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Depression in multiple sclerosis: The utility of common self-report instruments and development of a disease-specific measure

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The ultimate objective of the present investigation was to improve the detection of depression in multiple sclerosis (MS) by comparing common self-report depression measures to a new, modified measure, which takes into account the contribution that symptoms of MS may have on individuals' reports. There has been a longstanding concern regarding the accurate assessment of depression in MS, particularly with regard to the overlap of MS symptomatology and neurovegetative depression symptoms on self-report questionnaires, which may lead to an overdiagnosis of depression in MS. To address these difficulties, we previously proposed a "trunk and branch" of depression in MS. This model allows for the delineation of what symptoms are most reflective of depression in MS. By identifying these symptoms, it was possible to develop a modified Beck Depression Inventory (BDI) in which only the items found to be most related to depression in MS are included in the new measure, the MS Specific BDI (MS-BDI). We compared this measure to common self-report instruments (Beck Depression Inventory–Second Edition, BDI–II; Beck Depression Inventory–Fast Screen, BDI–FS; Chicago Multiscale Depression Inventory, CMDI). Results suggest that cutoffs of 4 on the BDI–FS and 23 on the CMDI Mood subscale are most useful when screening for depression in MS, with a sensitivity for both of 100%, while a cutoff of 19 on the BDI–II, a cutoff of 22 on the CMDI Evaluative scale, and a cutoff of 8 on the MS-BDI had high specificities, suggesting they can be used as to assist in diagnosing depression in MS.

Keywords: Multiple sclerosis; Depression; Assessment; Beck Depression Inventory; Self-report.

Depression is a common and debilitating symptom associated with multiple sclerosis (MS). Point prevalence rates reported in the literature range from 27% to 54% (for a full review, see Arnett, Barwick, & Beeney, 2008; Minden & Schiffer, 1990, 1991). Multiyear prevalence rates have also been found to be as high as 42% to 62% (see Nyenhuis et al., 1995), with lifetime prevalence rates ranging from 22% to 54% (see Patten, Fridhandler, Beck, & Metz, 2003). Given its grave impact, proper detection and effective treatment of depression in MS are paramount. However, many investigators have cautioned that adequate detection of depression among chronic medical illnesses such as MS is difficult given the overlap of neurovegetative symptoms of depression and symptoms of the illness. In fact, MS is a disorder for which many of the cardinal symptoms of depression are also hallmarks of the disease. As such, self-report depression instruments applied to this population may not differentiate medical and psychological factors. Many common physical symptoms of MS (e.g., gait change, visual problems, bladder and bowel incontinence, muscle spasticity or stiffness, and numbness/tingling in the extremities) are easily recognizable as being

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caused by MS. However, there are many other frequent symptoms of MS (e.g., fatigue, sleep disturbances, sexual dysfunction, and concentration difficulties) that can easily be misconstrued as symptoms of depression and blur assessment (Strober & Arnett, 2010).

Given this, several studies have examined the use of common self-report measures, which include such neurovegetative symptoms, when assessing depression in MS. To date, these have primarily focused on measures such as the Beck Depression Inventories (Aikens et al., 1999; Avasarala, Cross, & Trinkaus, 2003; Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003; Mohr et al., 1997; Moran & Mohr, 2005; Sullivan, Weinshenker, Mikail, & Bishop, 1995) and the Chicago Multiscale Depression Inventory (CMDI; Chang et al., 2003; Nyenhuis et al., 1995). Although these questionnaires have been shown to be valid in the general population, they, for the most part, have not been standardized for use with MS and may have limited validity when used in this context.

Investigators interested in assuring accurate assessment of depression in medical populations have taken many approaches to remedy this situation. For one, various modifications to the cutoffs of existing measures have been suggested. These modifications typically consist of raising or lowering the cutoff of the measure depending on which cutoff results in prevalence rates closer to the expected prevalence or which cutoff produces optimal accuracy as assessed by receiver operating characteristics (ROC) procedures. Other approaches have involved modifying the measure itself, usually by removing items that are thought to be more related to the medical condition. The removal of somatic symptoms has been a popular approach, because inclusion of them may inflate the total score and be reflective of the medical condition rather than depression.

