

Why Depression Goes Unrecognized in Multiple Sclerosis Patients

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Depression is very common among people with multiple sclerosis (MS). Unfortunately, many MS patients with depression do not receive a diagnosis of depression or adequate treatment for the condition. This study was undertaken to investigate screening tools used to assess depression in MS patients as well as the presentation of depression in MS. A total of 20 MS patients from the Texas Tech University Health Sciences Center MS clinic were screened for depression using the Two Question Screen (2QS), Beck Depression Inventory–Short Form (BDI-SF), and Patient Health Questionnaire–9 (PHQ-9). They were also evaluated for a possible major depressive episode (MDE). Results from each screening method were then compared with the corresponding findings from the MDE evaluation for each patient. In addition, each individual's depressive symptoms were quantified, characterized, and compared with screening results. The three depression screening tools yielded inconsistent results. The 2QS correlated best with the MDE evaluation findings. In addition, the number of overlapping symptoms in each patient was proportional to the likelihood of having a positive depression screen. The 2QS appears to be the best diagnostic tool available for detecting depression in MS patients. Clinicians also must be able to identify atypical signs of depression and overlapping symptoms between MS and depression and offer appropriate therapies for their management. Int J MS Care. 2009;11:154–159.

It has been well documented that depression rates in people with multiple sclerosis (MS) are higher than those in the general population.^{1,2} Rates of depression are also higher in MS patients than in people with other chronic illnesses and other neurologic conditions.^{3,4} Despite this evidence, depression is often either not recognized or not treated in this population. One study found that 25% of MS patients had symptoms of depression that were ignored.⁵ Mohr et al.⁶ showed that over 60% of depressed MS patients were not given antidepressant therapy. This study investigated why depression often goes unrecognized and undertreated in the MS patient population.

The effects of untreated depression, whether occurring alone or in the presence of MS, are debilitating, resulting in diminished quality of life.⁷ In addition to social stress, depression also causes cognitive impairments.⁸ These impairments include delayed information

processing and decreased working memory capacity.⁹ Finally, depression has been shown to interfere with MS treatment programs, hampering successful therapeutic management of the disease.¹⁰ Clearly, improving the recognition and treatment of depression in MS patients can enhance their quality of life, better control depressive and nondepressive MS symptoms, and improve therapeutic outcomes.

In order to properly diagnose depression in MS patients, physicians must first be able to recognize both typical and atypical presentations of symptoms in that population. Although the *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV)* sets forth specific criteria for the diagnosis of a major depressive episode (MDE), many MS patients present with a combination of symptoms that do not qualify them for this diagnosis, such as weepiness, loss of emotional control, and irritability.^{11,12} Furthermore, the diagnosis of depression in those with MS is often complicated by the overlapping of symptoms between depression and MS itself. Overlapping symptoms include fatigue, psychomotor retardation, sleeping problems, and decreased ability to concentrate.⁴ This can make it difficult for the

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clinician to successfully recognize true depression. Second, effective depression screening tools specifically designed for MS patients must be used so that physicians can recognize which patients need to be evaluated further. In recent years, assessment scales such as the Beck Depression Inventory (BDI), the Patient Health Questionnaire–9 (PHQ-9), and the Two Question Screen (2QS) have all been used to assess depression status in MS patients. Because this population is underdiagnosed, however, these tools may not be as effective as was once thought.¹³ Finally, patients themselves may deny or not recognize their own depression. The effects of atypical presentation of depression, overlapping of symptoms, and masking of depression by patients, as well as the effectiveness of depression assessment scales, were explored in this study.

Methods

Participants

Participants in this study were regular attendees of the MS clinic at the Texas Tech University Health Sciences Center (TTUHSC) in Lubbock. Each patient was made aware of the purpose of the study and how the information would be used. The patient then provided written consent to participate. Inclusion criteria for participants were 1) age of at least 18 years, 2) written consent provided by the patient to participate, and 3) documented evidence of an MS diagnosis. All subtypes of MS were included in the study (progressive, relapsing-remitting, and progressive-relapsing). Exclusion criteria were 1) an inability to speak English, 2) significant cognitive impairment, 3) normal bereavement, and 4) other psychiatric disorders such as schizophrenia and bipolar disorder. The baseline characteristics of the study participants are shown in Table 1.

