Tools and Strategies for Ongoing Assessment of Depression: A Measurement-Based Approach to Remission

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The goal of treatment for major depressive disorder is remission, but many patients do not achieve complete remission, and few reach sustained remission (ie, recovery). However, systematically using clinical strategies such as implementing measurement-based care tactics and following treatment algorithms can improve the accuracy of ongoing assessment of depressive symptoms, better inform treatment decisions, and make sustained remission more likely. Measurement-based care tactics include using assessment tools to measure medication adherence, side effects, depressive symptoms, and suicide risk. Particularly useful in clinical practice are the Frequency, Intensity, and Burden of Side Effects–Rating (FIBSER) questionnaire; the 9-item Patient Health Questionnaire (PHQ-9); and the 16-item Quick Inventory of Depressive Symptomatology (Clinician-Rated or Self-Report versions; QIDS-C or QIDS-SR). The use of these measurements at regular patient visits can be combined with the use of treatment algorithms so that appropriate treatment selections are made on the basis of assessment tool results at critical decision points in follow-up. This article includes an example of how, at each treatment step, assessments can be made and results used to monitor progress toward remission, efficacy of dosage, and tolerability and to make informed, evidence-based treatment decisions.

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Many patients who are treated for major depressive disorder (MDD) do not achieve remission. However, 2 strategies that physicians can employ to improve outcomes are systematically measuring patients' progress and following proven sequenced treatment algorithms. The measurement tools and tactics described in this article can assist clinicians in making treatment decisions that help patients move toward remission.

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REMISSION AS THE TREATMENT GOAL IN MAJOR DEPRESSION

In the treatment of MDD, outcomes are classified as response, remission, recovery, relapse, and recurrence.[1] *The Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision (*DSM-IV-TR*)[2] describes full remission as having no significant signs or symptoms of the disorder during the past 2 months; the *DSM-IV-TR* describes partial remission as occurring when symptoms are present but the full criteria for a major depressive episode are not met, or when a period without any significant symptoms occurs but lasts less than 2 months.[2] Achieving remission is the goal of acute treatment, and sustaining remission (ie, achieving recovery) is the ultimate treatment goal. *Relapse* is the return of a depressive episode during remission, and *recurrence* is the return of a depression episode during recovery.

For more than a decade, remission of all symptoms has been the standard goal in the treatment of MDD. Remission should include resolution of both emotional and physical symptoms. The goal of remission places emphasis on restoration of the patient's full functional capacity, which includes return to work, resumption of hobbies and personal interests, and restoration of personal relationships.[3] Aiming for remission and recovery helps the patient to feel that he or she is not only moving away from the illness but also moving toward symptom-free status and a return to previous levels of functioning.

Remission is the goal of depression treatment because failing to achieve remission has negative consequences.

For Clinical Use

- To encourage remission, clinicians should use patient information gathered via measurement-based care in conjunction with algorithm recommendations.
- A systematic measurement strategy using appropriate assessment tools should be used to evaluate patients' symptoms, adverse events, and medication adherence at critical decision points throughout the treatment of MDD.
- Clinicians should be persistent when treating MDD because several treatment steps may be needed for some patients to reach remission.

First, in both psychiatric and primary care settings, relapse rates are 2 to 3 times higher in patients with major depression who do not achieve complete remission compared with those who do.[4,5] Other well-established consequences for patients who fail to achieve and sustain remission include an increased number of chronic depressive episodes,[6] a shorter duration between episodes,[6] and continued impairment in work and relationships.[7] Further, increased mortality, medical comorbidity, and suicide attempts are associated with unresolved depressive symptoms.[8,9]

Despite the serious potential consequences of incomplete remission of MDD, remission is still too rare. Among patients who start an antidepressant medication for acute depression, about half do not even respond to initial therapy, and remission is seen in only one third of patients.[10] About 30% may not reach remission after a series of treatment trials.[11] Accurate measurement of depressive symptoms can help clinicians monitor a patient's progress toward remission and make appropriate treatment choices that encourage remission.