Evaluation of self-report depression measures in MS such as the BDI have examined the optimal cutoffs as well as the benefit of removing potentially confounded items. More specifically, Sullivan et al. (1995) concluded that the BDI was more heavily weighted by the cognitive, affective, and behavioral components relative to somatic symptoms of depression and therefore valid in MS in its original form. When utilizing ROC analyses they found that the standard cutoff of 9 on the BDI resulted in a sensitivity of 88% but an extremely low specificity of 46%. They suggested that the cutoff be raised to 13 for optimal accuracy. However, even with this cutoff, their sensitivity (71%) and specificity (79%) indicate that a false-negative rate of nearly 30% still remains. Mohr et al. (1997) examined individual items of the BDI and suggested that the fatigue, work difficulty, and concerns about health items be removed as their endorsement was inflated due to MS symptomatology. However, these investigators did not compare the items between nondepressed and depressed MS. These items may be likely to be endorsed by MS patients regardless of whether or not they are depressed. In contrast to this, Aikens et al. (1999) suggested that removal of such items was not warranted as their exclusion did not enhance the reliability (i.e., Cronbach's alpha) of the BDI in MS in comparison to controls, depressed, and medically ill comparison groups. McGuigan and Hutchinson (2006) also found that removing confounded items (fatigue and lack of energy) had negligible effects. Finally, Moran and Mohr (2005) sought to determine whether or not somatic complaints on the BDI were related to depression or MS and whether such complaints would remit if depression was treated. They found that all items of the BDI showed a reduction with treatment. These investigators concluded that all items of the BDI may be sensitive to changes in depression in MS.

The Beck Depression Inventory–Fast Screen (BDI–FS) was more recently developed as a measure for use in medical populations and does not include any neurovegetative symptoms. Benedict et al. (2003) found that the BDI–FS differentiated depressed from nondepressed MS and showed good concurrent validity with the BDI (r = .85) and Center for Epidemiological Studies-Depression Scale (r = .86). In previous investigations with a primary care sample, a cutoff of 4 was found to be the optimal cutoff and to have a sensitivity of .97 and specificity of .99 (Steer, Cavalieri, Leonard, & Beck, 1999).

The Chicago Multiscale Depression Inventory (CMDI) was designed specifically for conditions such as MS and allows for the separation of mood, evaluative, and vegetative symptoms. Chang et al. (2003) performed comparative confirmatory factor analysis and differential item functioning analysis with 433 MS patients and the original standardization sample of the CMDI and were able to replicate the same five-factor structure with the MS group as Nyenhuis et al. (1998) found. They found few items that were endorsed differently by the MS group. Despite this, it should be noted that all scales were significantly higher for the MS group than the standardization sample, suggesting some generalized inflation. This is somewhat consistent with Nyenhuis et al.'s (1995) finding that all subscales and the total CMDI were significantly higher in a depressed sample than in an MS community sample, while all but the mood subscale were higher in MS than in a healthy control sample. Nyenhuis et al. (1995) suggested that assessing depression using only the mood subscale

may be best practice and may result in more accurate prevalence rates that are not inflated due to the inclusion of nonmood symptoms. These investigators substantiated this hypothesis by showing that the point prevalence rate of depression in MS was lowered to 17.7% when utilizing the mood subscale alone compared to 26.6% when using the total CMDI. This prevalence of 17% is closer to the point prevalence found when employing more stringent criteria such as structured clinical interviews. For instance, Feinstein and Feinstein (2001) and Patten, Beck, Williams, Barbui, and Metz (2003) found prevalence rates of 17% and 16%, respectively, using such interviews. These findings suggest that utilizing only the mood subscale of the CMDI may be a more accurate reflection of the prevalence of depression in MS when neurovegetative symptoms are not inflating reports.