Screening Tools

Each participant completed three depression screenings: the short form of the BDI (BDI-SF), PHQ-9, and 2QS. At the end of the interview, the results of the screens were tabulated and the patient was evaluated for the occurrence of an MDE using the *DSM-IV* criteria. Sensitivities, specificities, and positive and negative predictive values were computed for each screen using the MDE criteria as the standard for comparison.

Beck Depression Inventory–Short Form

The BDI-SF is a self-report depression scale that has been shown to be an appropriate screening tool for MS

Table 1. Baseline characteristics of study participants at time of interview (N = 20)

Characteristic	Value
Age, mean (SD), y	44.1 (13.6)
Gender	
Female, No. (%)	17 (85%)
Male, No. (%)	3 (15%)
Race	
Caucasian, No. (%)	17 (85%)
Hispanic, No. (%)	3 (15%)
Currently taking antidepressants/ anxiolytics, No. (%)	6 (30%)

patients. It consists of 13 items that ask the patient to indicate the degree to which they have various depressive symptoms. Each item has four responses scaled from 0 to 3, with a score of 3 indicating the most severe degree. The BDI-SF covers components of depression such as mood, anhedonia, cognitive changes, suicidal ideation, fatigue, and appetite. The 21-item and 7-item (fast screen) versions of the BDI have both been used to screen for depression in the MS population, while the 13-item version has been validated to screen for moderate-to-severe depression in the inpatient setting.^{14,15} A score above 10 on the BDI-SF was considered to be positive. This screen was completed first, with the patient isolated from others.

Two Question Screen

The 2QS was administered next. In this screening method, patients are asked if they have felt depressed or anhedonic at any time during the previous 2 weeks. An affirmative answer to either of these questions yields a positive screen. The 2QS has been shown to be a sensitive screening tool for diagnosing high-risk individuals for depression in primary-care settings. After a positive screen, however, it is recommended that the patient be evaluated for other symptoms of depression.¹⁶

Patient Health Questionnaire–9

The patient was then assessed with the PHQ-9, which was modeled after the nine symptom criteria for an MDE. The score for each criterion ranges from 0 to 3 and correlates with the frequency of the occurrence of each symptom (not at all, several days, more than half the days, or nearly every day). The maximum possible score is 27, with a higher score indicating increased severity. A score of 10 or above was considered positive.¹⁷

Symptom Mapping

The quality and quantity of depressive symptoms were noted for each participant. The specific symptoms and frequency of their occurrence were recorded and then compared with the participant's scores on depression screenings.

Patient Follow-up

If participants received a positive score on any of the screening tests, they were asked if they would consider treatment, either pharmacologic or psychotherapeutic. Those who were already receiving some form of therapy were asked if they would like to continue with their current treatment or make changes to their therapeutic plan.

Results

This was an information-gathering study designed to gather data on depressive symptoms in a group of MS patients from the Lubbock area.

A total of 23 MS patients were interviewed, of whom 3 were excluded because their diagnoses were retracted. All 20 participants completed all three depression screenings and were evaluated for the diagnosis of an MDE. The total number of positive screens was 29 of 60. Ten

patients (50%) screened positively for the PHQ-9, 13 patients (65%) for the 2QS, and 6 patients (30%) for the BDI-SF. The total number of negative screens was 31. Ten patients (50%) screened negatively for the PHQ-9, 7 patients (35%) for the 2QS, and 14 patients (70%) for the BDI-SF (Fig. 1). The mean (SD) score on the BDI-SF was 7.6 (6.0), and that on the PHQ-9 was 9.9 (6.9).

