

# Remission, Residual Symptoms, and Nonresponse in the Usual Treatment of Major Depression in Managed Clinical Practice

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**Background:** Although published guidelines recommend the continuation of treatment for depression until full remission of symptoms and restoration of functioning, little is known about how often remission is achieved in usual practice and the precipitants of treatment termination when treatment outcome has not been optimal.

**Method:** A naturalistic study design examined 1859 patients receiving treatment for DSM-III-R major depression between 1995 and 1997 in the national provider network of a managed behavioral health organization (MBHO). Symptom and impairment ratings by clinicians were used to group patients into full remission, partial remission, and no response. Claims data were used to characterize treatment and identify comorbid medical conditions.

**Results:** According to clinician ratings, approximately 27% to 39% of patients achieved full remission. Medical and substance use comorbidity and hospital admission were more common in those with a partial response to treatment. Only half of patients without a treatment response received a trial of medication during their treatment. Patient choice was the most common reason for termination of treatment, although nearly 40% of clinicians concurred with patients' decisions even when symptoms had not improved.

**Conclusion:** Although rates of full remission were comparable to those in clinical trials of antidepressants, results suggest that clinicians may fail to recommend continuation and maintenance treatment consistent with best practice guidelines and that unsuccessful treatment often does not include antidepressant medication.

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**C**urrent standards of care state that the primary goal of treatment for major depression is the complete remission of symptoms and restoration of functioning. The acute phase of treatment ends when full remission has occurred, whereas partial response and no response initiate modifications and enhancements following 4 to 6 weeks of active treatment.<sup>1,2</sup> Considerable evidence suggests that termination of treatment in the presence of residual depressive symptoms is associated with poorer long-term outcomes,<sup>3-5</sup> lower functioning, and higher risk of work impairment.<sup>6</sup>

Estimates of partial recovery range from 30% to 40% and those for full remission from 20% to 40% in clinical trials and other outcome studies.<sup>5,7,8</sup> Although specific criteria for recovery, relapse, and recurrence have become accepted,<sup>9</sup> partial recovery with residual symptoms is often defined as the presence of more symptoms than that allowed for full remission but fewer than those that define nonresponse to treatment.<sup>5</sup>

Some have suggested that clinicians use specific criteria to define full and partial remission in a manner similar to that used in clinical trials of antidepressants. For

example, a score of 7 or less on the Hamilton Rating Scale for Depression (HAM-D), a Clinical Global Improvement rating of 1 (very much improved), or a 70% reduction in any patient-rated symptom scale would suggest terminating treatment or beginning maintenance treatment.<sup>10</sup> Guidelines on the duration of treatment of major depression are sufficiently clear that they can be measured, suggesting that clinician performance against guidelines might also be measured.

Although limited in number, published studies suggest that treatment of major depression may rarely conform to guidelines calling for at least 4 months of active treatment after remission of symptoms and functional impairments.<sup>11,12</sup> Inadequate duration of care may stem from several factors—not all of which are tied to clinician decision making. Patients often drop out of treatment before achieving full remission because they “feel better” or become “hopeless” about improvement. Ongoing problems with restrictive mental health benefits and reimbursement rates or the perception of undue influence by managed care may also influence the duration of treatment by affecting both patient and clinician decisions. However, some evidence also suggests that clinicians may be unaware of or reject published clinical guidelines.<sup>13</sup> Absent from the literature is research on the extent to which full remission is the goal of clinicians treating major depression and the extent to which they believe that goal is achieved.

The goal of the present study is to examine the rate at which full remission is achieved by privately practicing clinicians treating major depression in the network of a national managed behavioral health organization (MBHO) and to examine the factors associated with suboptimal outcome. MBHOs are the predominant system of care for employed individuals<sup>14</sup> and little is known about the outcomes achieved by clinicians practicing in these settings. The present study addresses 3 questions related to these outcomes: (1) What is the rate at which clinicians report the achievement of full remission of depressive symptoms and functional impairments? (2) What factors are associated with suboptimal outcome? and (3) What are the reasons for termination of treatment when outpatient treatment has not been optimal?

## METHOD

The study is a naturalistic study of clinician-rated outcomes among patients treated for major depressive disorder in a national MBHO, United Behavioral Health (UBH). UBH pays clinicians on a fee-for-service basis and reviews care every 5 to 10 sessions for concordance with treatment guidelines. The present report is part of a larger study of therapeutic choice in the treatment of depression involving 10 large, self-insured employers who consented to the use of their administrative health

care data for research. Data from 4 (284,903 insured individuals) of the 10 employers were used for this report because these employers had also previously agreed to participate in a quality improvement program referred to as Goal Focused Treatment Planning and Outcomes (GFTPO) in which clinicians routinely rate the outcome of concurrent treatment and at termination.

