9*	14.3*	13.6*		
Other	11.8	44.6*	.0†	.0†	.0†	.0†	.0†	.0†		
Stimulus Dosing Strategy									373.2	<.0001
Titration	48.1	88.0*	.0†	93.7*	.0†	97.6*	.0†	4.6		
No titration	51.9	12.0†	100.0*	6.3†	100.0*	2.4†	100.0*	95.4*		
Stimulus Dosage Level										
High or maximal dose	50.4	35.9‡	66.1†	31.3‡	97.9*	22.0‡	28.6‡	95.5*,†	119.1	<.0001
Average intensity	75.7 (26.0)	73.3 (19.2)†	87.8 (21.7)*,†	62.0 (30.7)‡	98.3 (7.2)*	56.2 (24.1)‡	56.8 (24.1)‡	98.7 (2.6)*	24.4	<.0001
Number of Treatments	7.2 (3.0)	8.2 (2.6)*	6.1 (3.5)†	6.8 (3.0)*,†	5.4 (2.1)†	8.1 (3.1)*	8.6 (2.5)*	6.2 (2.9)*,†	9.2	<.0001
Treatment Duration (days)										
ECT treatment period	16.4 (9.3)	19.5 (10.0)*	14.3 (10.4)*,†	14.1 (7.2)*,†	12.0 (7.0)†	18.3 (9.3)*,†	19.2 (6.1)*	15.5 (10.2)*,†	5.7	<.0001
Duration per treatment	2.3 (.7)	2.4 (.8)	2.4 (1.0)	2.1 (.5)	2.2 (.8)	2.2 (.4)	2.2 (.4)	2.4 (.7)	1.4	.23

Data are expressed as % or mean (SD).

ECT, electroconvulsive therapy.

[a]Average stimulus dosage is the average electrical dosage across all treatments of a patient, and is expressed as a percentage of maximal device output. High dosage reflects an average charge per treatment that was 80% or greater of maximal device output. ECT treatment period is the number of days from start to end of the acute treatment phase with ECT. Duration per treatment is the treatment period divided by the number of treatments the patient received. Study sites with different superscript symbols (*,†,‡) above mean or percentage values differed significantly in post hoc comparisons, whereas study sites with overlap in superscript symbols did not differ.

[b]χ^2 and p values refer to the main effect of study site in χ^2 analyses conducted with categoric measures (df = 6). χ^2 analyses were conducted on all variables except average intensity of electrical stimulation, number of treatments received, and the treatment duration measures.

[c]F and p values refer to the main effect of study site in one-way analyses of variance (ANOVAs) on continuous variables (df = 6,340). ANOVAs were conducted on the average intensity of electrical stimulation, number of treatments received, and the treatment duration measures.

fective disorder, and more days intervening between last treatment and clinical assessment were consistent predictors of inferior clinical outcome. In bivariate analyses, each of these variables was significantly associated with each of the primary clinical outcome measures (data not shown).

The presence of a comorbid personality disorder was the patient variable with the largest and most consistent associations with clinical outcome. In the intent-to-treat sample, the response, $remit_{10}$, and $remit_7$ rates in those without versus those with a comorbid Axis II disorder were 68.95% versus 50.51%, 52.42% versus 32.32%, and 35.08% versus 18.18%, respectively. Although the diagnosis of a comorbid Axis II disorder had a substantial effect on clinical outcome, the response and remission rates were still markedly below those expected for ECT among patients who did not have a comorbid Axis II disorder. Furthermore, the associations of Axis II comorbidity and ECT clinical outcomes were undoubtedly exaggerated. The SCID-II interview was conducted immediately after the ECT course. This timing confounded the identification of Axis II disorders with the effects of ECT on depressive symptoms and memory. When the intent-to-treat sample was further restricted to patients without a comorbid Axis I or Axis II disorder (n = 157), the response and remission rates were still below expectations (response: 72.6%, $remit_{10}$: 54.10%, and $remit_7$: 37.8%). Thus, the relatively low rates of response and remission could not be attributed to greater prevalence of comorbid Axis I or Axis II disorder in this community sample.

The treatment variables did not have significant associations with any of the three primary outcome measures, except for a component of the interaction between electrode placement and stimulus dose titration (Table 5). Among patients treated with RUL ECT, titration of electrical dose was associated with higher rates of $remission_{10}$ [$\chi^2(1) = 4.79$, $p < .03$; odds ratio (OR) = .54, 95% confidence interval (CI) .31–.94] and $remission_7$ [$\chi^2(1) = 4.79$, $p < .03$; OR = .54, 95% CI .31–.94], relative to use of a fixed (nontitrated) electrical dose. These analyses also indicated that there were no site differences in the primary outcome measures.

Reasons for Terminating ECT

The low remission rates and the absence of associations between clinical outcome after ECT and the number of treatments administered (Table 5) raised the issue of the rationale for discontinuing treatment. In research contexts, as a consequence of ensuring that an adequate treatment trial is given before declaring lack of benefit, patients who do not remit typically receive more treatment than remitters (Petrides et al 2001; Sackeim et al 1993, 2000).

