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Predictors of Major Depression Six Months After Admission for Outpatient Treatment

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Abstract

Objective—This study examined the rate and predictors of major depression six months after outpatient mental health admission.

Methods—Assessments were conducted at admission and three and six months later among 166 participants. Antidepressant treatment adequacy and depression outcomes were assessed at follow-ups.

Results—Predictors of major depression at six months included nonremission status at three months (odds ratio [OR]=3.56, $p=.003$), inadequacy of early pharmacotherapy (OR=2.73, $p=.009$), worse physical functioning measured by the 36-Item Short-Form Health Survey (OR=.975, $p<.001$), and being unmarried (OR=2.54, $p=.031$).

Conclusions—The findings support the effects of baseline physical disability, marital status, early treatment adequacy, and early remission on the course of major depression. The identification of individuals who do not receive intensive pharmacotherapy or who have not recovered by three months may provide opportunities for interventions to optimize six-month outcomes and to prevent the development of a persistent depression.

Unremitting depression is a prevalent and insidious public health problem (1,2) for which an effective approach has not been identified. Recent data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study demonstrate that algorithms using augmentation or switching medications to treat resistant depression have limited efficacy (3,4). This study assessed predictors of sustained major depression among adults receiving care in community outpatient settings. This study expanded on earlier research documenting the predictors of early recovery (5) to identify adults who are at risk of sustained depression at six months, after early pharmacotherapy and baseline predictors of course of depressive illness have been accounted for during the three months after admission to a mental health clinic.

More than two decades ago, Keller and colleagues (6) reported that 45% of patients admitted to academic centers for treatment of an index episode of depression continued to meet criteria for major depression six months later. Less is known about the course of depression in community-based psychiatric settings. In this study we examined the rates of persistent major depression six months after treatment had been sought at community clinics. Since Keller and colleagues' study of 1986, better-tolerated antidepressants have been developed and implemented in the field.

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In an earlier study, we identified predictors of early (three-month) “recovery”, which was defined as two weeks with no or only minimal symptoms of depression (5). Early recovery was independently associated with less severe depression, adequate antidepressant treatment, being female, and married. Building on this previous work, we hypothesized that sustained major depression at six months after admission would be predicted by lack of achievement of early recovery and by depression severity at admission, duration of the index episode, and intensity of early pharmacotherapy between baseline and six months.

Methods

Outpatient mental health clinics were selected from Westchester County, New York, to maximize socioeconomic and ethnic diversity. Six clinics (an outpatient department of a teaching hospital; a voluntary-sector hospital-based clinic; three county-funded clinics, and a freestanding voluntary-sector clinic) were selected to participate in a study of the course and outcome of major depressive disorder.

Individuals 18 years and older who were admitted consecutively to participating clinics during between October 1, 1995, and December 31, 1997, were invited to participate in a two-stage screening process in the same period to identify new admissions with major depressive disorder as defined by *DSM-IV*. Individuals who screened positive for depression on the Center for Epidemiological Studies Depression Scale were reinterviewed with the Structured Clinical Interview for *DSM-IV* to establish the major depression diagnosis. Antidepressants of the selective serotonin reuptake inhibitor (SSRI) class were widely available during this period. The Institutional Review Board of Weill Cornell Medical College approved study procedures. Written informed consent was obtained before study assessments were conducted.

A total of 166 participants who met criteria for major depressive disorder and were reinterviewed three and six months after admission constituted the study sample. This group of participants is a subsample of the larger study (7). At admission and at the six month follow-up, participants were administered the 17-item Hamilton Rating Scale of depression (HAM-D) to assess depression severity, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) to measure pain, social functioning, and physical functioning, and the Cornell Services Index (8) to catalogue recent use of medical and mental health services.

The three- and six-month assessments evaluated depressive symptom severity and treatment adequacy with scales from the Longitudinal Interval Follow-up Evaluation (LIFE) (9). The LIFE's Psychiatric Status Rating (PSR), used in the original study conducted by Keller and associates (6), offers a 6-point scale to rate depression severity from 1 to 6 relative to full major depression criteria on a weekly basis. In our study, we defined remission status as having a PSR score of 1 or 2 (having no symptoms or having no more than a mild degree of one symptom), whereas major depression was defined as having a PSR score of 3 or more for the preceding two weeks. A PSR score of 3 either indicates a partial remission from an index episode with clinically significant persistent symptoms or a recurrence of depressive symptoms that does not meet full criteria for major depression of a patient who had been in remission for depression. The two-week duration criterion for remission is shorter than the six-month period required for achieving full recovery in the longer-term observational study reported by Keller (10). However, this criterion is consistent with shorter-term treatment studies, including those assessing the impact of residual symptoms on subsequent course of depression. The prognostic importance of being symptom free for a minimum of two weeks is supported by evidence that incomplete remission predicts a poorer course of depression (11).

