Validation of Mood Measures for People with Multiple Sclerosis

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Background: *Valid assessments are needed in order to identify anxiety and depression in people with multiple sclerosis (MS). The objective of this study was to assess the validity of questionnaire measures of mood in people with MS.*

Methods: *People with MS were recruited from a clinic database and asked to complete and return a questionnaire containing the Beck Anxiety Inventory (BAI), Beck Depression Inventory–II (BDI-II), and Hospital Anxiety and Depression Scale (HADS). Those who returned the questionnaire were invited to complete a structured clinical interview, which was blind to the results of the questionnaire.*

Results: *The BDI-II and HADS were both found to be valid measures to detect depression and anxiety in people with MS. An optimum cutoff score of 23 for the BDI-II yielded high sensitivity (85%) and high specificity (76%). An optimum cutoff score of 11 for the HADS demonstrated high sensitivity and specificity for both the Anxiety subscale (sensitivity 90%, specificity 92%) and the Depression subscale (sensitivity 77%, specificity 81%). The BAI had high sensitivity (80%) but poor specificity (46%) for detecting anxiety.*

Conclusion: *The BDI-II and HADS can be used to identify mood disorders in people with MS. Int J MS Care. 2014;16:105–109.*

Depression and anxiety are reported to have a severe negative impact on people with multiple sclerosis (MS)^{1,2} and are associated with a reduction in quality of life.³ As a result of under-identification of these disorders, access to treatment is low, despite evidence that psychological and psychopharmacologic treatments can be effective.² Valid screening measures are needed to identify people with MS who may have depression or anxiety, which requires further evaluation.

The relationship between depression, anxiety, and MS is complex. It is influenced by several factors, including disability,⁴ adjustment to illness,⁵ and social support.⁶ However, there are concerns about the assessment measures used, as many items are affected by the symptoms of MS. There are commonalities in symptoms of mood disorders and MS, such as fatigue and pathologic cry-

ing.⁷ These shared symptoms make differential diagnosis more difficult and may compromise the validity of questionnaire measures. This also limits the ability to determine the prevalence of anxiety and depression in people with MS. Clinical interviews have the advantage that they allow greater exploration of the possible overlap between mood disorders and the symptoms of MS. However, in clinical practice, screening is usually performed by health-care professionals who are not experts in mental health disorders, and therefore standardized questionnaires are used because they require less expertise in administration and interpretation.

Some attempts have been made to validate measures of anxiety and depression commonly used in clinical practice.^{8,9} However, these studies have not used a gold standard comparison, which is necessary to assess criterion-related validity. Within psychiatric disorders the gold standard is considered to be a structured diagnostic interview. Mohr et al.¹⁰ evaluated a very brief screening battery comprising two questions: “During the past two weeks, have you often been bothered by feeling down, depressed, or hopeless?” and “During the past two weeks, have you often been bothered by little interest or pleasure in doing things?” Using a positive answer to either question had 99% sensitivity in relation to major

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depressive disorder on the Structured Clinical Interview for the DSM-IV (SCID) (specificity 87%, positive predictive value 72%, negative predictive value 99%). However, it seems that both assessments were administered by the same researcher and the assessment was conducted over the telephone. In clinical practice it is more usual to use standardized questionnaires in a face-to-face situation. Honarmand and Feinstein¹¹ also used the SCID to validate the Hospital Anxiety and Depression Scale (HADS) in people with MS. They found that using a cutoff score of 8 on the HADS subscales had 90% sensitivity (specificity 87%) for detecting major depression and 89% sensitivity for detecting generalized anxiety disorder (specificity 81%). Quaranta et al.¹² evaluated a scale developed specifically for people with MS, the Multiple Sclerosis Depression Rating Scale, and the Beck Depression Inventory (BDI) in relation to psychiatric interview. They found that both showed good diagnostic accuracy in relation to DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders [Fourth Edition]*) criteria for a diagnosis of “depression with major depression-like episodes” and “mood disorder associated with a general medical condition with depressive manifestations.” There were no significant differences between the two scales in the area under the curve (AUC). The BDI correctly classified 82% of those with depression with major depression-like episodes (cutoff 27, sensitivity 38%, specificity 99%) and 75% of those with mood disorder associated with a general medical condition with depressive manifestations (cutoff 11, sensitivity 86%, specificity 83%). However, these validation studies need replication in independent samples.

The aim of this study was to validate measures of anxiety and depression commonly used in clinical practice with people with MS, by comparing the measures to a gold standard diagnostic interview.

Methods

The study was granted ethical approval by the Leicestershire, Northamptonshire, and Rutland Research Ethics Committee and by the Nottingham University Hospitals NHS Trust Research and Development Department.

Participants were recruited from a database of patients with MS who had consented to be contacted regarding research. Participants were excluded if they had been diagnosed within the last 3 months, were involved in other studies of mood, were unable to give informed consent, or did not understand and speak English.