In the intent-to-treat sample, the treating psychiatrist indicated that ECT was terminated due to full clinical response in 213 of 316 patients (67.4%) for whom a reason for termination was documented (Table 6). In contrast, the treating psychiatrist indicated that ECT was terminated because of lack of response in only 31 of 316 patients (9.8%). For these patients, additional treatment was not expected to be of benefit. Only 2 of these 31 patients were rated by the research evaluator as meeting remission criteria, but 5 of the 31 patients (16.1%) met response criteria. Of the 213 patients determined by the treating psychiatrist to have achieved a full response, 81.6% were classified as meeting the research response criteria; however, only 66.8% and

Table 3. Efficacy of ECT Treatments by Site[a]

Variable	Total Sample $n = 347$	Site I $n = 92$	Site II $n = 59$	Site III $n = 48$	Site IV $n = 43$	Site V $n = 41$	Site VI $n = 35$	Site VII $n = 22$	F or χ^{2b}	p
Intent-to-Treat Sample										
HRSD										
Pre-ECT	31.3 (6.9)	31.2 (6.0)	31.4 (8.4)	31.4 (6.8)	31.0 (6.5)	30.4 (7.0)	33.3 (8.1)	30.0 (5.0)	.77	.60
Post-ECT	13.3 (8.8)	13.7 (9.0)	13.3 (9.5)	13.4 (8.1)	14.9 (10.0)	12.0 (7.4)	10.9 (7.8)	15.0 (8.5)	1.14	.34
Percent change	56.5 (28.0)	56.0 (27.1)	55.4 (33.7)	57.1 (25.4)	52.4 (28.4)	58.4 (26.5)	66.2 (23.3)	50.0 (27.7)	.94	.46
BDI										
Pre-ECT	35.4 (11.7)	36.9 (11.9)	35.1 (11.1)	35.1 (12.6)	34.2 (11.7)	34.1 (10.3)	37.0 (12.4)	32.8 (13.1)	.64	.70
Post-ECT	15.1 (12.8)	16.7 (15.2)	14.0 (11.0)	15.2 (13.0)	18.4 (12.0)	10.8 (9.4)	12.4 (12.0)	19.5 (13.9)	2.35	.03
Percent change	54.8 (36.0)	54.7 (38.3)	57.7 (31.0)	52.0 (40.5)	44.1 (32.9)	67.3 (30.0)	64.3 (31.1)	36.7 (43.7)	2.55	.02
Categorical clinical outcomes										
$Remission_7$	30.3	30.4	32.3	25.0	25.5	31.7	42.9	22.7	4.42	.62
$Remission_{10}$	46.7	45.7	48.4	43.8	44.7	48.8	57.1	36.4	2.92	.82
Response	63.7	62.0	61.3	68.8	57.5	70.7	74.3	50.0	6.01	.42
Completer Sample										
HRSD										
Pre-ECT	31.5 (6.7)	31.3 (5.9)	31.0 (8.3)	32.5 (5.7)	31.0 (6.8)	30.3 (6.8)	33.6 (7.5)	30.8 (5.3)	.84	.54
Post-ECT	11.5 (7.8)	12.0 (8.0)	10.3 (7.7)	12.6 (7.9)	12.7 (9.2)	10.5 (6.2)	9.5 (7.2)	14.1 (8.4)	1.23	.29
Percent change	63.4 (23.1)	61.8 (24.1)	66.2 (23.6)	62.1 (21.2)	60.2 (22.9)	64.2 (21.7)	71.4 (21.7)	54.7 (25.7)	.97	.45
BDI										
Pre-ECT	35.3 (11.6)	36.4 (11.8)	35.1 (11.5)	35.7 (11.6)	34.9 (12.0)	33.9 (10.3)	36.8 (12.7)	31.0 (11.9)	.57	.76
Post-ECT	13.0 (11.6)	15.2 (14.0)	11.1 (9.1)	12.3 (8.7)	16.2 (12.1)	10.1 (9.5)	9.9 (9.5)	18.5 (15.6)	2.32	.03
Percent change	60.8 (34.7)	57.9 (37.9)	64.8 (29.3)	58.0 (41.1)	53.4 (28.3)	68.9 (31.3)	70.6 (26.3)	41.0 (44.7)	1.68	.13
Categorical Clinical Outcomes										
$Remission_7$	38.1	35.7	42.5	32.3	36.0	37.1	53.6	26.7	4.13	.66
$Remission_{10}$	55.7	54.3	62.5	45.2	60.0	54.3	67.9	40.0	4.27	.64
Response	73.0	70.0	72.5	77.4	68.0	80.0	82.1	53.3	5.25	.51

Data are expressed as mean (SD) or %.

ECT, electroconvulsive therapy; HRSD, Hamilton Rating Scale for Depression; BDI, Beck Depression Inventory.

[a]Pre-ECT and post-ECT refer to scores before and after the completion of treatment with ECT, respectively. Percent change reflects division of the difference between these scores by the pre-ECT (baseline) score and multiplying the result by 100. In post hoc comparisons there were no significant differences among the study sites for any measure.

[b]F and p values for the main effect of study site are reported from one-way analyses of variance (pre-ECT scores) and analyses of covariance (post-ECT and percent change scores) on the HRSD and BDI measures. Sample size for the BDI was 318 for the total intent-to-treat sample and 230 for the completer sample due to missing values. Likelihood ratio χ^2 values and associated p values are reported for the main effect of study site in logistic regression analyses on categoric outcome measures controlling for the number of days between end of ECT and clinical assessment.

49.2% were classified as meeting $remit_{10}$ and $remit_7$ criteria, respectively.

The discrepancies between the treating psychiatrist and the research evaluator could have been due to the evaluator assessing clinical outcome at a later date than the treating psychiatrist, such that some of the improvement observed by the treating psychiatrist had been lost. To test whether this possibility contributed to the discrepancy, three ANOVAs were conducted with the sample restricted to those patients for whom the treating psychiatrist stated that ECT was terminated owing to full response or lack of response ($n = 244$). In each case, the dependent measure was the number of days from the end of ECT until the research evaluator HRSD interview. The independent variables were the treating psychiatrist's determination that the patient did or did not fully respond to ECT and the research outcomes categorization as meeting or not meeting response, $remit_{10}$, or $remit_7$ criteria. There were no significant effects in any of these ANOVAs, thus indicating that the latency to HRSD interviews was not different among patients for whom the treating psychiatrist's and research evaluator's outcome designations were congruent or discrepant. For example, among the patients whom the treating psychiatrist judged as fully responding to ECT, the latency to the HRSD interview averaged 3.28 days (SD = 3.07) in patients categorized as meeting $remit_{10}$ criteria ($n = 134$) and 3.91 days (SD = 2.93) in patients who did not meet $remit_{10}$ criteria ($n = 79$) [$t(211) = 1.47$, $p = .14$].