## Data Sources

Data were extracted from 3 sources: (1) mental health claims data from UBH, (2) clinician and patient outcomes ratings from the GFTPO program, and (3) medical claims data from the 4 employers' health plans. Since GFTPO is focused exclusively on treatment that involves psychotherapy or psychotherapy in combination with medication treatment, outcome ratings are not available for patients treated only with medication. Measures derived from these sources were merged such that outcome ratings for a specific treatment episode were matched to mental health and medical claims from the time period of the episode.

## Sample

The sample consisted of all adult patients (N = 1859) diagnosed with DSM-III-R major depression and included all episodes of care between 1995 and 1997. The index episode was the earliest in the study period for those individuals having more than 1 treatment episode. The diagnosis of major depression by mental health specialists has been shown to be accurate in routine practice, with 74% to 76% of diagnoses verified by structured interviews.<sup>15,16</sup> A recent study by UBH found that 88% of major depression diagnoses were corroborated by a patient-completed checklist of DSM-IV symptoms.<sup>13</sup>

## Measures

The primary measures in this study are the rates of (1) full remission, (2) partial remission, and (3) no response based on symptom ratings of clinicians at the time of termination. Ratings were made on a 6-point scale where 1 = worse, 2 = somewhat worse, 3 = unchanged, 4 = somewhat improved, 5 = greatly improved, 6 = resolved. Residual symptoms and functional impairments were defined as a rating of “somewhat improved.” No response was defined as ratings of “worse,” “somewhat worse,” or “unchanged.” Impairments in functioning were included in our definition of “residual” and “nonresponding” symptoms, although they are typically not in clinical trial definitions of treatment response. Inclusion of functional impairments allowed us to approximate guideline definitions of complete and partial response to treatment and incorporated a broader array of problems that affect clinicians' decisions regarding the duration of treatment.<sup>1</sup>

Clinicians made their ratings on a termination form in which 23 depressive symptoms and functional impairments are listed. Clinicians are only required to rate symp-

Table 1. Prevalence of Treatment Response by Different Definitions of Remission

Definition	Total Sample (N = 1859)		Sample With Both Patient and Provider Ratings (N = 620)				Kappa
	Provider Ratings		Provider Ratings		Patient Ratings		
	N	% Remitted	N	% Remitted	N	% Remitted	
0 residual symptoms	494	26.6	226	36.5	176	28.4	.20*
1 residual symptom	727	39.1	300	48.4	296	47.7	.27*
2 residual symptoms	973	52.3	386	62.3	409	66.1	.38*
3 residual symptoms	1177	63.3	436	70.3	509	82.1	.36*

\*p &lt; .05.

toms and functional problems that are the focus of treatment. Although this procedure leads to missing data, it is required to minimize administrative burden for busy clinicians. Outcome rating forms were faxed to UBH for data entry. UBH obtains outcome ratings from providers on 99% of closed episodes in the GFTPO program.

A secondary measure of outcome status was available for a subset of patients (N = 620) who responded to a single mailed survey and who rated improvement on the same scale as clinicians. Given the low response rate to the survey, significant opportunity for response bias exists. Therefore, patient outcome ratings were used only as a concordance check on clinician ratings. Patients responding to the survey are more likely to be female ( $\chi^2 = 11.0$ ,  $df = 1$ ,  $p < .0009$ ) and were more likely to be rated by their clinician as still depressed or partially improved at the end of treatment ( $\chi^2 = 34.2$ ,  $df = 2$ ,  $p < .0001$ ).

Clinicians also indicated the cause for treatment termination by selecting 1 of 11 reasons: (1) benefit maximum reached, (2) changed clinicians, (3) lack of medical necessity, (4) insurance changed, (5) patient discontinued treatment, (6) patient moved, (7) treatment goals met, (8) treatment goals partially met—clinician concurred with termination decision, (9) clinician discontinued treatment (other reason), (10) patient death, or (11) other reason.

Mental health claims gave age, sex, diagnosis, and treatment characteristics including the presence or absence of combined medication and psychotherapy, use of acute inpatient care, and use of intermediate care, namely, day treatment and residential care, and the total number of outpatient visits. In addition, medical claims (as opposed to mental health claims) were available on a subset of 925 patients.