Potential participants were sent information about the study and a questionnaire containing three assess-

ments to complete and return by mail. These were as follows:

- Beck Anxiety Inventory (BAI)¹³: a 21-item self-report measure of the symptoms of anxiety. Items were rated on a 4-point scale. A score of 16 or above indicates anxiety.
- Beck Depression Inventory–II (BDI-II)¹⁴: a 21-item self-report measure of the severity of depressive symptoms. It includes somatic and cognitive-affective symptoms, and each item is rated on a 4-point scale. Scores of 19 or above indicate depression. It has been validated with people with MS who have been recently diagnosed¹⁵ and those who have had MS for several years.¹²
- Hospital Anxiety and Depression Scale (HADS)¹⁶: a 14-item self-report measure with two subscales. A score of 8 or above on either subscale indicates possible anxiety or depression. The HADS has been found to have high sensitivity and specificity in relation to clinical interview¹¹ and to other mood rating scales⁸ in people with MS.

All participants were interviewed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN)¹⁷ by an independent researcher who was blind to the questionnaire scores. The SCAN is a structured clinical interview that provides diagnostic classifications based on the *International Classification of Diseases, 10th Revision* (ICD-10)¹⁸ and *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision)* (DSM-IV-TR).¹⁹ After the interview, participants were classified as having a diagnosis of depression (major depressive disorder, dysthymic disorder) or anxiety (generalized anxiety disorder, specific phobia) using the ICD-10 and DSM-IV-TR criteria. Interviews were conducted as soon as possible after the questionnaires were received. Data were gathered on demographic characteristics for each participant, including the level of disability using the Guy's Neurological Disability Scale.²⁰

Results

Of the 60 participants who completed the questionnaires, 34 also completed the interview. The demographic characteristics of the participants are shown in Table 1. The distributions of scores on the questionnaires are also shown in Table 1.

On the SCAN, 13 participants (38%) were identified as depressed and 10 (29%) as anxious. The sensitivity and specificity of the questionnaire measures were determined using the predefined cutoff points on questionnaires. Results are shown in Table 2. The results showed that the BDI-II and HADS Anxiety subscale had accept-

Table 1. Characteristics of study participants (N = 34)

Characteristic	Value
Gender, No. (%)	
Men	10 (29)
Women	24 (71)
Type of MS, No. (%)	
Relapsing-remitting	19 (55.9)
Secondary progressive	10 (29.4)
Primary progressive	4 (11.8)
Unknown	1 (2.9)
Age, mean (SD), y	48.5 (11.1)
Years since diagnosis, mean (SD)	11.9 (8.6)
Disability, mean (SD) score	
Guy's Neurological Disability Scale	18.1 (8.3)
Mood measure, mean (SD) score	
BAI	14.4 (9.8)
BDI	19.0 (13.4)
HADS-Anxiety	7.2 (5.4)
HADS-Depression	8.1 (5.9)

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; HADS, Hospital Anxiety and Depression Scale; MS, multiple sclerosis.

able sensitivity (>80%) and all measures had acceptable specificity (>60%). The positive predictive value was generally low (56–61%), but negative predictive values were acceptable ($\geq 82\%$). The AUC was statistically significant, but the correspondence between measures was low for the HADS Depression subscale (kappa statistic, 0.41).

A receiver operating characteristic (ROC) curve was used to determine the optimum cutoff score for each of the measures—the score that yielded the best balance between sensitivity and specificity. Results are shown in Table 3 and ROC curves in Figures 1 and 2. The results showed that the BAI (cutoff 9/10), BDI-II (cutoff 22/23), and HADS Anxiety subscale (cutoff 10/11) had acceptable sensitivity (>80%), but the BAI did not have

acceptable specificity (46%). The positive predictive value of the BAI was low (38%), but negative predictive values of all measures were acceptable ($\geq 85\%$). The AUC was statistically significant, but the correspondence between measures was low for the BAI (kappa statistic, 0.20).

Discussion

The sample was representative of the general population of people with MS in terms of age and gender, but with slightly fewer participants with secondary progressive MS than would be expected.²¹ The screening questionnaires were always administered before the psychiatric interview, and the time interval between the two was not recorded. Although it was generally within 2 weeks, this was not always possible, and some patients may have changed during the intervening period.

The BDI-II and the HADS were found to have good criterion validity for screening mood disorders in people with MS, although the optimum cutoff scores were slightly higher than those recommended in the test manuals. The BAI was not found to be valid for screening for anxiety in people with MS.

The assessment of validity of the BDI-II in recently diagnosed people with MS¹⁵ suggested that a lower cutoff score of 13 was needed, as opposed to the higher score of 23 in the present study. It may be that as more symptoms arise with the development of MS, there is greater overlap with the symptoms of depression, and therefore the cutoff scores need to change as the disease progresses. An alternative explanation is that people with MS who have been recently diagnosed may meet the criteria for an adjustment disorder rather than depression.¹⁹ The optimum cutoff score identified was also higher than that recommended by Quaranta et al.,¹² who also studied patients late after onset. It may be that differences arose owing to the different psychiatric interview methods used.