With these considerations in mind, we previously developed a "trunk and branch" model of depression in MS to aid in our conceptualization and assessment and guide future development of a disease-specific depression measure in MS (Strober & Arnett, 2010; see Figure 1). In such models, the "trunk" symptoms are those commonly found in both depressed and nondepressed MS patients. These symptoms are thus impacted more by MS than depression per se. The "branch" symptoms are those less impacted by the illness and as such are thought to be endorsed by depressed individuals in this model. Proper identification of what is common in MS and what may exceed expectations is necessary in developing such models. Moreover, symptoms that appear more related to depression in MS need to be identified.

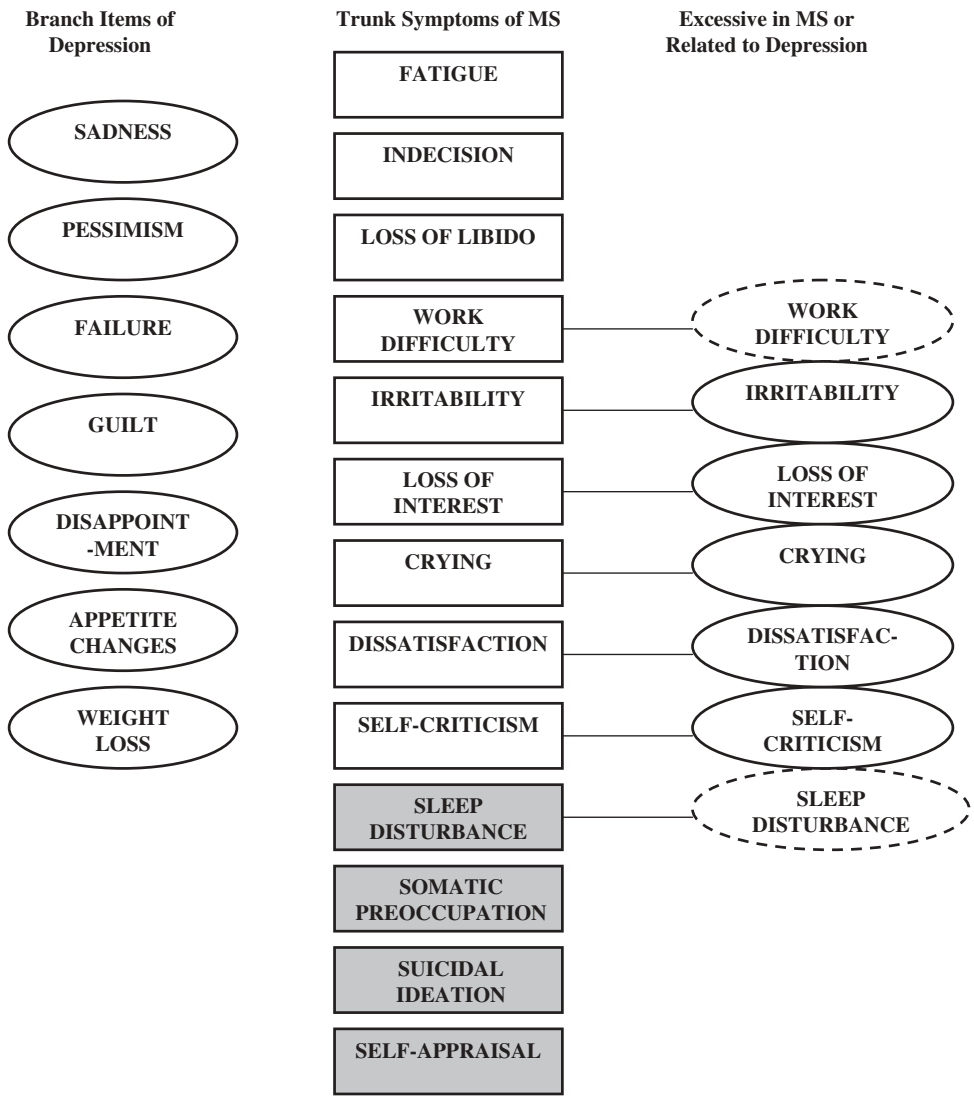

Figure 1. "Trunk and branch" model of depression in multiple sclerosis (MS). Shaded grey boxes are symptoms that were not identified either as a "trunk" or as a "branch" symptom in the previous investigation.

