Why Do Some Depressed Outpatients Who Are in Remission According to the Hamilton Depression Rating Scale Not Consider Themselves to Be in Remission?

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ABSTRACT

Objective: In treatment studies of depression, remission is typically defined narrowly, based on scores on symptom severity scales. Patients treated in clinical practice, however, define the concept of remission more broadly and consider functional status, coping ability, and life satisfaction as important indicators of remission status. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services project, we examined how many depressed patients in ongoing treatment who scored in the remission range on the 17-item Hamilton Depression Rating scale (HDRS) did not consider themselves to be in remission from their depression. Among the HDRS remitters, we compared the demographic and clinical characteristics of patients who did and did not consider themselves to be in remission.

Method: From March 2009 to July 2010, we interviewed 274 psychiatric outpatients diagnosed with *DSM-IV* major depressive disorder who were in ongoing treatment. The patients completed measures of depressive and anxious symptoms, psychosocial functioning, and quality of life.

Results: Approximately one-half of the patients scoring 7 and below on the HDRS (77 of 140 patients for whom self-reported remission status was available) did not consider themselves to be in remission. The self-described remitters had significantly lower levels of depression and anxiety than the patients who did not consider themselves to be in remission ($P < .001$). Compared to patients who did not consider themselves to be in remission, the remitters reported significantly better quality of life ($P < .001$) and less functional impairment due to depression ($P < .001$). Remitters were significantly less likely to report dissatisfaction in their mental health ($P < .01$), had higher positive mental health scores ($P < .001$), and reported better coping ability ($P < .001$).

Conclusions: Some patients who meet symptom-based definitions of remission nonetheless experience low levels of symptoms or functional impairment or deficits in coping ability, thereby warranting a modification in treatment. The findings raise caution in relying exclusively on symptom-based definitions of remission to guide treatment decision-making in clinical practice.

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In describing treatment outcome for depression, a distinction is made between response and remission. Treatment *response* is commonly defined as a 50% or greater improvement in scores on symptom measures such as the Hamilton Depression Rating Scale (HDRS),[1] whereas *remission* is usually defined as a score below a predetermined cutoff score on the scale. Through the years, many cutoff scores have been used on the HDRS to define remission[2,3]; however, since the publication of the recommendations of Frank and colleagues,[4] a general consensus emerged to define remission on the 17-item HDRS as a score of 7 or less. A more recent consensus conference suggested that, when the HDRS is used as the primary outcome measure, a cutoff of 5 or 7 be used to define remission.[5]

Recognizing remission among patients who have responded to treatment is clinically important, because the presence of residual symptoms in treatment responders predicts an increased likelihood of relapse[6–9] and greater psychosocial morbidity.[10–13] In consideration of the clinical significance of residual symptoms, experts in the treatment of depression have suggested that achieving remission of symptoms should be viewed as the primary goal.[14–23]

Symptomatic remission has been defined as a complete or near-complete absence of symptoms.[5,22,23] The distinction between a complete and near-complete absence of symptoms itself might be meaningful, although this distinction has not received much empirical attention. In a report from the Collaborative Depression Study, Judd and colleagues[24] found that, compared to asymptomatic patients, patients with minimal levels of residual symptoms were at greater risk for relapse. In an earlier study from our clinical research group, Zimmerman and colleagues[25] found that, compared to patients scoring 3 through 7 on the HDRS, those who scored 0 to 2 reported less impaired psychosocial functioning and better quality of life. More recently, Nierenberg et al[26] found that the presence of mild residual symptoms in patients scoring below the cutoff used to define remission on the Quick Inventory of Depressive Symptomatology (QIDS)[27] significantly predicted relapse. These findings are consistent with our clinical observations that some patients with low levels of symptoms still do not consider themselves to be in remission and, despite low symptom severity, request a modification to their treatment. In other research from our group, we surveyed patients' opinion of the factors they considered important in defining remission from depression.[28] The patients considered a return to normal level of functioning, coping with the daily stressors of life, and the presence of features of positive mental well-being such as self-confidence and optimism as equal if not more important indicators of remission as a resolution of depression symptoms.