COMBATING TREATMENT-RESISTANT MDD WITH MEASUREMENT-BASED CARE

Several issues contribute to treatment-resistant MDD, but they can be tackled with a system of ongoing assessment and treatment modifications as well as patient involvement. Treatment efficacy and tolerability issues can result in MDD that does not respond to treatment and patients who become nonadherent to medication. For example, treatment may be unnecessarily prolonged without response, have poor long-term efficacy, or result in intolerable side effects that may increase when doses are adequate or combination therapies are used.[12]

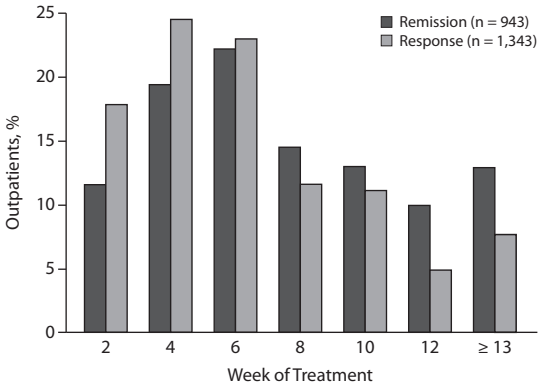
Methodically monitoring patient progress and using this information when making treatment decisions can help combat tolerability and efficacy issues. Systematically using measurement tools to monitor progress and guide treatment choices is known as *measurement-based care*. In this type of care, itemized symptom rating scales or measurement tools provide more sensitive measures of the patient's clinical status than global judgments by the clinician or patient, and these more precise measures then provide a more accurate foundation on which clinicians can make decisions about modifying treatment. Measurement-based care is optimally implemented by adhering to a set visit schedule; regularly monitoring symptom improvements, side effects, and medication adherence; and using a set dose titration and a treatment algorithm. *Critical decision points* in the algorithm provide a timetable for clinicians to evaluate patients' response, tolerance of side effects, and functioning, and to make treatment changes accordingly.

For patients with MDD to achieve remission, a series of assessment and treatment steps may be necessary during the acute phase of treatment. Depression treatment has acute, continuation, and maintenance phases. The acute phase of treatment has traditionally been described as lasting 6 to 12 weeks; patients who achieve remission then move on to a continuation phase of 4 to 9 months, followed by a long-term maintenance phase for those who have chronic or recurrent major depressive disorder.[13] During the acute phase of treatment,[3] a sequence or combination of treatments will be needed if the first-line therapy is not successful; decisions will need to be made using assessments of symptoms and response at each treatment step.[14,15]

Evidence from the Texas Medication Algorithm Project (TMAP)[16] and from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial[10,11,17] supports the view that achieving remission is facilitated if the strategies of using a systematic symptom rating measurement approach and a treatment algorithm are implemented.[18,19] The TMAP trial was a large prospective study that used a 7-stage algorithm and carried out assessments at 6 critical decision points in the acute phase.[18,20] The STAR*D trial was carried out in real-world settings and used an algorithm of 4 treatment steps and a measurement-based approach at every treatment interaction to assess symptoms, identify adverse events or side effects, and monitor patient adherence.[11]

The measurement-based approach used in the STAR*D trial[17] included, for example, measurement of symptoms with the 17-item Hamilton Depression Rating Scale ($HDRS_{17}$)[21] at baseline and exit (week 12) of the first treatment level and measurement of symptom severity with the 16-item Quick Inventory of Depressive Symptomatology, Self-Report (QIDS-SR)[22] at each treatment visit throughout the acute phase of treatment. With this measurement system, clinicians obtained information that was useful in the decision-making process when choosing treatments.

Figure 1. Response and Remission Rates as Defined by QIDS-SR Scores by Treatment Week in Level 1 of STAR*D[a,b]



[a]Reprinted with permission from Trivedi et al.[10]
[b]Response was defined as ≥ 50% reduction in QIDS-SR score from baseline; remission was defined as QIDS-SR score ≤ 5 at endpoint.
Abbreviations: QIDS-SR = Quick Inventory of Depressive Symptomatology, Self-Report; STAR*D = Sequenced Treatment Alternatives to Relieve Depression.