Medical claims were used to identify individuals receiving treatment for 7 chronic medical conditions concurrent with their depression treatment: arthritis, back problems, diabetes, gastrointestinal problems, lung disease, heart disease (angina or coronary artery disease), and hypertension. These conditions were selected because they were also investigated in the Medical Outcomes Study and have been associated with poorer outcomes.<sup>17,18</sup>

Table 2. Prevalence of Residual and Unimproved Symptoms in 1859 Patients With Major Depression

Symptom or Functional Impairment	N	% Residual	% Unimproved
Social functioning impairment	921	44.5	20.2
Coping impairment	1244	40.4	14.5
Anxiety	1240	39.9	13.7
Unrealistic appraisal of control	510	39.6	19.6
Depressed mood	1739	36.8	12.8
Concentration impairment	563	36.6	14.9
Appetite disturbance	560	33.4	22.9
Occupational functioning impairment	769	32.5	25.0
Sleep disturbance	807	32.2	18.2
Suicidal risk and self-endangering	512	22.9	16.0

## RESULTS

Rates of full remission were estimated for the full sample (N = 1859) and for the subsample for which both clinician and patient ratings were available (N = 620). Remission rates allowing 0, 1, 2, or 3 residual symptoms are shown in Table 1.

Under the most conservative definitions (0 or 1 residual symptom), 27% to 39% of depressed cases were considered remitted at the time of discharge. More liberal definitions (2 or 3 residual symptoms) gave higher estimates of remission in the range of 52% to 63%. Patient ratings showed comparable remission rates ranging from 28% to 48% when confined to conservative definition. Among the subset with patient and clinician ratings, concordance was low but statistically significant using the kappa statistic, a chance-corrected index of agreement.<sup>19</sup>

Given that rates of remission are closely tied to how full remission and partial remission are defined, we chose a conservative definition of full remission that reflects the fact that symptoms were rated in this study only when they were the focus of treatment. Because of the centrality of ratings to the goals of treatment, patients with no more than 1 residual symptom and having no unchanged or worsening symptoms were classified as "fully remitted." Any patient with 2 or more residual symptoms and with 0 symptoms rated as unchanged or worsening were classified as in partial remission. Any patient with at least

Table 3. Correlates of Residual Symptoms

Characteristic	Full Remission N = 727	Partial Remission N = 503	No Response N = 629	$\chi^2$ or (F)
Age, mean, y	37.4	36.9	36.0	(1.5)
Males, %	28.4	27.8	30.1	0.77
DSM diagnostic group (4th digit), %				
Recurrent	53.0	55.5	59.0	5.0
DSM diagnostic severity (5th digit), %				
Mild	33.3	29.2	32.1	2.3
Moderate	55.3	54.9	51.2	2.6
Severe without psychotic	32.6	36.8	45.8	25.2**
Severe with psychotic	6.3	6.0	10.2	9.6**
Partial remission	7.7	6.4	5.6	2.7
Full remission	4.5	1.4	1.6	15.6**
Comorbid diagnoses, %				
Alcohol abuse	2.5	3.8	6.0	11.2**
Other substance abuse	2.2	2.2	5.4	13.5**
Anxiety disorder	19.1	16.7	19.1	1.4
Psychotic disorder	5.1	6.0	7.0	2.2
Medical diagnoses, % <sup>a</sup>				
Arthritis	4.1	3.8	4.1	0.04
Back problems	5.6	6.5	7.2	0.7
Diabetes	0.3	3.0	1.9	7.2*
Gastrointestinal	7.0	8.4	8.4	0.8
Lung disease	14.4	18.3	19.3	3.1
Heart disease	5.6	4.6	6.9	1.4
Hypertension	3.5	4.9	5.9	2.1
Any chronic	29.9	35.0	37.1	4.0
Service characteristics of episode, %				
Medication only <sup>b</sup>	1.4	0.4	1.1	2.9
Psychotherapy only	56.3	54.5	52.3	2.1
Combined treatment	42.4	45.1	46.6	2.5
Used intermediate care	1.8	1.0	2.1	2.1
Used inpatient care	6.7	8.6	15.0	26.8**
No. of outpatient units of service, mean	17.4	15.9	16.6	(1.6*)
Duration of episode, mean, d	201.8	186.4	177.2	(3.8**)

<sup>a</sup>N = 925.<sup>b</sup>Although Goal Focused Treatment Planning and Outcome is focused on depression care involving psychotherapy, a few cases of treatment involving only medication were admitted into the program.

\*p &lt; .05; \*\*p &lt; .01.