These research findings and clinical observations lead to the present study from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, in which we examined

Clinical Points

- Approximately one-half of depressed patients scoring in the remission range on the Hamilton Depression Rating Scale (HDRS) did not consider themselves to be in remission from their depression.
- Remission is a broader construct than symptom level, a construct that includes other indicators of clinical status such as functioning, quality of life, resiliency in coping with stress, and a general sense of well-being.
- That such a high proportion of HDRS remitters did not consider themselves to be in remission raises questions about the validity of the HDRS definition of remission.

the question of why some minimally depressed patients consider themselves to be in remission whereas others do not. We hypothesized that, among patients who are considered to be in remission according the HDRS, those who considered themselves to be in remission would have lower levels of symptoms, more features of positive mental health, better psychosocial functioning, greater life satisfaction, and better ability to cope with daily stress than patients who did not consider themselves to be in remission.

METHOD

The sample consisted of 274 psychiatric outpatients who were being treated for *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*), major depressive disorder in the Rhode Island Hospital Department of Psychiatry outpatient practice. The Rhode Island Hospital outpatient group predominantly treats individuals with medical insurance on a fee-for-service basis, and it is distinct from the hospital's outpatient residency training clinic, which predominantly serves lower income, uninsured, and medical assistance patients. For approximately one-half of the patients, the diagnosis of major depressive disorder was based on the Structured Clinical Interview for *DSM-IV* (SCID),[29] whereas others were diagnosed on the basis of an unstructured clinical interview. The sample included 87 men (31.8%) and 187 women (68.2%) who ranged in age from 19 to 80 years (mean = 49.0, SD = 13.9). The Rhode Island Hospital Institutional Review Committee approved the research protocol, and all patients provided informed written consent. The study was conducted from March 2009 to July 2010.

The patients were rated by the authors on the 17-item HDRS and *DSM-IV* Global Assessment of Functioning scale. In a previous study, we found high interrater reliability when rating the HDRS (intraclass correlation coefficient = .97).[30] Patients completed 7 self-report scales: a demographic form, the Clinically Useful Depression Outcome Scale (CUDOS),[31] the QIDS,[27] the Clinically Useful Anxiety Outcome Scale (CUXOS),[32] the Patient Global Index of Severity of Depression (PGI),[33] the psychosocial functioning and quality of life subscales of the Diagnostic Inventory for Depression (DID),[34] and the Remission from Depression Questionnaire (RDQ).[35]

The demographic form included a question regarding the patient's perception of whether they were currently in remission from depression (0 = yes, 1 = no). The term *remission* was not defined for patients; thus, they were left to answer the question based on their personal conceptualization of remission.

The CUDOS is a brief measure of depression severity that assesses the *DSM-IV* symptoms of major depressive disorder.[31] Each of the 16 symptom items is rated on a 5-point Likert scale to indicate the frequency of the symptom during the past week. A Likert rating was preferred in order to keep the scale brief. The scale's internal consistency reliability coefficient and test-retest reliability were high. The CUDOS was more highly correlated with other measures of depression than with measures of the other symptom domains, thereby supporting the scale's convergent and discriminant validity.

The QIDS is also a reliable and valid measure of the *DSM-IV* symptom criteria of major depressive disorder.[27] The 16 symptoms are assessed by groups of 4 statements, and the respondent selects the item that best describes how they have been feeling. Each item is scored from 0 to 3, and the total score ranges from 0 to 27, because only the highest score is used from items that are components of a single *DSM-IV* criterion. For example, only the highest value of the insomnia and hypersomnia items contributes to the total score. The QIDS has demonstrated high levels of reliability and has been shown to be sensitive to change in several controlled treatment studies.

The CUXOS is a general measure of psychic and somatic anxiety rather than a disorder-specific scale.[32] The scale was intended to be useful in the management of depressed patients, who often report high levels of anxiety in the absence of a specific anxiety disorder, as well as in monitoring patients with a variety of diagnosed anxiety disorders. The CUXOS consists of 20 items, 6 items assessing psychic anxiety and 14 assessing somatic anxiety, that are rated on a Likert scale similar to the CUDOS. The scale had high internal consistency and test-retest reliability and was more highly correlated with other self-report measures of anxiety than with measures of depression, substance use problems, eating disorders, and anger. The CUXOS was more highly correlated with clinician severity ratings of anxiety than depression and anger, and CUXOS scores were significantly higher in psychiatric outpatients with anxiety disorders than other psychiatric disorders.