The identification of these symptoms was accomplished by examining endorsement patterns on a self-report depression measure, the BDI, among depressed and nondepressed individuals with MS and healthy, nondepressed controls. In doing so, the following "branch" symptoms were identified: sadness, pessimism, sense of failure, guilt, disappointment, and changes in appetite and/or weight. Symptoms such as fatigue, indecision, loss of libido, work difficulty, irritability, loss of interest, crying, dissatisfaction, and self-criticism were found to be "trunk" symptoms, suggesting that these symptoms are common in MS and are present among both depressed and nondepressed individuals. However, certain "trunk" symptoms were also found to be more severe among those who were depressed, suggesting that while they are common in MS, they may still be indicative of depression. These included: irritability, loss of interest, crying, dissatisfaction, and self-criticism (see Figure 1 for full model). Finally, four symptoms—namely, sleep disturbance, somatic preoccupation, suicidal ideation, and self-appraisal—were not identified as either "trunk" or "branch" symptoms, suggesting that they were not more common either among individuals with MS or among those who were depressed, respectively.

Based on this model, we decided to extend these findings and examine the clinical utility of a revised BDI that only includes the above-mentioned seven "branch' items and the five "trunk" symptoms that were more severe among the depressed sample, as these 12 items are purported to be most indicative of depression in MS. We hypothesized that this revised BDI would have greater specificity than existing measures in detecting depression in MS, given its inclusion of items most indicative of depression in MS. More specifically, we examined the accuracy, derived prevalence rates, and optimal cutoffs of commonly used self-report depression measures (BDI–II, BDI–FS, CMDI) in comparison to this new revised MS Specific BDI (MS-BDI). Based on these findings, we provide recommendations to assist practitioners in assessing depression in MS by providing suggested cutoffs when using common self-report depression measures in screening or diagnosing depression in MS. Please see Strober and Arnett (2010) for more detailed information regarding the study methods and sample.

RESEARCH DESIGN AND METHOD

Participants

Multiple sclerosis participants were recruited through the Western Pennsylvania chapter of the National MS Society and local support group meetings for MS. Exclusionary criteria included history of alcohol/drug abuse; history or current diagnosis of a neurological disorder besides MS (for MS participants); severe visual or motor impairment that may impede cognitive testing that was conducted for purposes outside the scope of the present investigation; evidence of a premorbid learning disability; and severe physical or neurological impairment that would have made evaluation difficult. Inclusion criteria included a diagnosis of definite MS based on the Polman et al. (2010) criteria per patients' neurologists. All procedures were approved by the Institutional Review Board of the Pennsylvania State University.

Procedure

Participants underwent an extensive neuropsychological evaluation as part of an ongoing study examining the contributors to and consequences of depression in MS. A psychosocial interview was conducted on the same day and prior to testing. The battery consisted of cognitive tests interspersed with self-report measures of depression, anxiety, fatigue, and psychosocial factors. Participants and significant others also completed additional self-report questionnaires the week prior to testing. Finally, a structured clinical interview focusing on criteria for *Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM–IV)* major depressive disorder was conducted at the completion of the testing session.

Measures

Structured Clinical Interview for DSM–IV Axis I Disorders–Patient Edition (SCID; First, Spitzer, Gibbon, & Williams, 1995*)*

The SCID for DSM–IV Major Depressive Disorder (MDD) was conducted by the same examiner as the one who administered the testing battery. All examiners were doctoral-level students in clinical psychology trained to criterion in administering the SCID as part of their training. The examiner conducting the interview did so following the five-hour neuropsychological battery and was kept blind to patients' self-report data.

State Trait Anxiety Inventory (STAI; Spielberger & Gorsuch, 1983*)*

The STAI is a 40-item measure divided into two 20-item scales to assess both present (state) and

longstanding (trait) anxiety. Ratings are based on a 4-point Likert scale. Patients are asked to describe how they feel at the present moment (state) as well as how they generally feel (trait).

