Patient Health Questionnaire-9 to Screen for Depression in Outpatients With Multiple Sclerosis

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***Depression is common in multiple sclerosis (MS), with a reported lifetime prevalence of 25–50% and a median point prevalence of 14%. Identification and validation of brief screening tools is essential. The objective of this study was to determine whether the self-administered Patient Health Questionnaire-9 (PHQ-9) is a potentially useful screening tool for depression in an MS clinic population. The PHQ-9 is an increasingly used clinical tool that is brief and specifically queries the American Psychiatric Association's* Diagnostic and Statistical Manual of Mental Disorders IV: Text Revision *(DSM-IV-TR) depression criteria, making it easier for the clinician to diagnose depressive disorders. It has been validated in multiple medical and neurological populations. A total of 248 patients were given the PHQ-9 in the clinic waiting room, and 225 (mean age 43 years, 69% women) provided full responses. Rates of PHQ-9 depression are reported based on two scoring methods. With syndrome-based PHQ-9 scoring, 26 patients (12%) met criteria for either major depression (n = 15, 7%) or subthreshold major depression (n = 11, 5%). With a cut score of ≥10, 19% met criteria for significant depression. Both results are comparable to reported prevalence rates of depression in the MS literature. Twenty patients meeting syndromal depression criteria on the PHQ-9 were available for formal psychiatric evaluation, and all were diagnosed with a depressive disorder. Depressive symptom profiles revealed a low frequency of frank depressed mood and a preponderance of somatic symptoms, particularly fatigue and sleep disturbance. These preliminary results suggest that the PHQ-9 may be a useful tool in screening for depression in outpatients with MS. A formal validation study is indicated.* **Int J MS Care. 2007;9:99–103.**

Of the affective disorders known to be associated with multiple sclerosis (MS), depression is the most common.[1] Patients with MS are found to have a lifetime prevalence of depressive disorders of up to 50%,[1,2] which is higher than the 12.9% lifetime prevalence among patients with other chronic medical conditions.[3] The median point prevalence of major depression reported in the literature is 14%.[1] Despite abundant evidence that depressive disorders are a frequent source of morbidity in MS and that efficacious treatments are available,[4] these symptoms are often poorly documented and treated. This situation may be partly related to confounding of somatic symptoms of MS, most notably fatigue, with those of depression. Furthermore, MS neurologists may be unaware of depression screening measures that are brief and reliable. Most of the previous work on depression screening in MS has been done with the Beck Depression Inventory (BDI), a 20-item dimensional measure of depressive symptoms.[5,6] Although it is frequently used and extensively validated, the BDI is limited in that it does not screen specifically for the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders IV: Text Revision* (DSM-IV-TR)[7] depression criteria, and numerical cutoff scores are not firmly established, thus limiting its usefulness in facilitating the diagnosis of depressive disorders in clinical settings.

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The Patient Health Questionnaire (PHQ) is a self-report measure for DSM-IV psychiatric disorders that has been validated in multiple medical clinic populations, including primary care and obstetrics/gynecology (Figure 1).[8,9] PHQ-9 is the 9-item depression module that is keyed to DSM-IV major depression criteria.[10] It may be scored categorically to diagnose major depressive and subclinical depressive disorders, or it may be used as a continuous numerical measure to assess and track severity of depressive symptoms. The criterion-based scoring system helps to avert confounding of somatic symptoms in medical populations and greatly facilitates rapid review and depressive disorder diagnosis by the busy physician. In addition to the above clinical settings, the PHQ-9 has been validated in chronic renal failure/hemodialysis,[11] traumatic brain injury,[12] and stroke[13] patients and in various ethnic groups.[14] It has been translated and validated in Spanish,[15] and it has been documented to be valid in tracking response to depression treatment.[16]

Given the multiple potential advantages of PHQ-9 in medical and neurological populations, this study aimed to gain preliminary information about its clinical utility in a university hospital MS center.

Methods

As part of a clinic quality-of-life screening project sponsored by the New York Area Chapter of the National MS Society, 248 consecutive patients attending the New York–Presbyterian Hospital Weill Cornell Medical Center MS Clinic were given the PHQ-9 to fill out in the waiting room.