Another potential cause of the discrepancy between the treating psychiatrist and the research evaluator in clinical outcome designation was differential effects of comorbid Axis I or Axis II conditions. Hypothetically, by discounting symptoms attributable to a comorbid psychiatric disorder, the treating psychiatrist might have viewed many more patients as fully responding to ECT, whereas ratings of the research evaluator might have been more influenced by the comorbid pathology; however, there was no evidence that Axis I or II comorbidity contributed to the discrepancies in outcome classification. For example, among the 134 patients who met $remit_{10}$ criteria and were judged to have fully responded by the treating psychiatrist, 20.15% had a comorbid Axis II condition, whereas this rate was 29.11% among the 79 patients who did not meet $remit_{10}$ criteria but were judged to be full responders by the treating psychiatrist [$\chi^2(1) = 2.2$, $p = .14$]. The comparable rates for the presence of either an Axis I or Axis II comorbid disorder were 48.5% and 55.7%, respectively [$\chi^2(1) = 1.0$, $p = .31$].

Table 4. Relationships of Patient Factors to Primary Clinical Outcome Measures[a]

	HRSD % Change		Remission$_{10}$				Remission$_7$			
Variables	F	p	χ^2	p	Odds Ratio	95% CI	χ^2	p	Odds Ratio	95% CI
Intent-to-Treat Sample										
Site	1.04	.40	2.5	.87			4.7	.58		
Interval to assessment (days)	40.84	<.0001	21.0	<.0001	15.7	4.8–54.9	8.7	.003	6.4	1.9–23.6
Age (years)	.49	.48	.7	.40			.2	.70		
Inpatient status (inpatient)	12.12	.0006	1.7	.19			.2	.65		
Cumulative medical burden	1.29	.26	.1	.71			.2	.64		
Episode duration (wk)	3.64	.06	4.5	.03	4.5	1.1–19.2	5.5	.02	6.0	1.3–28.0
History of previous ECT (no)	.88	.35	.9	.34			.1	.82		
Psychosis (no)	1.30	.25	.1	.81			.1	.72		
Schizoaffective disorder (no)	6.76	.01	4.5	.03	.2	.0–.9	4.2	.04	.2	.0–.9
Axis I disorder (no)	.85	.36	1.8	.18			5.4	.02	.5	.3–.9
Axis II disorder (no)	13.38	.0003	10.5	.001	.4	.2–.7	9.2	.002	.4	.2–.7
Completer Sample										
Site	1.47	.19	6.9	.33			6.1	.41		
Interval to assessment (days)	4.17	.04	2.0	.16			.6	.44		
Age (years)	.70	.41	.1	.71			.0	.89		
Inpatient status (inpatient)	1.20	.28	.3	.62			.1	.82		
Cumulative medical burden	.70	.41	.4	.54			1.2	.28		
Episode duration (wk)	9.17	.003	6.5	.01	8.2	1.6–46.0	8.4	.004	11.9	2.2–70.6
History of previous ECT (no)	.02	.88	.4	.53			.4	.53		
Psychosis (no)	.57	.45	.1	.79			.1	.75		
Schizoaffective disorder (no)	5.97	.02	3.8	.05	.2	.0–1.0	5.4	.02	.1	.0–.7
Axis I disorder (no)	.46	.50	2.0	.16			3.1	.08		
Axis II disorder (no)	6.34	.01	5.9	.01	.4	.2–.9	9.3	.002	.3	.2–.7

HRSD, Hamilton Rating Scale for Depression; CI, confidence interval; ECT, electroconvulsive therapy.

[a] F and p values for HRSD % change refer to the results of the simultaneous linear regression analysis on the percentage change in scores on the HRSD from before the start of the ECT course until after the ECT course. χ^2 and associated p values, and odds ratios and 95% CIs for the odds ratios refer to the results of logistic regression analyses conducted on rates of remission, defined by either the remission$_{10}$ or remission$_7$ criteria.

Clinical Outcome Immediately after ECT: Completer Sample

The analyses reported above were repeated for the completer group, which comprised patients for whom the treating psychiatrist indicated that a full course of ECT had been given. There was no meaningful change in the pattern of site differences in patient demographic and clinical characteristics, and no site differences emerged in rates of response, remission, or the extent of clinical improvement (Table 3). The response and remission

Table 5. Relationships of Treatment Factors to Primary Clinical Outcome Measures[a]