As in the Collaborative Study of the National Institute of Mental Health (NIMH), antidepressant intensity was measured with the 5-point Composite Antidepressant Scale (CAD), with ratings modified to include newer classes of antidepressants (5). Adequate treatment was defined as a weekly CAD score of 3 or more for a minimum of four consecutive weeks for one or more antidepressants. The three- and six-month follow-up assessments were conducted whether or not participants had continued treatment in the clinic from which they had been recruited.

Data analyses were conducted to construct a parsimonious and clinically informative model describing the likelihood of major depression at six months after admission based on the hypothesized predictors: early treatment adequacy, remission from depression at three months as defined by a PSR score of 1 or 2, and log-transformed duration of the index episode. Before the multivariate analysis was conducted, we made bivariate comparisons to identify associations between nonremission and baseline clinical variables.

Results

The study sample represents adults who completed the three- and six-month follow-up interviews. Of the sample of adults who completed the baseline assessment, 67% (166 of 247) completed both three- and six-month follow-up assessments. The group unavailable for follow-up assessments was younger ($t=-2.17$, $df=245$, $p<.05$) than the participating sample. The mean \pm SD age of participants was 46.8 \pm 18.0. The 166 participants had a mean level of education of 13.3 \pm 2.8 years. Sixty-nine percent of the sample (114 of 166) were female, 14% (24 of 166) were black, 12% (20 of 166) were of Hispanic descent, 74% (122 of 166) were white, and 63% (105 of 166) filled a prescription and took at least one dose of prescribed antidepressants.

Of the 166 participants, 39% (64 participants) met PSR criteria for major depression at six months. Specifically, 33% (55 participants) of the sample had depression at three months and continued to be depressed (PSR scores of 4 or 5) at six months, 13% (21 participants) had been in a partial or full remission at three months but were depressed at six months, and 15% (26 participants) were depressed at three months but in remission at six months.

Seventy-one percent of patients (117 participants) had index episodes less than 12 months at the six-month follow-up, with the mean length of episode being 13.3 \pm 16.8 months. Twenty percent (34 participants) had index episodes greater than six months but less than 12 months. The 122 participants who had a prior episode of major depression had 2.93 \pm 3.1 prior episodes.

In bivariate analyses (see Table 1), participants who achieved six-month remission status (both newly remitted and sustained remission) had better baseline physical functioning ($t=-3.79$, $df=162$, $p<.05$), had reported less pain ($t=-2.52$, $df=162$, $p<.05$), had fewer prior hospitalizations ($\chi^2=7.21$, $df=1$, $p=.007$), had shorter length of index episode of major depressive disorder (log transformed) ($\chi^2=2.61$, $df=161$, $p=.010$), and were married ($\chi^2=7.47$, $df=2$, $p=.006$). Half of the participants with depression in remission or not in remission reported continued mental health treatment at six months. As noted in Table 1, meeting criteria for personality dysfunction did not distinguish participants whose depression was in remission versus not in remission at six months.

Among participants who reported adequate antidepressant treatment therapy in the first three months, 49% (40 of 81 participants) continued to meet criteria for depression at six months compared with 73% (62 of 85) who had no pharmacotherapy or whose antidepressant treatment did not meet the threshold for adequacy. Also, among participants who reported using antidepressant therapy between three and six months, 73% (77 of 105) met criteria for

an adequate dosage for four weeks. Receiving adequate pharmacotherapy between months 3 and 6 was not associated with depression outcome at six months.

Multivariate analyses of predictors of remission included the hypothesized predictors and variables with significant bivariate relationships: marital status, physical functioning, pain, number of prior hospitalizations, HAM-D rating at admission, duration of index episode, three-month depression status (remitted or not remitted), and treatment adequacy. Of these predictors, being unmarried, having a greater number of previous hospitalizations, and having worse physical functioning were independent predictors of depression status at six months (model 1, Table 2). When both three-month nonremission status and three-month inadequate pharmacotherapy treatment were added to the model, the number of previous hospitalizations did not remain a significant predictor of major depression at six months.