Table 1. Sample Assessment Tools to Implement Measurement-Based Care for Major Depressive Disorder

Measurement	Assessment Tool
Medication adherence and reasons for nonadherence	BMQ[23]
Side effects	FIBSER[24]
Symptomatic improvement	QIDS-C/QIDS-SR[22]
	PHQ-9[28]
	BDI[29]
Suicidal ideation and associated suicidal symptoms	CHRT
	CAST

Abbreviations: BDI = Beck Depression Inventory; BMQ = Brief Medication Questionnaire; CAST = Concise Associated Symptoms Tracking; CHRT = Concise Health Risk Tracking; FIBSER = Frequency, Intensity, and Burden of Side Effects–Rating; PHQ-9 = Patient Health Questionnaire; QIDS-C/QIDS-SR = Quick Inventory of Depressive Symptomatology, Clinician-Rated/Self-Report.

Information from the STAR*D trial provides some lessons about treatment. First, without the benefit of the measurement-based system, many patients who ultimately responded to the initial treatment and achieved remission might have unnecessarily been switched to another medication or received more than 1 treatment (Figure 1).[10] Further, over the 4 treatment steps of the trial, remission rates were 36.8% in Step 1, 30.6% in Step 2, 13.7% in Step 3, and 13.0% in Step 4, and these rates suggest that clinicians should aggressively optimize treatment early because later treatment steps are less likely to produce remission.[11]

Finally, after each acute treatment step, patients who achieved remission could go on to 1 year of naturalistic follow-up, during which they were monitored less closely using measurement-based care than they had been in the acute phase; medication management was determined by clinician judgment and usually not QIDS assessments.[11] Relapse rates after each treatment step escalated from 40.1% after Step 1 to 55.3% after Step 2, 64.6% after Step 3, and 71.1% after the final step, and the time to relapse became steadily shorter.[11] Some relapses could possibly have been avoided with more aggressive measurement-based care during this follow-up phase. Patients who had achieved complete remission before entering the follow-up phase consistently had lower relapse rates than those who had not.

The STAR*D study identified critical decision points (weeks 4, 6, 9, and 12) at which changes in treatment tactic were considered on the basis of data from the measurement-based care strategy.[19] In clinical practice as well, using assessment tool data at critical decision points can aid in deciding when to declare a treatment a failure, what to do with patients who have achieved partial improvement, how long to continue successful treatment, and when to discontinue successful treatment.

MEASUREMENT-BASED CARE TACTICS AND TOOLS TO OPTIMIZE TREATMENT

Measurement-based care tactics include monitoring adherence, side effects, and symptom improvement; adhering to a set visit schedule; and using critical decision point guides when making changes in dosage or treatment step or phase.[16] Assessment tools are available to implement the patient-monitoring tactics used in a measurement-based care strategy (Table 1). The purpose of these tools is to provide accurate information about the patient's clinical status and any treatment barriers. This information can be used to personalize and optimally implement treatment.

Measuring Adherence to Medication

A patient medication adherence questionnaire, such as the Brief Medication Questionnaire (BMQ),[23] can provide an estimate of the patient's adherence to medication since the last contact and can provide information about the reasons for nonadherence. Patients are often reluctant to tell a clinician that they have not taken medication regularly but may be more comfortable providing that information in a self-report. If a patient has missed 3 or more of the previous 14 days of medication, clinicians can assume a significant level of nonadherence. If nonadherence was due to concern about side effects, those side effects can be measured and addressed accordingly. Unless adherence is low because of intolerable side effects, the current treatment regimen can be continued, and the reason for nonadherence (eg, stigma) can be dealt with.