	HRSD % Change		Remission$_{10}$				Remission$_7$			
Variables	F	p	χ^2	p	Odds Ratio	95% CI	χ^2	p	Odds Ratio	95% CI
Intent-to-Treat Sample										
Site	1.29	.26	3.7	.72			4.5	.61		
Interval to assessment (days)	57.93	<.0001	31.3	<.0001	26.2	8.0–91.7	14.0	.0002	9.9	2.9–35.1
Waveform (sine)	.12	.72	1.0	.31			2.1	.15		
Electrode placement (4 levels)	.83	.48	.3	.96			1.0	.79		
Titration (no)	1.40	.24	.5	.47			0	.95		
Electrode placement × titration	.52	.67	4.1	.25			2.8	.43		
Electrical dosage	.64	.42	0	.91			0	.90		
No. of treatments	1.32	.25	2.6	.11			0	.97		
Completer Sample										
Site	2.70	.02	12.3	.06			6.6	.36		
Interval to assessment (days)	9.30	.003	4.7	.03	4.5	1.2–18.5	1.3	.25		
Waveform (sine)	4.13	.04	4.8	.03	4.7	1.2–22.2	3.5	.06		
Electrode placement (4 levels)	.62	.61	.6	.89			.6	.89		
Titration (no)	2.98	.09	1.2	.28			.3	.61		
Electrode placement × titration	.88	.45	4.3	.23			1.7	.64		
Electrical dosage	.14	.71	.5	.47			0	.84		
No. of treatments	15.00	.0001	13.9	.0002	42.0	5.7–362.7	3.1	.08		

HRSD, Hamilton Rating Scale for Depression; CI, confidence interval.

[a] F and p values for HRSD % change refer to the results of the simultaneous linear regression analysis on the percentage change in scores on the HRSD from before the start of the electroconvulsive therapy (ECT) course until after the ECT course. χ^2 and associated p values, and odds ratios and 95% CIs for the odds ratios refer to the results of logistic regression analyses conducted on rates of remission, defined by either the remission$_{10}$ or remission$_7$ criteria.

Table 6. Concordance of Treating Psychiatrist's Reasons for Termination of ECT with Research Ratings of Clinical Outcome

Clinical Research Rating	Full Response (n = 213)	Lack of Response (n = 31)	Withdrawal of Consent (n = 31)	Cognitive Impairment (n = 17)	Illness or Complication (n = 14)	Insurance Limitations (n = 5)	No Information (n = 31)
Response							
Yes	173 (81.2)	5 (16.1)	10 (27.8)	10 (58.8)	3 (21.4)	3 (60.0)	17 (54.8)
No	40 (18.8)	26 (83.9)	26 (72.2)	7 (41.2)	11 (78.6)	2 (40.0)	14 (45.2)
$Remission_{10}$							
Yes	134 (62.9)	2 (6.5)	5 (13.9)	5 (29.4)	3 (21.4)	0 (.0)	13 (41.9)
No	79 (37.1)	29 (93.5)	31 (86.1)	12 (70.6)	11 (78.6)	5 (100.0)	18 (58.1)
$Remission_{7}$							
Yes	91 (42.7)	2 (6.5)	2 (5.6)	3 (17.7)	0 (.0)	0 (.0)	7 (22.6)
No	122 (57.3)	29 (93.5)	34 (94.4)	14 (82.4)	14 (100.0)	5 (100.0)	24 (77.4)

Data are expressed as n (%). ECT, electroconvulsive therapy.

rates improved by 7.8%–9.3% in the completer sample relative to the intent-to-treat sample, depending on the measure. Among completers, 73.0% were classified as responders, and 55.7% and 38.1% met $remit_{10}$ and $remit_{7}$ criteria, respectively. Time from end of treatment to HRSD evaluation continued to be associated with clinical outcome (Tables 4 and 5). The patient features of episode length, diagnosis of schizoaffective disorder, and presence of an Axis II disorder continued to show associations with poorer outcome (Table 4), and no new associations with patient features emerged; however, new associations were seen between treatment variables and clinical outcome. Among completers, clinical outcome was now poorer among patients who received a larger number of treatments. Patients who were treated exclusively with brief pulse stimulation had superior outcomes compared with those who received sine wave stimulation. There were indications that patients for whom titration was the strategy used for dose determination had outcomes superior to those of patients who did not receive titrated dosing. As before, dosage titration seemed to be of specific benefit when RUL ECT was administered.

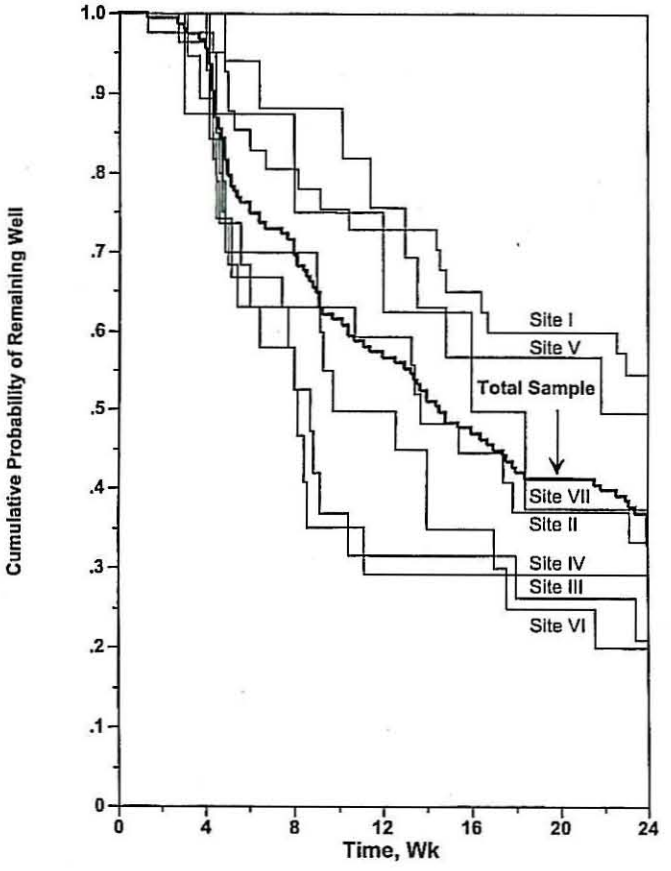

Figure 2. Kaplan-Meier estimates. Proportion of patients who remitted after electroconvulsive therapy and remained well during the 24-week follow-up period for the total sample (n = 154) and for each of the seven sites.