We conducted post hoc analyses to explore whether the absence of an effect in the three- to six-month period was due to either the more chronic patients' receiving persistently intense pharmacotherapy or remitted patients' discontinuing pharmacotherapy before this period. A bivariate analysis examining the relationships between baseline chronicity based on a median split of duration of index episode (median=48 months) and medication adherence during the second three months did not reveal an association ($p=.646$).

Discussion

Among adults seeking community mental health treatment for major depression, fewer than four out of ten had a sufficiently significant reduction in depressive symptoms to be considered in remission six months after clinic admission, whether or not antidepressant treatment had been used. The rate of remission was the same as for those assessed at three months (5). Only one in five adults who sought care achieved remission at both three and six months. Participants in remission at three months were more than three times as likely as those without a three-month remission to be in remission at six months. One-third of participants met criteria for major depression at both three and six months. These findings support the importance of early nonremission as a predictor of sustained depression for at least six months. It is likely that participants who are in the large clinical trials focusing on optimal treatment of resistant or chronic depression could be identified after the first three months of treatment.

Our findings suggest that early adequacy of pharmacotherapy and early pharmacotherapy response are important independent predictors of depression outcomes at six months. Recent findings from the STAR*D trial demonstrate that individuals who responded after only eight weeks of treatment (considered early responders) were the group of individuals who typically achieved remission. The STAR*D study supports 12 weeks as a clinically meaningful period to monitor response. Clinical trials are documenting that patients who do not respond early are at greater risk of later treatment failure, which highlights the need for continued, early aggressive monitoring of patients (12).

The data from this naturalistic community-based study underscore the potential prognostic importance of early response to pharmacotherapy. Only adequate pharmacotherapy during the first three months predicted six-month remission. Early remission independently predicted status at six months regardless of later treatment adequacy (at three and six months). Nevertheless, we cannot explain why later treatment adequacy during the three months after clinic admission was not a significant predictor of six-month remission.

Regardless of the lack of an association between adequate pharmacotherapy during the second three months and six-month outcomes, these findings are consistent with the recommendations of the American College of Neuropsychopharmacology Task Force, that

monitoring and appropriately altering an individual's treatment regimen are necessary for improved chances of remission and recovery. These treatment factors combined with prior course of illness (hospitalizations) and physical health status differentiate who achieves remission within six months of seeking care. The construct of sustained depression at six months is related to the construct of chronic depression. Whereas chronicity has been used traditionally to describe the duration of a depressive episode, the syndrome of chronic depression (1,6) is closely tied to that of treatment resistance (1,4,13). Among participants in this study, the duration of the index episode, whether measured as a continuous variable or through a median split, did not predict persistence to six months. Our results can determine neither the extent to which participants with persistent depression at six months were treatment resistant before study entry nor the persistence of the index major depressions subsequent to the six-month assessment.

Our study has several limitations. First, we were unable to report fully on the efficacy and quality of treatment or to determine patient- and clinician-related factors that may have influenced whether antidepressants were continued. Second, we cannot ascertain the types of treatment offered beyond the antidepressant therapy dosage and duration and the number of psychotherapy visits. In the absence of data with more frequent assessment about changes in symptom severity, we cannot ascertain whether participants experienced more frequent switches into or out of major depression and whether transient fluctuations influenced depression status at six months. The fact that these data were collected over a decade ago may limit their relevance today. Nevertheless, a more recent study found that between 1987 and 1997, the number of individuals treated with antidepressant medications increased substantially, from 37% to 75%, which was primarily attributable to the introduction of SSRIs (14). Nevertheless, these data on prescription rates did not consider the duration of pharmacotherapy or classify treatment by adequacy. Weilburg and colleagues (15) conducted a secondary analysis of a pharmacy database and found an association between SSRI treatment and adequacy of antidepressant treatment; nevertheless, only 54% of the outpatients with depression treated only by psychiatrists met minimum dosage and duration criteria for adequacy. This percentage is higher than the recent finding that only 31% of 801 patients who met criteria for depression had had an adequate antidepressant trial at entry into an NIMH trial for chronic depression (13). Unfortunately, the more frequent prescription of antidepressants has not been associated with an increase in adequacy of treatment for nearly half of the patients who seek outpatient care for depression.