Measuring Side Effects

When selecting a first-line treatment, clinicians should specifically ask patients about their tolerance for potential medication side effects; thereafter, the Frequency, Intensity, and Burden of Side Effects–Rating (FIBSER) questionnaire[24]

Table 2. Characteristics of Tools for Assessing Depressive Symptoms

Assessment Tool	Remission Score	Items, No.	Rater
BDI[29]	≤ 9	21	Patient
$HDRS_{17}$[21]	≤ 7	17	Clinician
MADRS[27]	≤ 10	10	Clinician
QIDS-C/QIDS-SR[22]	≤ 5	16	Clinician/patient
PHQ-9[28]	≤ 4	9	Patient

Abbreviations: BDI = Beck Depression Inventory; $HDRS_{17}$ = 17-Item Hamilton Depression Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; PHQ-9 = Patient Health Questionnaire; QIDS-C/QIDS-SR = Quick Inventory of Depressive Symptomatology, Clinician-Rated/Self-Report.

is a useful 3-question self-report tool to assess side effects and is in the public domain.[25] The questionnaire addresses frequency, intensity, and burden of side effects, but, in general, the burden score ($FIBSER_B$) is most useful in monitoring and guiding treatment. A low score of 0 or 2 is acceptable and indicates that current treatment can continue unless concerns about safety or symptom severity exist. An intermediate score of 3 to 4 means that side effects require attention such as a possible dose decrease, and a high score of 5 or 6 indicates that the current treatment is unacceptable and a change such as decreasing the dose or switching medication is needed.

Measuring Depressive Symptoms

Many tools are available to assess depression symptoms, but only the most commonly used ones are discussed here. These scales are used to monitor the patient's progress toward remission. Unfortunately, a 50% improvement from baseline in symptoms is sometimes used as an outcome measure; however, patients who respond with a 50% improvement may still have significant symptoms, depending on baseline severity.

The tools for assessing symptoms of depression have different characteristics (Table 2). The HDRS[21,26] is lengthy and is rarely used in clinical practice although commonly used in research. The Montgomery-Asberg Depression Rating Scale (MADRS),[27] which encompasses the main diagnostic criteria for MDD, is also commonly used in research settings.

In clinical practice, all of the following rating scales are useful for monitoring patients on an ongoing basis: the 9-item Patient Health Questionnaire (PHQ-9)[28]; the 16-item Quick Inventory of Depressive Symptomatology, Clinician-Rated (QIDS-C) and the QIDS-SR[22]; and the Beck Depression Inventory (BDI).[29]

The PHQ-9[28] captures all 9 domains of MDD criteria and assesses how often the patient has been bothered by symptoms in the last 2 weeks. Scores range from 0 to 27. A score of ≥ 9 indicates that the patient is not responding to medication and doses should be increased until maximum doses are reached if side effects are not problematic. Patients with scores ranging from 5 to 8 may have their medication increased or maintained at the same dosage starting at week 4. If scores are < 5, patients may be maintained at the same dosage starting at week 4 if side effects are not problematic.

The QIDS-C and QIDS-SR[22] (available in the public domain[25]) also contain the 9 domains of MDD criteria. Scores again range from 0 to 27, and, because the QIDS tools assess both frequency and intensity of symptoms, they provide a more finely nuanced assessment than the PHQ-9. A score of ≤ 5 indicates remission and generally leads to a recommendation to continue current treatment, a score of ≥ 9 indicates significant symptoms and suggests that a change of treatment should be considered, and a score of 6 to 8 indicates partial response and suggests either considering a treatment change or continuing with the current treatment for longer to see if subsequent results produce the desired outcome.

The BDI[29] is a self-report questionnaire that measures the intensity of depressive thoughts and attitudes.

Conducting Other Assessments

Several other assessment tools have been developed and include the Concise Health Risk Tracking (CHRT) scale (M. H. Trivedi, MD; S. R. Wisniewski, PhD; D. W. Morris, PhD; et al, manuscript submitted), which assesses suicidal ideation, and the Concise Associated Symptoms Tracking (CAST) scale (M. H. Trivedi, MD; D. W. Morris, PhD; M. Fava, MD; et al, manuscript submitted) that monitors symptoms associated with suicide. These tools are in line with US Food and Drug Administration warning labels for antidepressants.

Scheduling Assessments

In consultation with the patient, clinicians should initially attempt to select a first-line treatment that is likely to be effective for and tolerable to the patient.[14] Patients should then be assessed for adequacy of response every 2 weeks for the first 6 weeks of each treatment step, or as often as possible. Telephone follow-up assessments may also be used at the clinician's discretion. After 6 weeks, patient visits should be scheduled every 3 weeks until the patient experiences remission or a change in treatment strategy is made. Once remission is achieved, the clinician should assess the patient every 3 months.