The DID[34] is a self-report scale designed to assess the *DSM-IV* symptom inclusion criteria for a major depressive episode, assess psychosocial impairment due to depression, and evaluate subjective quality of life. The 6-item psychosocial functioning subscale assesses the amount of difficulty symptoms of depression have caused in usual daily responsibilities, relationships with significant others such as spouse, relationships with close family members, relationships with friends, participation in leisure activities,

and overall level of function. Items are rated on a 5-point Likert scale (0 = no difficulty, 4 = extreme difficulty). The quality of life subscale assesses satisfaction with the same areas covered by the psychosocial functioning scale as well as global satisfaction with mental health and physical health. Items are rated on a 5-point Likert scale (0 = very satisfied, 4 = very dissatisfied). The DID quality of life and psychosocial impairment subscales achieved high levels of internal consistency and test-retest reliability.

The RDQ consists of 41 items assessing multiple components of remission, such as positive mental health, symptom levels, and coping ability.[35] The items refer to the prior week and are rated on a 3-point rating scale (not at all or rarely true, sometimes true, often or almost always true). In the present study, we examined the positive mental health and coping subscales, both of which have high internal consistency and test-retest reliability.

Data Analysis

Among patients who scored 7 and below on the 17-item HDRS, we compared patients who did and did not consider themselves to be in remission. The independent variables were examined categorically as well as continuously. We a priori defined as indicators of clinically significant functional impairment scores of 2 or higher, indicating at least moderate impairment. A score of 3 or higher on the quality-of-life items indicated dissatisfaction in that domain. Based on prior research, a score of 20 and higher on the CUXOS and CUDOS indicated clinically significant levels of anxiety and depression.[31,32] A cutoff of 5 was used to identify remission on the QIDS.[36] *t* Tests were used to compare groups on continuously distributed variables, and χ^2 tests were used to compare categorical variables.

RESULTS

The mean score on the 17-item HDRS for the entire sample was 8.6 (SD = 6.9). Approximately one-half of the sample scored 7 or below on the HDRS and were considered to be in remission (n = 142, 51.8%). Self-reported remission status was missing for 2 patients. Slightly more than one-half of the patients scoring 7 and below on the HDRS considered themselves to be in remission (n = 77, 55.0%).

In the sample scoring 7 and below on the HDRS, we compared the 77 patients who did and the 63 patients who did not consider themselves to be in remission. There was no difference between groups in sex (67.5% vs 68.3%, $\chi^2 = 0.01$, not significant [NS]) or age (51.6 ± 12.2 years vs 47.7 ± 14.3 years, $t_{138} = -1.7$, NS). The data in Table 1 show that the self-described remitters had significantly lower levels of depression and anxiety than the patients who did not consider themselves to be in remission. In addition, the remitters were significantly more likely to score below 20 on the CUDOS (93.4% vs 61.9%, $\chi^2 = 20.7$, $P < .001$) and CUXOS (88.2% vs 47.6%, $\chi^2 = 26.8$, $P < .001$) and to be in the remission range on the QIDS (68.8% vs 27.0%, $\chi^2 = 24.3$, $P < .001$).

The data in Table 2 show that, across all functional domains, the self-described remitters reported significantly less functional impairment due to depression ($P < .001$). In addition, the remitters were significantly less likely to report moderate functional impairment in at least 1 specific area (21.1% vs 55.6%, $\chi^2 = 17.7$, $P < .001$), as well as significantly less likely to report moderate impairment on the global rating of impairment (9.2% vs 44.4%, $\chi^2 = 22.7$, $P < .001$). Results were similar for the quality-of-life analyses. That is, compared to patients who did not consider themselves to be in remission, the remitters reported significantly better quality of life across all domains (Table 3). Moreover, the

Table 1. Symptom Severity in Depressed Outpatients in Remission According to the 17-Item Hamilton Depression Rating Scale Who Do and Do Not Consider Themselves to Be in Remission

Symptom Severity Scale, Mean (SD) Scores	Self-Reported Remission (n = 77)	Self-Reported Nonremission (n = 63)	*t* Value
Patient Global Rating of Severity	0.9 (0.9)	1.4 (0.9)	3.6*
Clinically Useful Depression Outcome Scale	7.0 (7.2)	17.3 (11.3)	6.3*
Clinically Useful Anxiety Outcome Scale	9.4 (10.1)	21.6 (14.5)	5.6*
Quick Inventory of Depressive Symptomatology	4.9 (3.3)	9.0 (4.4)	6.2*
17-item Hamilton Depression Rating Scale	2.8 (2.3)	4.3 (1.8)	4.3*

*$P < .001$.