Clinical Outcomes during Follow-up

Of the 162 patients in the intent-to-treat sample who met $remit_{10}$ criteria, 145 patients were clinically monitored until they met criteria for relapse or the completion of the 24-week follow-up. Nine patients were followed for a shorter period but were lost to follow-up without meeting relapse criteria, and eight patients did not consent to post-ECT clinical monitoring. Ninety-

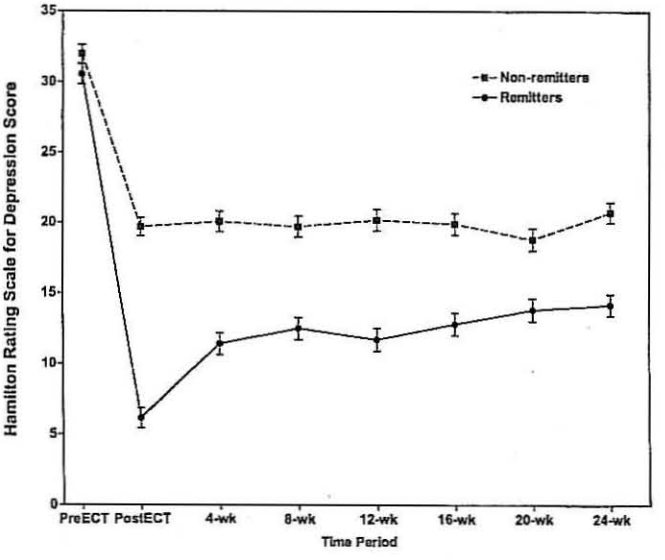

Figure 3. Depression severity scores. Hamilton Rating Scale for Depression (HRSD) scores for patients who did (n = 162) and did not (n = 185) meet $remit_{10}$ criteria immediately after electroconvulsive therapy (ECT). Scores are for the period before and immediately after ECT and at 4-week intervals during follow-up. Missing observations were imputed with a longitudinal mixed-model analysis.

nine of the 154 remitted patients (64.3%) relapsed (Figure 2). The median time to relapse was 8.6 weeks. Patients who relapsed (6.1 ± 2.6) did not differ from patients who did not relapse (6.3 ± 2.6) in post-ECT HRSD scores [$t(152) = -.3$, $p = .79$]. At the time of relapse, the mean HRSD score was 23.2 ± 5.4, whereas at the end of follow-up HRSD scores averaged 6.3 ± 4.8 in patients who did not relapse [$t(148) = 19.3$, $p < .0001$]. The Kaplan-Meier analysis indicated that the sites differed in survival time [log-rank, $\chi^2(6) = 16.4$, $p = .01$]. Across the seven sites, the relapse rate ranged from 46.3% to 78.9% (Figure 2).

The overall model in the parametric analysis on survival time was significant [likelihood ratio, $\chi^2(16) = 45.5$, $p < .0001$]. Site [$\chi^2(6) = 14.5$, $p = .02$], psychotic depression [$\chi^2(1) = 5.2$, $p = .02$], comorbid Axis I disorder [$\chi^2(1) = 7.4$, $p < .007$], comorbid Axis II disorder [$\chi^2(1) = 6.5$, $p = .01$], and number of ECT treatments in the acute phase [$\chi^2(1) = 4.3$, $p < .04$] were each associated with survival time. When we retested these variables after controlling for site, all except number of ECT treatments maintained significant associations. Compared with those who did not relapse, relapsed patients had higher rates of psychotic depression (31.1% vs. 22.2%) and comorbid Axis I (43.4% vs. 27.0%) and Axis II (23.2% vs. 14.3%) disorders. Strength of continuation pharmacotherapy was not associated with relapse; however, only 46.8% of relapsed patients and 53.3% of nonrelapsed patients were rated as receiving an adequate dosage of an established antidepressant medication. Of note, use of continuation ECT was frequent but equally represented among patients who did (43.9%) and did not relapse (49.0%).

Of the 185 patients who did not meet $remit_{10}$ criteria, 20 patients did not complete 12 weeks of follow-up and were excluded from characterization of post-ECT course. Of the remaining 165 patients, 92 (55.8%) never met remission criteria during follow-up. Of the 26 patients who met $remit_{10}$ criteria at one follow-up assessment, 5 continued through follow-up without meeting relapse criteria, 15 subsequently met relapse criteria, and relapse status could not be determined in 6 patients. The remaining 47 patients met $remit_{10}$ criteria at two or more consecutive assessments. Of this group, 32 patients continued without relapse, 14 patients subsequently met relapse criteria, and relapse status could not be determined for 1 patient. Thus, of the 158 patients who did not meet $remit_{10}$ criteria immediately after ECT and for whom follow-up data were complete, 37 (23.4%) met remission criteria and did not relapse during follow-up.

The longitudinal mixed-model analysis indicated that among patients who did not remit after ECT there was no change in average HRSD scores from the end of the acute ECT course through the completion of the 24-week follow-up (Figure 3). In contrast, among patients who met $remit_{10}$ criteria, there was a marked increase in HRSD scores at the first follow-up (4 weeks) after the end of ECT [$t(1818) = 6.22$, $p < .0001$]. The 4th week of follow-up was the modal point of relapse. Compared with the 4th week of follow-up, HRSD scores of ECT remitters were further increased at the 20th [$t(1818) = 2.59$, $p < .01$] and 24th [$t(1818) = 3.11$, $p < .002$] weeks. Relative to pre-ECT baseline, nonremitters ($n = 185$) had an average improvement in HRSD scores of 36.6% ± 23.3% at post-ECT and of 34.5% ± 28.8% at the 24-week follow-up. The ECT remitters averaged a 79.3% ± 9.5% decrease in symptom scores after ECT and a 52.3% ± 30.2% decrease at the end of follow-up. Based on HRSD scores at the end of the 24-week follow-up, 153 of the total sample of 347 patients (44.1%) were classified as responders, 78 of 347 (22.5%) met $remit_{10}$ criteria, and 56 of 347 (16.1%) met $remit_7$ criteria.