Conclusion

Recognizing sociodemographic and clinical characteristics that are predictive of major depression in community outpatient mental health care may help in the early identification of individuals who are particularly susceptible to sustaining poor outcomes. In addition, the importance of early adequate pharmacotherapy and response to treatment in predicting the course of depression supports an emphasis on early care as a gateway potential prevention of persistent depressive symptoms.

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Table 1
Baseline characteristics of participants whose major depression was in remission or not in remission six months after outpatient admission^a

Descriptor	All participants (N=166)		Participants in remission (N=64)		Participants not in remission (N=102)		Test statistic	df	p
	N	%	N	%	N	%			
HAM-D score (M±SD) ^b	19.54±4.56		18.62±4.75		20.12±4.13		t=2.15	162	.033
SF-36 score (M±SD) ^c									
Social functioning ^d	47.57±12.83		45.40±9.6		48.95±14.30		t=-1.79	162	.075
Physical functioning ^e	76.06±27.32		85.44±19.61		70.10±29.83		t=3.75	162	<.001
Bodily pain ^f	60.57±31.76		67.61±31.08		56.09±31.51		t=2.37	162	.019
Clinical Anxiety Scale (M±SD) ^g	9.61±5.89		8.07±5.00		10.00±6.00		t=-1.96	138	.052
Duration of index episode									
(log-transformed M±SD)	2.01±1.27		1.69±1.14		2.21±1.30		t=2.61	161	.010
Previous hospitalizations (M±SD)	.93±1.56		.40±.90		1.25±1.78		t=3.51	162	.001
Personality dysfunction (M±SD) ^h	4.26±2.39		3.91±2.42		4.48±2.36		t=1.51	163	.131
3-month pharmacotherapy treatment									
Adequate	81	49	41	51	40	49	χ ² =9.72	1	.002
Inadequate	85	51	23	27	62	73			
3-month depression status									
In remission	54	33	35	65	19	35	χ ² =23.30	1	<.001
Not in remission	112	67	29	26	83	74			

^aRemission was defined as a Longitudinal Interval Follow-up Evaluation (LIFE) Psychiatric Status Rating of less than 3; nonremission was defined as a LIFE Psychiatric Status Rating of 3 or more.

^bPossible scores on the 17-item Hamilton Rating Scale for Depression range from 0 to 53, with higher scores indicating more severe depression.

^cMedical Outcomes Study 36-Item Short-Form Health Survey

^dPossible scores range from 0 to 100, with higher scores indicating performance of normal social activities without interference from physical or emotional problems.

^ePossible scores range from 0 to 100, with higher scores indicating performance of all types of physical activities, including the most vigorous, without limitations resulting from health issues.

^fPossible scores range from 0 to 100, with higher scores indicating no pain or limitations because of pain.

^gPossible scores range from 0 to 24, with higher scores indicating greater anxiety.

^hPossible scores range from 0 to 12, with higher scores indicating higher distress in regard to interpersonal problems. This variable is a sum of the interpersonal sensitive, interpersonal ambivalence, and aggression subscales of the Inventory of Interpersonal Problems.

Table 2
Hierarchical logistic regression results predicting major depression six months after baseline^a

Variable	OR	Wald CI	p
Model 1 ^b			
Unmarried	3.17	1.45–6.94	.004
Poor physical functioning ^c	.98	.96–.99	<.001
Prior hospitalizations	1.31	1.03–1.66	.026
Model 2 ^d			
Unmarried	2.54	1.09–5.92	.031
Poor physical functioning ^c	.98	.96–.99	<.001
Prior hospitalizations	1.25	.97–1.59	.085
3-month nonremission	3.56	1.28–5.80	.003
3-month inadequate treatment	2.73	1.53–8.28	.009

^aMajor depression was defined as a Longitudinal Interval Follow-up Evaluation Psychiatric Status Rating of more than 3.

^bWald $\chi^2=34.4$, $df=4$, $R^2=25.5\%$

^cMeasured with the Medical Outcomes Study 36-Item Short-Form Health Survey

Wald $\chi^2=53.0$, $df=5$, $R^2=37\%$