Table 2. Psychosocial Functioning in Depressed Outpatients in Remission According to the 17-Item Hamilton Rating Scale for Depression Who Do and Do Not Consider Themselves to Be in Remission

Psychosocial Functioning Domain, Mean (SD)	Self-Reported Remission (n = 77)	Self-Reported Nonremission (n = 63)	*t* Value
Work performance	0.3 (0.6)	0.9 (0.8)	4.9*
Marital relationship	0.6 (0.8)	1.3 (1.2)	3.6*
Family relationships	0.3 (0.6)	1.0 (0.9)	5.3*
Friendships	0.3 (0.7)	0.9 (0.9)	3.8*
Leisure	0.4 (0.7)	1.2 (1.0)	4.8*
Global rating of impairment	0.6 (0.7)	1.5 (1.0)	5.9*

*$P < .001$.

Table 3. Quality of Life in Depressed Outpatients in Remission According to the 17-Item Hamilton Rating Scale for Depression Who Do and Do Not Consider Themselves to Be in Remission

Quality of Life Domain, Mean (SD)	Self-Reported Remission (n = 77)	Self-Reported Nonremission (n = 63)	*t* Value
Work performance	1.0 (1.1)	1.6 (1.0)	3.7*
Marital relationship	0.9 (1.0)	1.7 (1.2)	3.8*
Family relationships	0.8 (1.0)	1.3 (0.9)	3.3*
Friendships	0.7 (1.0)	1.3 (1.0)	3.0**
Leisure	1.0 (1.1)	1.7 (1.1)	3.8*
Mental health	0.9 (1.0)	1.9 (1.0)	5.7*
Physical health	1.1 (1.1)	1.9 (1.1)	4.4*
Global rating of life satisfaction	0.9 (0.8)	1.7 (0.9)	5.3*
Global rating of quality of life	1.0 (0.7)	1.6 (0.7)	5.7*

*$P < .001$.
**$P < .01$.

remitters were significantly less likely to be dissatisfied in at least 1 specific area (21.1% vs 56.5%, $\chi^2 = 18.4$, $P < .001$) although not significantly less likely to report dissatisfaction on the global rating of quality of life (1.3% vs 7.9%, $\chi^2 = 3.7$, P = NS). Remitters were significantly less likely to report dissatisfaction in their mental health (7.9% vs 25.8%, $\chi^2 = 8.2$, $P < .01$). Finally, the remitted patients had higher scores on the positive mental health subscale of the RDQ (17.4 ± 5.0 vs 12.4 ± 5.3, $t_{138} = 5.7$, $P < .001$) and on the coping subscale of the RDQ (4.0 ± 1.6 vs 3.0 ± 1.4, $t_{135} = 3.8$, $P < .001$).

DISCUSSION

Experts recommend remission as the primary goal in the treatment of depression. The corollary to recommendations to "treat till remission" is that treatment should be modified until remission is achieved. This has been the approach followed in studies such as the Combining Medications to Enhance Depression Outcomes (CO-MED)[37] and Sequenced Treatment Alternatives to Relieve Depression (STAR*D),[38] in which pharmacologic interventions were changed at predefined intervals if symptomatic remission was not achieved. For example, in the CO-MED trial, patients receiving bupropion and escitalopram or venlafaxine and mirtazapine had their dosages increased after 4 weeks of treatment if QIDS scores were above 5 and again 2 weeks later if QIDS scores were still above 5. Thus, the failure to achieve symptomatic remission triggered automatic dosage increases (as long as the medication was tolerated), and patients scoring below the symptom-based remission cutoff did not have their medication changed.

We do not agree with recommendations to modify treatment if remission has not been attained, and we reject the corollary to continue the present course of treatment if the remission threshold has been reached, when the definition of remission is based exclusively on symptom status. We consider remission to be a broader construct than symptom level alone, a construct that includes other indicators of clinical status such as functioning, quality of life, resiliency in coping with stress, and a general sense of well-being. The present results are consistent with the hypothesis that remission as defined by a cutoff of 7 on the HDRS is overinclusive. One-half the patients in the present study who were HDRS remitters did not consider themselves to be in remission from depression. It is not surprising that, compared to the patients who did not consider themselves to be in remission, the self-described remitters reported lower levels of symptoms, better functioning, better quality of life, better coping ability, and better overall mental health. This is consistent with our clinical experience and explains why some patients with low levels of symptoms, in the so-called remission range of symptom severity, nonetheless are interested in modifications in their treatment.