Discussion

We have provided evidence that ECT is substantially less effective in community practice than previously assumed from the results of clinical trials. Whereas the rate of remission in clinical trials is typically reported to be on the order of 70%–90% (American Psychiatric Association 2001; Petrides et al 2001; Sackeim et al 1993, 2000), the intent-to-treat remission rates from a large cohort of adults treated with ECT in community facilities were in the range of 30%–47%. The disparity between clinical outcomes in research and community settings was more marked for remission than for response rates. The low rates of remission are of particular concern given the long-term outcomes of patients who did not remit with ECT. Only a small minority of such patients achieved sustained remission during the subsequent 6 months.

The low remission rates in community practice might be explained by patient selection. Patients with comorbid psychiatric and medical conditions that are associated with poorer ECT outcome might represent a larger proportion of clinical populations than research samples. For example, we found that comorbid personality disorders, which occurred in more than one quarter of the sample, were associated with poor response to ECT. In controlled trials of ECT for major depression, patient selection criteria tend to limit the number of participants with various complicating comorbid disorders (e.g., neurologic disorders, substance abuse) (McCall et al 2000a); however, broader patient selection does not seem sufficient to account for the low remission rates. Although statistically significant associations were observed between several patient features and immediate post-ECT outcome, the amount of variance explained was modest. Indeed, the remission rates were substantially below expectations when the sample was restricted to patients without a comorbid Axis I or Axis II disorder.

Treatment adherence is known to impact on clinical outcomes in the pharmacologic and behavioral treatment of depression (Katon et al 2002; Sood et al 2000) and more generally in medicine (Haynes et al 2002; McDonald et al 2002). Indeed, depression has been repeatedly shown to be a risk factor for nonadherence to medical treatment (DiMatteo et al 2000). Poor patient adherence is unlikely to account for the low remission rates. Unlike pharmacotherapy, which is self-administered, other than agreeing to, and in the case of outpatients, showing up for treatment, the administration of ECT requires minimal active patient participation. Withdrawal of consent was the leading cause of premature termination of ECT according to the treating psychiatrist's report; however, when a completer sample was selected on the basis of the treating psychiatrist's view that a complete course of ECT had been administered, the remission rates were still disappointing.

Premature treatment termination is a more likely explanation of the remission rates. In controlled trials, a minimum number of treatments is usually required before patients are considered nonremitters, and in those patients who show clinical improvement, ECT is usually continued until detailed symptom assessments show a plateau in additional benefit (Petrides et al 2001; Sackeim et al 1993, 2000). In the community cohort, treating psychiatrists often terminated ECT before remission was achieved. Approximately one half of the cases that the treating psychiatrists determined to have had a full response did not meet

the strict remission criteria. The frequent termination of ECT in patients who had considerable residual symptoms might have been due to the use of symptom reduction as the target for treatment, as opposed to remission. Alternatively, some providers might have aimed for more complete improvement but might not have been aware of the residual symptoms. Systematic and thorough assessment of symptomatic status might help lower the risk of terminating treatment before remission has been achieved. In practice, premature treatment termination deprives patients of the full benefit of ECT and puts them at risk to lose the gains they have achieved. Indeed, in the first systematic follow-up of a large cohort of patients who did not remit with ECT, the rate of sustained remission was low. Because treatment resistance and intolerance are the leading indications for use of ECT in major depression (American Psychiatric Association 2001), it is not surprising that not achieving remission with ECT augers a poor prognosis. The guiding principle should be to deliver no more or less treatments than are needed to achieve maximal clinical gains. Too few treatments can result in incomplete improvement, chronic symptomatology, and heightened risk of relapse. Additional treatments beyond the point of maximal improvement do not seem to reduce the relapse risk (Barton et al 1973) but can contribute to adverse cognitive effects.

We found little evidence that technical aspects of ECT administration were associated with clinical outcomes. Although the community sites varied widely in many aspects of ECT administration, there were no site differences in short-term effectiveness. The incomplete symptomatic improvement in many patients might have limited the possibility of observing associations with technical factors or patient features. In addition, none of the sites routinely used forms of ECT that are known to have reduced efficacy (Sackeim et al 1987, 1993). Rather, the site differences in factors such as choice of electrical waveform, electrode placement, and dosing strategy are more likely to produce differences in cognitive side effects. Relationships between technical factors and cognitive outcomes will be addressed in a forthcoming report.

A high rate of relapse shortly after ECT has been observed in most recent reports (Grunhaus et al 2001; Sackeim et al 1990, 1993, 2000, 2001) and confirmed in this study. Controlled research has shown that intensive pharmacotherapy reduces this relapse rate (Sackeim et al 2001). The majority of patients who remitted after ECT received continuation pharmacotherapy that was rated as inadequate. The extent to which this low intensity of pharmacotherapy was due to medication intolerance or prescribing preferences could not be determined. Other work in community samples has shown that patients often receive inadequate levels of pharmacotherapy and psychotherapy in the acute treatment of major depression (Keller et al 1982, 1986).

Although the response and remission rates we observed would be considered high for routine pharmacologic treatment of major depression, the remission rates were well below expectations for ECT. When coupled with the relapse rate, it was evident that only a small percentage of patients who received ECT achieved a sustained remission. We suggest that rather than intrinsically reflecting limitations of ECT, this pattern reflects limitations in the delivery of care. In particular, the low remission rate might be due largely to premature termination of the acute ECT course in patients who show significant but incomplete benefit. The high relapse rate might be due to insufficient intensity of continuation treatment in ECT remitters.