1 unchanged or worsening symptom was classified as a nonresponder. Using these cutoff scores, 39.1% (N = 727) were classified as achieving full remission, 27% (N = 503) as achieving partial remission, and 33.8% (N = 629) as nonresponders (these numbers correspond to the "1 residual symptom" row in Table 1).

The areas most likely to show partial improvement were social functioning and impairments in coping. The areas remaining unimproved tended to be impairments in occupational functioning and appetite disturbance. The rates of residual symptoms and nonimprovement are shown in Table 2 for the 10 most commonly rated symptoms and functional deficits.

Patient characteristics were then correlated with outcome status and the results are shown in Table 3 with chi-square tests for the equivalence of proportions and F tests for means used to test differences between full remission, partial remission, and no-response groups. Outcome status was unrelated to the age and gender of the patient and whether or not the depression was diagnosed as single or recurrent episode. Poor outcomes were more common in

those with severe major depression and with alcohol and substance abuse or dependence comorbidity. Partial responders and nonresponders were 2 to 3 times more likely to have received a comorbid substance use disorder diagnosis.

Rates of recent treatment of chronic medical conditions were correlated with outcome status at the trend level ( $p < .10$ ), with rates exceeding 30% in the partial remission and no-response groups. Diabetes was the only condition that was significantly related to outcome status at the  $p < .05$  level. Lung disease (most commonly asthma) was the most common chronic medical condition examined in this study and was unrelated to outcome status.

Outcome status was largely unrelated to characteristics of treatment episodes (bottom of Table 3) and was not associated with more frequent outpatient sessions, which averaged 16 to 17 sessions in the full remission, partial remission, and unimproved groups. Type of treatment (psychotherapy only and combined treatment) was also unrelated to outcome status, although nonresponders were much more likely to have required inpatient care than persons achieving full or partial remission.

Finally, clinician-reported reasons for termination were tabulated within each outcome category, and differences were examined with chi-square tests. Patient discontinuation was the most common reason for termination among nonresponders, and this reason was highly associated with outcome status as shown in Table 4. As expected, termination by the clinician was also associated with outcome status. However, in a surprising 9% of cases, clinicians reported that they agreed with the termination decision and reported that treatment goals were met when their own ratings indicated the patient was still depressed. In an additional 14% of cases, clinicians concurred with treatment termination though they stated that treatment goals were partially met as shown in Table 4. In cases of partial remission, a total of 40.2% of terminations were with the agreement of the clinician and reported as "treatment goals met" or "treatment goals partially met." Other reasons such as exhaustion of mental health benefits, lack of medical necessity, patient moved, and patient death were infrequent and equivalent across outcome categories. Change in insurance status, change of clinicians, and the "other reason category" were infrequent reasons for discontinuation but were nonetheless significantly associated with outcome status as shown in Table 4.



**Table 4. Percentage of Provider-Reported Reasons for Treatment Termination by Outcome in 1859 Patients With Major Depression**

Reason for Termination	% Full Remission (N = 727)	% Partial Remission (N = 503)	% No Response (N = 629)	$\chi^2$
Benefit maximum reached	1.4	1.4	2.1	1.2
Changed clinicians	0.0	0.8	1.0	6.6*
Lack of medical necessity	1.0	1.2	2.2	4.1
Insurance changed	1.1	4.4	4.6	16.8*
Patient discontinued treatment	14.0	44.1	56.0	274.2*
Patient moved	1.2	2.4	1.6	2.4
Provider discontinued treatment	0.8	2.2	3.3	10.7*
Treatment goals met	66.0	19.7	9.2	548.2*
Treatment goals partially met and provider concurred with termination decision	10.3	20.5	14.0	25.1**
Patient death	0.3	0.2	0.3	0.1
Other reason	0.4	0.6	2.4	13.5*

\* $p < .05$ .  
\*\* $p < .01$ .