The results of this study have implications for efforts to adopt measurement-based care in clinical practice. While we embrace the concept of measurement-based care to guide treatment,[39,40] we believe that a focus on symptoms is overly narrow. A patient may be minimally symptomatic but still vulnerable to symptomatic relapse and deterioration in functioning because of issues related to marriage, a child's behavior, parental illness, or occupational stress. A modification of treatment by adding psychotherapy to help cope with these stressors may be recommended despite symptomatic remission. Or, a patient may be nearly asymptomatic but with residual fatigue and reduced concentration impacting their work performance. Again, a modification in treatment with a pharmacologic intervention targeting these features may be recommended despite falling into the remission range of the HDRS.[21] The bottom line is that the measurement-based care movement will need to carefully consider the desired goals of treatment and how to operationalize the concept of remission. Perhaps it is simply a matter of reducing the cutoff score to define remission on measures such as the HDRS, or perhaps the definition of remission should include nonsymptom-related elements.

While we believe that remission should be defined in broader terms than symptom level, we also recognize that the HDRS is likely to remain a scale widely used to define remission. Thus, we consider the implications of the findings for the definition of remission based on the HDRS. That such a high proportion of HDRS remitters did not consider themselves to be in remission raises questions about the validity of the HDRS definition. Consistent with patients' self-perceived failure to achieve remission from depression, one-half or more of these patients reported clinically significant functional impairment and dissatisfaction in 1 or more areas of their life and were not in the remission range on self-report measures of depression and anxiety. The present results are therefore consistent with prior research suggesting that a cutoff of 7 on the HDRS was too high to define remission.[25] Of course, if a lower cutoff is used to define remission on the HDRS, a smaller percentage of depressed patients will be considered to be in remission. How ready is the field to consider that the rate of remission in the acute phase treatment of depression is even lower than has been recently suggested in studies such as the STAR*D, which already found that the likelihood of patients' achieving and sustaining remission is modest?[41] There may be some resistance to lowering the cutoff to define remission, because it will appear that treatment is even less effective.

Before concluding, the limitations of the study should be recognized. First, we examined only the 17-item version of the HDRS. We focused on the 17-item HDRS because it is the most commonly used measure in antidepressant efficacy trials, and the cutoff used to define remission has been generally accepted. We would anticipate that our findings would be similar in studies of longer versions of the HDRS as well as other depression severity scales such as the Montgomery-Asberg Depression Rating Scale. Second, all of the assessments were cross-sectional. A longitudinal assessment to ascertain persistent improvement in the different domains would provide valuable information. Third, self-perceived remission status was based on the patients' response to a single question. We did not want to limit or

influence the patients' conceptualization of remission and therefore did not define the term. This very likely resulted in heterogeneity among patients in their definition of remission, thereby potentially introducing error variance. However, despite such error variance, expected differences were found between patients who did and did not consider themselves to be in remission. Fourth, the sample was drawn from a single large, general, adult outpatient, private practice setting, in which the majority of the patients were white, female, and in their 30s and 40s. Generalizability to samples with different demographic characteristics needs to be demonstrated. Fifth, we did not systematically record the treatments received by patients. Patients received different medications, and a subset of patients was receiving psychotherapy, thereby increasing the generalizability of the findings to routine clinical practice. However, we did not examine whether modifications in treatment differentiated HDRS remitters who did and did not consider themselves to be in remission from depression. This question would be useful to examine in future studies. And sixth, we did not assess diagnostic comorbidity. While we asked patients to indicate whether they considered themselves to be in remission from depression, perhaps the patients who did not consider themselves in remission were considering the symptoms associated with comorbid psychiatric disorders. The issue of diagnostic comorbidity and its impact on defining remission may be less relevant to industry-sponsored treatment trials because patients with comorbid conditions are often excluded.[42] However, in real-world clinical practice, the impact of comorbidity on defining remission, and how this might impact on algorithm-based treatment recommendations, warrants study.

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