The PHQ-9 queries each of the DSM-IV major depression criteria, including depressed mood; loss of

In the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all 0**	**Several days 1**	**More than half the days 2**	**Nearly every day 3**
1. Little interest or pleasure in doing things	☐	☐	☐	☐
2. Feeling down, depressed, or hopeless	☐	☐	☐	☐
3. Trouble falling asleep OR sleeping too much	☐	☐	☐	☐
4. Feeling tired or having little energy	☐	☐	☐	☐
5. Poor appetite OR overeating	☐	☐	☐	☐
6. Feeling bad about yourself OR that you are a failure OR that you have let yourself or your family down	☐	☐	☐	☐
7. Trouble concentrating on things such as reading the newspaper or watching television	☐	☐	☐	☐
8. Moving or speaking so slowly that other people could have noticed OR being so fidgety or restless that you have been moving around a lot	☐	☐	☐	☐
9. Thoughts that you would be better off dead OR of hurting yourself in some way	☐	☐	☐	☐

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

Figure 1. **Patient Health Questionnaire-9**

interest; disturbances in sleep, appetite, concentration, energy, self-esteem, and psychomotor agitation/retardation; and suicidal ideation. The items address the past 2 weeks and are scored on a 4-point scale (0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day). Responses of 2 or 3 meet threshold criteria and are counted toward making the diagnosis. For the purposes of this study, to provide an estimate of prevalence data on major depression and subthreshold major depression, the PHQ-9 was scored based on standardized criteria,[10] requiring that items 1 (loss of interest) and 2 (depressed mood) met threshold criteria. A total of ≥5 items at or above threshold (including items 1 or 2) qualified for a diagnosis of major depression, and 4 items (including 1 or 2) qualified for a diagnosis of subthreshold major depression. We chose to investigate subthreshold major depression, because a growing body of literature is documenting that subthreshold depressive symptoms adversely affect everyday functioning, are a risk factor for major depression, and are amenable to conventional depression treatments.[17] The authors of PHQ-9 also reported that a sum of all items >10 indicates moderate to severe depression in primary care and obstetric/gynecological samples. We also used this cutoff criterion, hypothesizing that the scoring method would give a higher prevalence estimate of depression based on the heavy somatic symptom burden in MS.

Of the 248 patients, 225 filled out usable questionnaires, with the remainder declining to participate or not giving complete information. The latter 23 patients did not differ in terms of demographic characteristics from those with complete data.

Based on a clinic algorithm, patients meeting criteria for depression were invited to have further depression evaluation by a physician dually boarded in psychiatry and neurology who worked in the MS clinic. These patients were given a semistructured interview and the Structured Clinical Interview for DSM-IV (SCID) depression module. Frequency distributions for depressive disorders based on the two criteria are reported. In addition, the mean scores and frequencies of at or above threshold scores for each PHQ-9 item are reported to provide symptom profiles of these patients. Finally, data on available follow-up psychiatric interviews are provided.

Results

Of the 225 patients, mean age was 43 years (standard deviation 12 years), 68% were women, and 91% were white. Frequencies of PHQ-9 depression diagnosis by categorical syndrome-based and continuous cut-score criteria are presented in Table 1.

Application of the continuous criterion estimated that 19% of clinic patients had moderate to severe depressive symptoms, compared to 12% of patients meeting criteria for a depressive disorder, either major or subthreshold major depression. The depressive symptom profiles of this MS sample are depicted in Figure 2, where the percentage of the sample who met threshold criteria ("more than half the days" or "nearly every day") is plotted for each of the symptoms. Not surprisingly, nearly one-third of patients endorsed high levels of fatigue, and one-fourth of them endorsed significant sleep disturbance. Of the two cardinal depression criteria, loss of interest (anhedonia) was nearly twice as frequent as depressed mood, which was reported at threshold levels in only 8% of patients. Only four patients (2%), all of whom had a major depressive disorder, had suicidal ideation at threshold levels.

Based on the results of the clinic screening protocol, the 26 patients who met PHQ-9 criteria for a depressive disorder were offered formal psychiatric evaluation. Twenty of them were evaluated formally, and the rest continued treatment with the clinic neurologist. All of these patients were found to have major depressive disorder, and, as clinically indicated, depression treatment was initiated or current treatment was augmented.

Discussion

This preliminary clinical study suggests that PHQ-9 is a useful screening tool in MS and warrants formal validation. Specifically, the proportion of MS clinic patients who scored above the cutoff for significant depression

Table 1. Estimated frequencies of depression based on two scoring criteria

Scoring methodology	Patients meeting threshold, %
PHQ-9 total score ≥10	19
Categorical diagnosis	
Major depression	7
Subthreshold major depression	5
Total (either disorder)	12