The results for each of the three depression screenings used were compared with those obtained using *DSM-IV* criteria for an MDE. Using MDE criteria as the standard, sensitivities, specificities, and positive (PV+) and negative (PV-) predictive values were calculated for each screen. The results of these measurements are shown in Table 2. The 2QS had a score of 100% in all categories and thus correlated best with the criteria for an MDE. The BDI-SF had a sensitivity of 46%, a specificity of 100%, a PV+ of 100%, and a PV- of 50%. It correlated least with the criteria for an MDE. The PHQ-9 scored 100% for specificity and PV+, 77% for sensitivity, and 70% for PV-.

The number of overlapping symptoms was assessed in each patient. Two patients (10%) had no overlapping symptoms, and three patients (15%) had only one. Participants in these two groups had negative results for all depression screens.

Another three patients (15%) had two overlapping symptoms, two (67%) of whom had positive screens. The same was true of the three patients (15%) who had three overlapping symptoms. All nine patients (45%) who had four overlapping symptoms had positive screens. Of the 13 participants who had positive depression screens, 4 (31%) did not want to be treated.

Discussion

Undertreatment of Depression

The fact that 65% of the study participants had positive results for one or more of the depression screening tools augments the evidence that MS and depression are closely linked. Notably, however, of the six participants who were currently receiving antidepressants, all but one had positive screens. These data indicate that even when depression is rec-

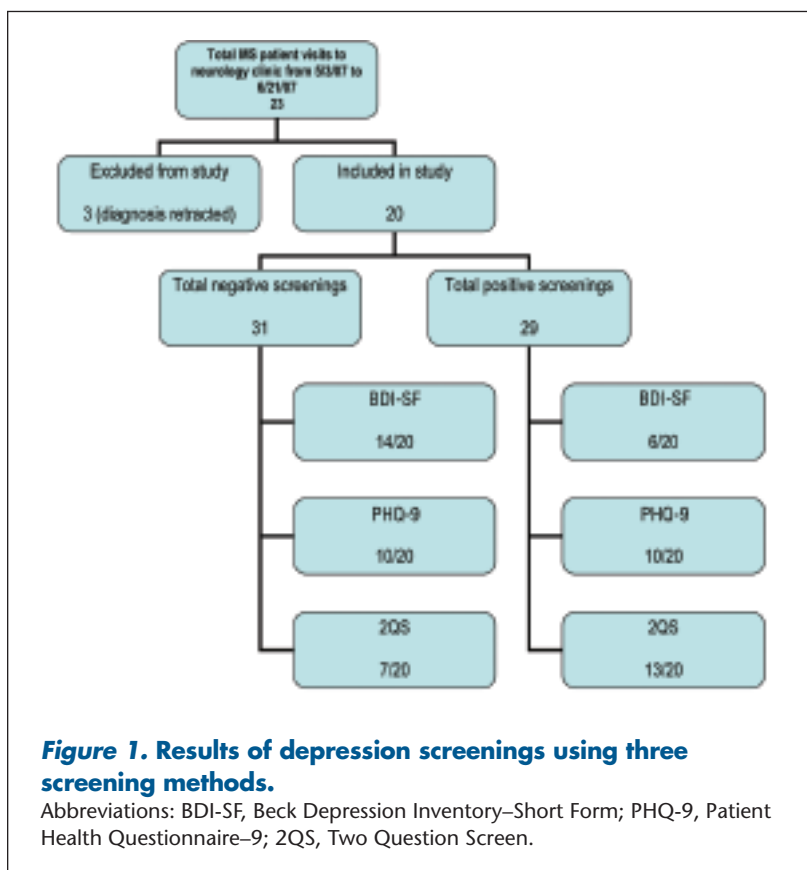


Table 2. Comparisons of three screening tests with major depressive episode diagnostic criteria

Test		Major Depressive Episode			Sensitivity (%)	Specificity (%)	PV+ (%)	PV- (%)
		Positive	Negative	Total				
BDI-SF	Positive	6	0	6	46	100	100	50
	Negative	0	14	14				
	Total	6	14	20				
2QS	Positive	13	0	13	100	100	100	100
	Negative	0	7	7				
	Total	13	7	20				
PHQ-9	Positive	10	0	10	77	100	100	70
	Negative	3	7	10				
	Total	13	7	20				

Abbreviations: BDI-SF, Beck Depression Inventory–Short Form; 2QS, Two Question Screen; PHQ-9, Patient Health Questionnaire–9.

ognized in this population, it is often not adequately treated. In these instances, there may be problems with dosing or with the specific medication given. In addition, psychotherapy can be helpful in managing depression along with drugs. It would be fruitful to evaluate the effectiveness of various antidepressants and psychotherapeutic methods in the MS patient population in the future to prevent depressive relapses.