## DISCUSSION

A preponderance of evidence and written guidelines suggests that treatment of major depression should be continued until full remission of symptoms and restoration of functioning.<sup>1,2</sup> Using a large sample of patients treated for depression in a national MBHO, the present study suggests that full remission and partial remission occur at rates comparable to those in clinical trials of antidepressant treatment, although active treatment extended beyond that of most trials (16–17 outpatient visits and 6 months' average duration).<sup>9</sup> Impairments in social and occupational functioning were the least likely to respond to treatment, consistent with other studies.<sup>20</sup>

Patients not responding to treatment were more likely to have been hospitalized but did not show less intense outpatient treatment as measured by frequency of visits and the likelihood of receiving combined psychotherapy and medication treatment. Instead, treatment failure was associated with discontinuation of treatment by the patient. Whether the poor response to treatment or other factors associated with poor outcome prompted patient dropout is unknown. When taken together with the fact that 46% of unimproved patients also did not receive a trial of medication in addition to their psychotherapy, findings of the present study suggest that guidelines for treating nonresponse are not routinely adhered to by clinicians. Whether the failure to combine medication with psychotherapy is due to reluctance on the part of non-M.D. therapists or due to the unwillingness of Americans to take psychiatric medications, as suggested by one national survey, is unknown (T. W. Croghan, M.D.; M. Tomlin, M.D.; B. A. Pescosolido, et al., unpublished data, 2001).

Another important area of discordance with treatment guidelines was evident in the finding that clinicians frequently agreed with treatment termination even in the face of poor outcomes. Despite clear evidence for the negative consequences of residual depressive symptoms, approximately 40% of those in partial remission and 23% with no response terminated from treatment with the agreement of the clinician. Clearly, more work is required on the training and education of practicing clinicians on objective criteria for detecting residual symptoms and their use in clinical decision making.<sup>21</sup>

Failure to achieve full remission was more likely to occur in those with severe depression, alcohol and substance use, and diabetes. Although a third of patients in the present study had a chronic medical condition, this is substantially less than the rate for major depression found in the Medical Outcomes Study<sup>17</sup> (65%). Persons with chronic medical disorders may be more likely to seek mental health care from primary care providers than specialty mental health care providers, even though it appears that depression-related outcomes may be worse.

The association between outcome status and alcohol and other substance use highlights the importance of assessing and aggressively treating these conditions. Since substance use disorder is likely to be underdiagnosed by clinicians treating depression, the true effects of comorbid substance use disorder on poor outcomes is probably underestimated in this study.

The present study suffers from some methodological drawbacks that are inherent in measuring outcomes in real-world practice settings. First, measures relied on clinician ratings that may be biased because they are submitted to an MBHO that both pays for and monitors care. In addition, training in the use of this unstandardized measure does not approximate that in research settings. Despite the lack of training, patient and clinician ratings were weakly but significantly correlated and rates of full remission were equivalent whether based on clinician or patient ratings. Nevertheless, there is no evidence as to whether the clinician ratings of outcome used in this study are correlated with measures of functional and health status, and conclusions about the implications of our results for patients' lives are not possible.

Despite these measurement problems, the fact that outcomes were measured from the clinicians' perspective adds to concerns about the decision making of clinicians that consent to termination of treatment in light of their own ratings of poor outcome. Further research is needed to understand factors influencing clinical decision making around treatment termination when outcomes have not been optimal.

Another limitation is that findings are derived from an observational design, thus limiting what can be concluded about the determinants of outcome in this population. For example, the fact that combined medication and psycho-

therapy or the frequency of outpatient sessions was unrelated to outcome status of the patient does not mean that these factors are unimportant determinants of depression outcome as has been demonstrated in controlled studies.<sup>22</sup> Rather, this study estimates the average or “typical” outcomes achieved in a representative sample of individuals receiving usual depression treatment—estimates that are lacking in studies of managed behavioral health care and which have implications for understanding the decision making of private practice network clinicians around duration of care.

Despite its limitations, the present study is the first to report estimates of treatment outcome in the real-world practice settings of a national MBHO. Results were reported in such a way as to show correspondence with estimates of full remission in clinical trials and to show the extent of adherence by clinicians to standards of care calling for treatment of major depression to the point of full remission of symptoms and restoration of functioning. Although rates of full remission appeared to correspond well to those achieved in most clinical trials of psychotherapy and antidepressant medication, these outcomes were achieved over longer time frames, and using more therapy sessions, than the usual 6- to 8-week trial period. Findings also raised questions about whether clinicians use full remission of symptoms as a guideline for termination. Organized systems of care, professional organizations, and consumer groups should consider training and education, monitoring, and feedback programs aimed at informing patients and clinicians regarding treatment guidelines and the potential consequences of premature termination of treatment, given the potential risk associated with repeated episodes of depression including higher health care and employer costs. Unknown from the present results is the extent to which suboptimal outcomes observed in routine practice are due to patient characteristics, the nature and severity of people’s depression, or the intensity and quality of care delivered by the clinician. Future research into these 3 factors as well as the cost implications of suboptimal outcomes in depression treatment may help systems of care recognize the importance of detecting and remedying care that is only partially successful.

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

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