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Abrams R (2002): Electroconvulsive Therapy, 4th ed. New York: Oxford University Press.

American Psychiatric Association (1994): *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Washington, DC: American Psychiatric Association.

American Psychiatric Association (2000): Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry* 157:1–45.

American Psychiatric Association (2001): The Practice of ECT: Recommendations for Treatment, Training and Privileging, 2nd ed. Washington, DC: American Psychiatric Press.

Barton J, Mehta S, Snaith R (1973): The prophylactic value of extra ECT in depressive illness. *Acta Psychiatr Scand* 49:386–392.

Beck AT, Steer RA, Brown GK (1996): *Beck Depression Inventory Manual*, 2nd ed. San Antonio, TX: Psychological Corporation.

Black DW, Bell S, Hulbert J, Nasrallah A (1988): The importance of Axis II in patients with major depression. A controlled study. *J Affect Disord* 14:115–122.

Casacalenda N, Perry JC, Looper K (2002): Remission in major depressive disorder: A comparison of pharmacotherapy, psychotherapy, and control conditions. *Am J Psychiatry* 159:1354–1360.

DeBattista C, Mueller K (2001): Is electroconvulsive therapy effective for the depressed patient with comorbid borderline personality disorder? *J ECT* 17:91–98.

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Dixon LB, Lehman AF, Levine J (1995): Conventional antipsychotic medications for schizophrenia. *Schizophr Bull* 21:567–577.

Farah A, McCall WV (1993): Electroconvulsive therapy stimulus dosing: A survey of contemporary practices. *Convuls Ther* 9:90–94.

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Folkerts HW, Michael N, Tolle R, Schonauer K, Mucke S, Schulze-Monking H (1997): Electroconvulsive therapy vs. paroxetine in treatment-resistant depression—a randomized study. *Acta Psychiatr Scand* 96:334–342.

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Gangadhar B, Kapur R, Kalyanasundaram S (1982): Comparison of electroconvulsive therapy with imipramine in endogenous depression: A double blind study. *Br J Psychiatry* 141:367–371.

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American Psychiatric Association (2001): The Practice of ECT: Recommendations for Treatment, Training and Privileging, 2nd ed. Washington, DC: American Psychiatric Press.

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American Psychiatric Association (2000): Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry* 157:1–45.

American Psychiatric Association (2001): The Practice of ECT: Recommendations for Treatment, Training and Privileging, 2nd ed. Washington, DC: American Psychiatric Press.

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Casacalenda N, Perry JC, Looper K (2002): Remission in major depressive disorder: A comparison of pharmacotherapy, psychotherapy, and control conditions. *Am J Psychiatry* 159:1354–1360.

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Dixon LB, Lehman AF, Levine J (1995): Conventional antipsychotic medications for schizophrenia. *Schizophr Bull* 21:567–577.

Farah A, McCall WV (1993): Electroconvulsive therapy stimulus dosing: A survey of contemporary practices. *Convuls Ther* 9:90–94.

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Gangadhar B, Kapur R, Kalyanasundaram S (1982): Comparison of electroconvulsive therapy with imipramine in endogenous depression: A double blind study. *Br J Psychiatry* 141:367–371.

Grunhaus L, Hirschman S, Dolberg OT, Schreiber S, Dannon PN (2001): Co-administration of melatonin and fluoxetine does not improve the 3-month outcome following ECT. *J ECT* 17:124–128.

Halliday G, Johnson G (1995): Training to administer electroconvulsive therapy: A survey of attitudes and experiences. *Aust N Z J Psychiatry* 29:133–138.

Hamilton M (1967): Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol* 6:278–296.

Haynes RB, McDonald HP, Garg AX (2002): Helping patients follow prescribed treatment: Clinical applications. *JAMA* 288:2880–2883.

Hermann RC, Dorwart RA, Hoover CW, Brody J (1995): Variation in ECT use in the United States. *Am J Psychiatry* 152:869–875.

Hewitt ME, Simone JV, U.S. National Cancer Policy Board (1999): *Ensuring Quality Cancer Care*. Washington, DC: National Academy Press.

Hoekstra JW, Pollack CV Jr, Roe MT, Peterson ED, Brindis R, Harrington RA, et al (2002): Improving the care of patients with non-ST-elevation acute coronary syndromes in the emergency department: The CRUSADE initiative. *Acad Emerg Med* 9:1146–1155.

Hollingshead AB (1975): *Four Factor Index of Social Status*. New Haven, CT: Yale University.

Janicak P, Davis J, Gibbons R, Ericksen S, Chang S, Gallagher P (1985): Efficacy of ECT: A meta-analysis. *Am J Psychiatry* 142:297–302.

Kalinowsky LB, Hoch PH (1946): *Shock Treatments and Other Somatic Procedures in Psychiatry*. New York: Grune & Stratton.

Katon W, Russo J, Von Korff M, Lin E, Simon G, Bush T, et al (2002): Long-term effects of a collaborative care intervention in persistently depressed primary care patients. *J Gen Intern Med* 17:741–748.

Keller M, Lavori P, Klerman G, Andreasen N, Endicott J, Coryell W, et al (1986): Low levels and lack of predictors of somatotherapy and psychotherapy received by depressed patients. *Arch Gen Psychiatry* 43:458–466.

Keller MB, Klerman GL, Lavori PW, Fawcett JA, Coryell W, Endicott J (1982): Treatment received by depressed patients. *JAMA* 248:1848–1855.