In order to treat any medical illness, the patient must want treatment and must agree to follow the physician's therapeutic plan. Without patient consent, no treatment is legally or ethically permitted. This certainly holds true for the treatment of depression. In this study, more than 30% of participants with positive screens did not want medical treatment for their depression even though their symptoms caused impairment in their daily activities. One patient felt this way because she did not want to add to her already long list of medications. Two other patients believed that they could deal with their depression on their own, without the use of medicines. Yet another patient was staunchly opposed to using medication even though she was weepy and very emotional during the entire interview. She said that she would rather "put on a face" and "tough it out."

When patients refuse recommended therapies, physicians should not pressure them but rather should try to educate them about their illnesses and inform them of the possible consequences of their decisions regarding treatment. Furthermore, these patients require frequent follow-up evaluations. In MS patients with depression,

psychotherapy can be offered as an alternative to those who decline pharmacotherapy.

Screening Methods

In this study, the individual screening methods yielded differing results. The results of the BDI-SF agreed the least with the criteria for an MDE. Although the 21-item and 7-item versions of the BDI have been shown to be useful depression screens for MS patients, the 13-item version seems to fall short of the task. Therefore, this instrument should not be used to screen MS patients for depression. Surprisingly, the 2QS correlated best with MDE criteria, although the PHQ was modeled on it. Thus the 2QS is the best diagnostic screening tool for depression in MS patients. In addition, of all the depression screening tests, the 2QS is the simplest and takes the least amount of time to complete. Thus it can be a very useful tool in physician offices with high volumes of patients and short turnaround times.

Overlapping Symptoms

The results of this study indicated that as the number of overlapping symptoms a person had increased, so did the likelihood that the person would screen positively for depression. Of the nine participants who had all four overlapping symptoms and consequently screened positively, only one-third were currently taking antidepressants. Thus, not only was the diagnosis of depression missed in most of the people in this group, but the three individuals receiving medication were not being treated effectively. One possible explanation for missed diag-

noses is that the primary focus of the physician is on the treatment of MS, with treatment of depression being a lower priority. It is clear that physicians are recognizing overlapping symptoms, but they may be attributing them to MS alone and failing to explore other causes. Whether the overlapping symptoms stem primarily from depression or result from the MS disease process is irrelevant. Apparently, treating MS alone does not effectively manage the symptoms of depression. Therefore, traditional MS therapy must be supplemented by antidepressant treatment and possibly psychotherapy as well.

Return to the Concept of Masked Depression

According to the *DSM-IV*, patients themselves must admit to feeling depressed or anhedonic in order to be considered clinically depressed. However, patients may be able to mask their depression. The concept of masked depression reached the height of its popularity in the 1970s. It was thought that in certain cases, depression manifested in the form of various nonspecific somatic complaints in the absence of abnormal mood. The theory was eventually discarded because of its broad reach and lack of conceptual clarity. It was further refuted with the release of the *DSM-III*, which called for more specific and descriptive sets of criteria for diagnosing mood disorders.¹⁸ An even broader definition of masked depression was applied to those who did not truly feel sad. Some researchers proposed that there were objective criteria to aid in the diagnosis of masked depression. These included somatic complaints in the absence of physical findings, major life events that could precipitate depression, depressive symptoms in the patient recognized by family members, and physical disease.¹⁹ Still others suggested that the “masking veneer” was dependent on culture, age, sex, and socioeconomic status. This same group found that skilled professionals, those in the middle and upper classes, and generally people living in the western hemisphere were more likely to mask depression and to have more psychosomatic complaints.²⁰ If masked depression truly exists, the only way to make the diagnosis is to unmask it. This can be done only by a physician who has followed a patient for a long time and has established a good relationship with him or her. Unfortunately, the diagnosis will inevitably be made retrospectively.¹⁹