Using Critical Decision Points

The information gathered via assessment tools at patient visits should be used to make treatment decisions at the critical decision points of weeks 2, 4, 6, 9, and 12, as was done in STAR*D.[10] Treatment options for partial response and nonresponse are available in treatment algorithms[15,16] and include maximizing dose and duration of treatment and seeking multi-neurotransmitter effects by switching or augmenting antidepressant medication. A combination of 2 antidepressant medications can be considered, particularly later in the treatment algorithm, but special attention must be paid to adverse events and side effect burden. After 2 treatment failures, atypical antipsychotic agents can be tried. Somatic treatments such as electroconvulsive therapy, vagus

Table 3. Example of a Measurement-Based Care Schedule Using Assessment Tools in the Acute Phase Treatment of Major Depressive Disorder[a]

Critical Decision Point (CDP)	Clinical Status		Plan
Week 0 (CDP #1)	$HDRS_{17} \geq 14$	Symptomatic	Initiate medication; adjust dose to lower end of therapeutic dose range or serum level
Week 4 (CDP #2)	QIDS-$C_{16} \leq 5$	Remission	Continue current dose
	QIDS-$C_{16} = 6–8$	Partial response	Continue current dose Consider increasing dose
		SEs intolerable	Continue current dose and address SEs Switch to another antidepressant
	QIDS-$C_{16} \geq 9$	Nonresponse	Increase dose Switch to another antidepressant
		SEs intolerable	Switch to another antidepressant
Week 6 (CDP #3)	QIDS-$C_{16} \leq 5$	Remission	Continue current dose
	QIDS-$C_{16} = 6–8$	Partial response	Increase/maximize dose Use augmentation
		SEs intolerable	Continue current dose and address SEs Switch to another antidepressant
	QIDS-$C_{16} \geq 9$	Nonresponse	Use augmentation Switch to another antidepressant
		SEs intolerable	Switch to another antidepressant
Week 9 (CDP #4)	QIDS-$C_{16} \leq 5$	Remission	Continue current dose
	QIDS-$C_{16} = 6–8$	Partial response	Increase dose Use augmentation Switch to another antidepressant
	QIDS-$C_{16} \geq 9$	Nonresponse or SEs intolerable	Switch to another antidepressant
Week 12 (CDP #5)	QIDS-$C_{16} \leq 5$	Remission	Go to follow-up phase
	QIDS-$C_{16} = 6–8$	Partial response	Switch to another antidepressant Increase dose and reevaluate in 2 weeks[b]
	QIDS-$C_{16} \geq 9$	Nonresponse or SEs intolerable	Switch to another antidepressant

[a]Reprinted with permission from Trivedi and Daly.[19]
[b]If after 12 weeks, the patient has not remitted but the clinician feels that 2 more weeks of treatment would be beneficial, treatment may be extended.
Abbreviations: $HDRS_{17}$ = 17-Item Hamilton Depression Rating Scale; QIDS-C = Quick Inventory of Depressive Symptomatology, Clinician-Rated; SEs = side effects.

nerve stimulation, and repetitive transcranial magnetic stimulation may be considered after 2 or 3 treatment failures.

Table 3[19] shows an example of how algorithm recommendations can be integrated with data from individual clinical status assessments at each critical decision point in the acute phase treatment of MDD; the algorithm recommendations are similar to those of STAR*D. For example, at week 4, if the patient's depression shows partial response as determined by a QIDS-C score of 6 to 8, the recommendation is to either continue the current dose or consider increasing the dose. The dosing tactic chosen would depend on evidence about adherence to medication from the BMQ and about side effect burden from the $FIBSER_B$ score.

CONCLUSION

When clinicians systematically use assessment tools to gauge depressive symptoms, adherence to medication, and side effects of treatment in patients with MDD, these measurements contribute to informed decisions when designing individual treatment programs. Using this strategy of measurement-based care with treatment algorithms may result in more patients being able to achieve remission. While remission is the standard goal of acute treatment, physicians must remember the old saying that "better is not well" and that recovery, or sustained remission, is the ultimate goal.

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

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