A Canadian validation of the HADS concluded that the measure was valid, but found that the optimum

Table 2. Classification of study participants using published cutoff scores

	BAI	BDI-II	HADS-Anxiety	HADS-Depression
Cutoff	15/16	18/19	7/8	7/8
Cases identified, No. (%)	12 (35)	18 (53)	16 (47)	17 (50)
Sensitivity (95% CI)	0.70 (0.49-0.94)	0.85 (0.58-0.96)	0.90 (0.60-0.98)	0.77 (0.50-0.92)
Specificity (95% CI)	0.79 (0.28-0.65)	0.67 (0.55-0.89)	0.71 (0.74-0.98)	0.67 (0.60-0.92)
PPV (95% CI)	0.58 (0.19-0.61)	0.61 (0.41-0.81)	0.56 (0.48-0.97)	0.59 (0.42-0.90)
NPV (95% CI)	0.86 (0.54-0.97)	0.88 (0.64-0.98)	0.94 (0.76-0.99)	0.82 (0.61-0.96)
AUC (95% CI)	0.77 (0.57-0.96)	0.89 (0.78-0.99)	0.94 (0.85-0.99)	0.88 (0.77-0.99)
Kappa statistic	0.47	0.48	0.52	0.41

Abbreviations: AUC, area under the curve; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; NPV, negative predictive value; PPV, positive predictive value.

Table 3. Classification of study participants using optimum cutoff scores

	BAI	BDI-II	HADS-Anxiety	HADS-Depression
Optimum cutoff	9/10	22/23	10/11	10/11
Cases identified, No. (%)	21 (62)	16 (47)	11 (32)	14 (41)
Sensitivity	0.80	0.85	0.90	0.77
Specificity	0.46	0.76	0.92	0.81
PPV	0.38	0.69	0.82	0.71
NPV	0.85	0.89	0.96	0.85
AUC	0.77	0.89	0.94	0.88
Kappa statistic	0.20	0.58	0.79	0.57

Abbreviations: AUC, area under the curve; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory–II; HADS, Hospital Anxiety and Depression Scale; NPV, negative predictive value; PPV, positive predictive value.

cutoff score was 8 rather than 11,¹¹ and consistent with the test manual. The discrepancy may be due to the use of a different clinical interview, since the SCID was used in the Canadian study, whereas the SCAN was used in the present study. Use of the higher cutoff scores on the BDI-II and HADS yielded the same level of sensitivity as the standard cutoffs but improved the specificity. The choice of cutoff will rest on the purpose of screening and whether it is important not to classify those with no mood disorder as possibly having a mood disorder. It may be appropriate to identify those with adjustment disorder if the resources are available to treat them. In clinical practice, this would usually mean that people receive further assessment and therefore would increase the assessment load but not have a detrimental effect on people's clinical care. These variations highlight the need for independent validation studies to confirm optimum cutoffs that may be applied across settings.

The BAI demonstrated poor agreement with the clinical interview. This is consistent with studies in

which the BAI has demonstrated poor agreement with alternative measures of anxiety.⁸ The BAI diagnosed anxiety more frequently than the clinical interview (47% vs. 29%). This overestimation may be due to the focus on physical symptoms of anxiety in the BAI, which leads to overlap with the physical symptoms of MS.

One of the limitations of the study is the small sample size, but despite this there was an approximately normal distribution of scores on questionnaires and a sufficient number of people who met the criteria for caseness. Screening for mood disorders is recommended for all those with a chronic physical illness,²² and these results indicate that the BDI-II and HADS are appropriate screening measures for people with MS. They may therefore be used to identify those who need further evaluation and treatment. However, it should be noted that screening programs have potential detrimental effects and may not necessarily result in improved care and outcomes for patients.^{2,23} Therefore, the value of using questionnaires to identify mood disorders in clini-

Figure 2. Receiver operating characteristic (ROC) curves to determine optimum cutoffs on questionnaires: classification of depression

A, Hospital Anxiety and Depression Scale (HADS) Depression subscale; B, Beck Depression Inventory (BDI). Diagonal segments are produced by ties.

cal settings needs to be evaluated. Although the measures used in this study demonstrated high sensitivity and specificity, they were not perfect, and some people were misclassified. Therefore, to be effective, any screening should be completed in conjunction with clinical judgment. In addition, the proposed cutoffs need to be confirmed in an independent sample of people with MS. □

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PracticePoints

- Questionnaire measures of mood need to be validated in people with MS.
- The Beck Depression Inventory–II and Hospital Anxiety and Depression Scale were found to be valid measures of mood in people with MS, and an optimum cutoff point was identified for each.
- The Beck Anxiety Inventory was found to be not suitable for screening for problems with anxiety in people with MS.