In this study, two patients displayed qualities of masked depression. One patient had negative results on all the screenings. During the interview, she seemed very

happy, energetic, and talkative. She repeatedly denied feeling depressed. She had just given birth to her second child and said she was very happy with her new baby. She denied any problems with work and stated that her family and social life were in good order. She had a history of postpartum depression after the birth of her first child, for which she was treated. At the time of the interview, she was not being treated for a psychiatric illness. One week after the interview, however, she was hospitalized for a psychiatric episode and resumed antidepressant treatment. The chances of suddenly developing a psychiatric illness serious enough to warrant hospitalization in the absence of substance abuse or a traumatic event seem small. It is more likely that the episode was caused by a long-standing psychiatric disease. The event may have indicated a more severe recurrence of postpartum depression, but it also could have been the unveiling of a masked depression.

Another patient also had a questionable screen. Like the patient described above, she had no positive screening results. At the time of the interview, however, her affect was abnormal in that she made little eye contact, seemed distracted, and had poor interaction with her child, whom she brought to the visit. Her responses to questions were short and quick. She took less than 1 minute to fill out the BDI-SF, which took other participants several minutes. She too had a history of previous postpartum depression for which she had received treatment. Other than fatigue, she had no complaints. Ultimately, it is impossible to know whether she was truly depressed, but patients presenting in this manner should

PracticePoints

- All MS patients should be appropriately evaluated for symptoms of depression. The Two Question Screen is the best available screening tool.
- Patients with symptoms of depression should be treated with pharmacotherapy, psychotherapy, or both.
- Clinicians should be able to identify atypical signs of depression and overlapping symptoms between MS and depression and offer appropriate therapies for their management.
- Because depression has been shown to interfere with MS treatment programs, successful treatment of depression can not only relieve depressive symptoms but also improve MS therapeutic outcomes.

be closely monitored for relapses and worsening of symptoms.

Finally, let us return to the weepy, emotional patient who refused antidepressant treatment. Although it is clear that she did not have masked depression, she met many of the criteria for it. As previously mentioned, she stated that she often “put on a face.” She said she was a nurse who grew up in West Texas and was raised to believe that life was hard and that depression was one of the obstacles a person had to overcome in life. It must be remembered that patients approach depression subjectively, and such individual differences must be considered when evaluating these patients for the disease.

Although some consider the concept of masked depression to be too vague and broad to be useful in a clinical setting, the number of atypical and undiagnosed depressions suggests that the *DSM-IV* may be too narrow in its assessment guidelines. Medicine is filled with diagnoses of exclusion, and it could be argued that masked depression falls into this category. In the end, the human mind, together with the physical and psychological factors that govern it, is too complex to be effectively evaluated with a checklist. Rather, the physician must use clinical acumen in addition to the *DSM* criteria to assess mood disorders.

Limitations

The main limitation of this study is its small sample size. Outliers may not have been readily recognized, reducing the accuracy of the results. Furthermore, the participants were from a single MS center, making the results difficult to generalize to a larger population.

Conclusion

Each physician caring for MS patients should make the diagnosis and treatment of depression in this population a priority. Each patient must be screened at every visit in order to map the progress of their mood, preferably using the 2QS. Treatment plans including pharmacotherapy, psychotherapy, or both must be continually evaluated for effectiveness and adjusted as needed. Depression is a disease like hypertension or diabetes, and it should be treated as such. It can be severely debilitating, imposing both physical and emotional burdens on the people it affects. The diagnosis of MS only worsens these problems. Effectively recognizing and treating depression will improve not only MS symptom management but also the quality of life of these patients, which is the ultimate goal of any therapeutic strategy. □

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