PHQ-9, 9-item Patient Health Questionnaire for depression

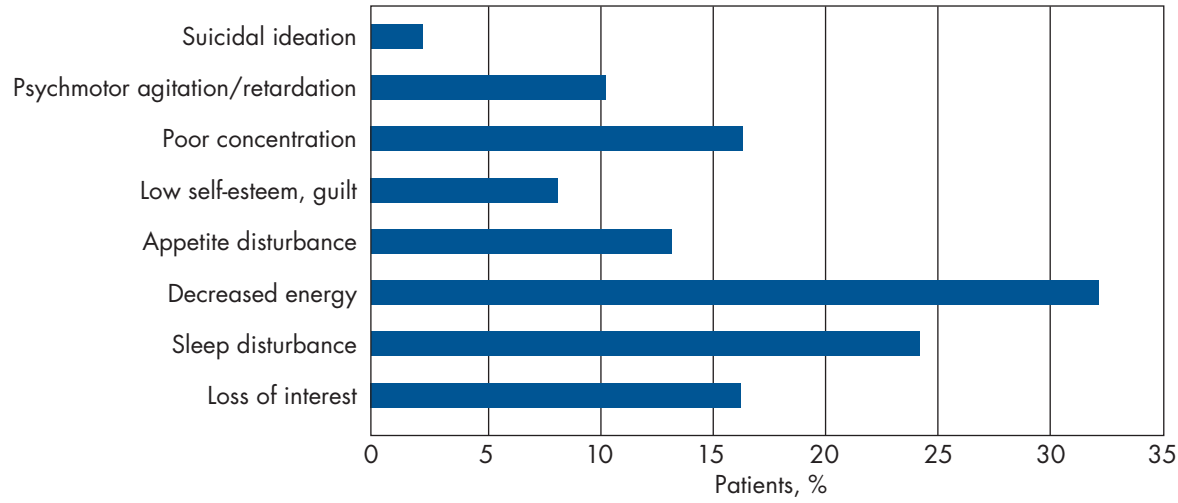

Figure 2. **Multiple sclerosis clinic patients meeting threshold criteria for each of DSM-IV major depression criteria queried by 9-item Patient Health Questionnaire for depression.**

with either of two PHQ-9 scoring criteria was similar to point prevalence rates previously reported in the literature (median 14%). With the more inclusive continuous scoring criterion for PHQ-9, the prevalence estimate was 19.1% for significant depressive symptoms, whereas the more conservative categorical scoring criteria revealed that 12% met criteria for either major or subthreshold major depression. All of the patients with a categorical depression diagnosis who had a formal psychiatric evaluation were diagnosed clinically with major depression, suggesting that the PHQ-9 may have a high degree of specificity for detecting depressive disorders.

An analysis of the individual major depression criteria symptoms revealed that MS patients experience a preponderance of somatic symptoms of depression, particularly fatigue and sleep disturbance. Fatigue and sleep disturbance are common in MS, independent of mood disturbances, and warrant close screening and treatment in their own right. Previous reports documented the prevalence of disabling fatigue to be 40% in MS patients,[18] similar to the proportion (33%) indicated by the PHQ-9 single-item query in this study. Indeed, we concurrently administered the Chalder Fatigue Scale (CFS)[19] physical fatigue subscale and found that the score on the PHQ-9 fatigue item bore a high degree of correlation with the CFS total score ($r = 0.84$, $P < .0001$). Thus, PHQ-9 enables screening for fatigue (and perhaps sleep disturbance) even when depression is not present.

Another interesting finding is that depressed mood as a cardinal symptom of depressive disorder in MS is relatively infrequent and that loss of interest or anhedonia is more likely to be a clinical indicator of depressive disorder. This may be related to the neurobiological disturbances associated with MS, including perturbations in subcortical and frontal systems that produce apathy, ie, diminished initiation, motivation, drive, and hedonic responsiveness. Indeed, recent evidence suggested that white matter volume loss in MS is associated with apathy and other neuropsychiatric symptoms and neuropsychological test impairment.[20] Thus, substantial overlap may exist between the loss-of-interest symptom of depression and apathy in MS, raising the question of whether different depressive "phenotypes" occur in this population that reflect different underlying pathologies.

In discussing the findings of this clinical study, its limitations must be considered. Most important, this is not a formal PHQ-9 validation or depression prevalence study in which all patients filling out the PHQ-9 underwent formal psychiatric evaluation (the gold standard) to verify the presence or absence of depression. Thus, we cannot comment on the specificity and sensitivity of PHQ-9 in the MS population. Furthermore, because of the clinical nature of the study, we cannot reliably relate PHQ-9 data to MS severity, because the latter was not formally documented with a standardized instrument. Also, other clinical variables were not available, such as medication treatments, neuropsychological testing, prior personal or family history of depression, and psychiatric

or medical comorbidities. Nonetheless, we found that PHQ-9 was generally well accepted by clinic patients, easy to fill out, and user-friendly for the clinical neurologists and other staff at the MS center. Based on these favorable initial data, we recommend a formal, multisite validity study of PHQ-9 in MS clinic populations. □

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