Latey R, Fahy T (1985): Electroconvulsive therapy in the Republic of Ireland 1982: A summary of findings. *Br J Psychiatry* 147:438–439.

Markowitz JC (1999): Developments in interpersonal psychotherapy. *Can J Psychiatry* 44:556–561.

McCall WV, Dunn AG, Kellner CH (2000a): Recent advances in the science of ECT: Can the findings be generalized? *J ECT* 16:323–326.

McCall WV, Reboussin DM, Weiner RD, Sackeim HA (2000b): Titrated moderately suprathreshold vs fixed high-dose right unilateral electroconvulsive therapy: Acute antidepressant and cognitive effects. *Arch Gen Psychiatry* 57:438–444.

McDonald HP, Garg AX, Haynes RB (2002): Interventions to enhance patient adherence to medication prescriptions: Scientific review. *JAMA* 288:2868–2879.

McIntyre R, Kennedy S, Bagby RM, Bakish D (2002): Assessing full remission. *J Psychiatry Neurosci* 27:235–239.

Medical Research Council (1965): Clinical trial of the treatment of depressive illness. Report to the Medical Research Council by its Clinical Psychiatry Committee. *Br Med J* 1:881–886.

Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack J, Rifai AH, et al (1992): Rating chronic medical illness burden in geropsychiatric practice and research: Application of the Cumulative Illness Rating Scale (CIRS). *Psychiatry Res* 41:237–248.

National Advisory Mental Health Council (1999): *Bridging Science and Service: A Report by the National Advisory Mental Health Council's Clinical Treatment and Services Research Workgroup*. Bethesda, MD: National Institute of Health.

Nelson JC (1999): A review of the efficacy of serotonergic and noradrenergic reuptake inhibitors for treatment of major depression. *Biol Psychiatry* 46:1301–1308.

O'Dea JF, Mitchell PB, Hickie IB (1991): Unilateral or bilateral electroconvulsive therapy for depression? A survey of practice and attitudes in Australia and New Zealand [see comments]. *Med J Aust* 155:9–11.

Olfson M, Marcus S, Sackeim HA, Thompson J, Pincus HA (1998): Use of ECT for the inpatient treatment of recurrent major depression. *Am J Psychiatry* 155:22–29.

Paykel ES (2002): Achieving gains beyond response. *Acta Psychiatr Scand Suppl*:12–17.

Petrides G, Fink M, Husain MM, Knap PRG, Rush AJ, Mueller M, et al (2001): ECT remission rates in psychotic versus nonpsychotic depressed patients: A report from CORE. *J ECT* 17:244–253.

Pippard J (1992): Audit of electroconvulsive treatment in two National Health Sservice regions. *Br J Psychiatry* 160:621–637.

Pippard J, Ellam L (1981): *Electroconvulsive Treatment in Great Britain, 1980*. London: Gaskell.

Prudic J, Olfson M, Sackeim HA (2001): Electro-convulsive therapy practices in the community. *Psychol Med* 31:929–934.

Prudic J, Sackeim HA, Devanand DP (1990): Medication resistance and clinical response to electroconvulsive therapy. *Psychiatry Res* 31:287–296.

Sackeim HA (2001): The definition and meaning of treatment-resistant depression. *J Clin Psychiatry* 62(suppl 16):10–17.

Sackeim HA, Decina P, Kanzler M, Kerr B, Malitz S (1987): Effects of electrode placement on the efficacy of titrated, low-dose ECT. *Am J Psychiatry* 144:1449–1455.

Sackeim HA, Haskett RF, Mulsant BH, Thase ME, Mann JJ, Pettinati HM, et al (2001): Continuation pharmacotherapy in the prevention of relapse following electroconvulsive therapy: A randomized controlled trial. *JAMA* 285:1299–1307.

Sackeim HA, Prudic J, Devanand DP, Decina P, Kerr B, Malitz S (1990): The impact of medication resistance and continuation pharmacotherapy on relapse following response to electroconvulsive therapy in major depression. *J Clin Psychopharmacol* 10:96–104.

Sackeim HA, Prudic J, Devanand DP, Kiersky JE, Fitzsimons L, Moody BJ, et al (1993): Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *N Engl J Med* 328:839–846.

Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, et al (2000): A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. *Arch Gen Psychiatry* 57:425–434.

Schoenbaum M, Unutzer J, Sherbourne C, Duan N, Rubenstein LV, Miranda J, et al (2001): Cost-effectiveness of practice-initiated quality improvement for depression: Results of a randomized controlled trial. *JAMA* 286:1325–1330.

Shapira B, Tubi N, Drexler H, Lidsky D, Calev A, Lerer B (1998): Cost and benefit in the choice of ECT schedule. Twice versus three times weekly ECT. *Br J Psychiatry* 172:44–48.

Sood N, Treglia M, Obenchain RL, Dulisse B, Melfi CA, Croghan TW (2000): Determinants of antidepressant treatment outcome. *Am J Manag Care* 6:1327–1336.

Thase ME, Ninan PT (2002): New goals in the treatment of depression: Moving toward recovery. *Psychopharmacol Bull* 36(suppl 2):24–35.

U.S. Department of Health and Human Services (1999): *Mental Health: A Report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, National Institutes of Health, National Institute of Mental Health.

U.S. Institute of Medicine Committee on Quality of Health Care in America (2001): *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press.

Unutzer J, Katon W, Sullivan M, Miranda J (1999): Treating depressed older adults in primary care: Narrowing the gap between efficacy and effectiveness. *Milbank Q* 77:225–256.

Weersing VR, Weisz JR (2002): Community clinic treatment of depressed youth: Benchmarking usual care against CBT clinical trials. *J Consult Clin Psychol* 70:299–310.