Beck Depression Inventory–Second Edition (BDI–II; Beck & Steer, 1987*)*

The BDI–II is a 21-item self-report inventory and a revision of the BDI–I. Modifications included allowing for responses indicating both increase and decrease in sleep and appetite as well as the removal of four items (body image, work difficulty, somatic preoccupation, and work difficulty). These items were replaced with items assessing agitation, worthlessness, loss of energy, and concentration difficulty. Patients rate themselves on a 4-point Likert scale ranging from 0 to 3 for the extent that they have experienced the symptom in the past two weeks.

Beck Depression Inventory–Fast Screen (BDI–FS; Beck, Guth, Steer, & Ball, 1997*)*

The BDI–FS was created for use within a medical sample. It consists of only seven items thought to be unconfounded by medical illness (sadness, pessimism, past failure, loss of pleasure, self-dislike, self-criticalness, and suicidal ideation). Patients rate themselves on a 4-point Likert scale ranging from 0 to 3 for the extent that they have experienced the symptom in the past two weeks.

Multiple Sclerosis Specific Beck Depression Inventory (MS-BDI)

The MS-BDI was based on previous findings when developing a "trunk and branch" model to assess depression in MS. It consists only of items on the BDI that were found to be more common or more severe among depressed individuals with MS. These items included: sadness, pessimism, sense of failure, guilt, disappointment, changes in appetite, changes in weight, loss of interest, crying, dissatisfaction, irritability, and self-criticism.

Identification of depressed group

Identification of depressed individuals was based on a diagnosis of MDD using the SCID interview. Eleven individuals met criteria for MDD and constituted the "depressed group." Depressed MS patients were not removed if their anxiety exceeded the cutoff on the STAI given the high comorbidity of depression and anxiety in this sample.

Identification of nondepressed group

The remainder of individuals who did not meet criteria for depression and whose anxiety was not 1.5 standard deviations or more above the mean on the STAI constituted the nondepressed MS group. The latter exclusion was due to the high comorbidity of depression and anxiety and the likelihood that, if we did not exclude nondepressed but anxious individuals when creating our criterion groups, they might be more likely to report depression on the other self-report depression measures used and provide us with less accurate sensitivity, specificity, and prevalence rates. This resulted in the removal of 19 patients, leaving a nondepressed MS sample of 70.

RESULTS

All statistical analyses were conducted using SPSS 21.0 computer software in conjunction with an algorithmic table designed in accordance with Streiner's (2003) publication regarding the sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and positive likelihood ratio (PLR) of diagnostic and screening tools.

Comparisons of depression and anxiety measures between the depressed and nondepressed MS groups were also conducted (see Table 1). Reports of depression and trait anxiety were significantly greater for the depressed MS group than the nondepressed group. There were no significant differences for current anxiety (STAI State scale) between the two groups.

Demographics of the two samples can be found in Table 2. There were no significant differences between the groups on age, education, or estimated IQ.

No significant differences were found between depressed and nondepressed MS on certain disease variables (symptom duration and diagnosis duration), while they were significantly different on their level of disease severity as measured by the Expanded Disability Status Scale (EDSS; see Table 3).

Initial examination of the relationship between the MS-BDI, common self-report depression measures, and depression proneness was established using Pearson correlation coefficients (see Table 4).

The MS-BDI was found to be moderately correlated with depression proneness, $r = .58$ and highly correlated with other self-report measures, rs ranging from .75 to .82, suggesting reasonably good convergent validity.

TABLE 1
Differences between depressed and nondepressed MS on depression and anxiety measures

Measure	*Depressed (N = 11) Mean (SD)*	*Nondepressed (N= 70) Mean (SD)*	*t-test, sig.*
BDI–II	21.81 (6.65)	8.97 (5.19)	$t(79) = -7.34$, $p < .001$
BDI–FS	6.91 (2.43)	1.94 (1.71)	$t(79) = -8.43$, $p < .001$
CMDI Mood	34.36 (9.40)	18.86 (5.26)	$t(79) = -5.34$, $p < .001$
CMDI Eval	29.45 (11.57)	16.71 (3.76)	$t(79) = -3.62$, $p = .004$
CMDI Veg	41.18 (7.01)	33.31 (8.76)	$t(79) = -2.84$, $p = .006$
CMDI Total	105.00 (25.36)	68.89 (13.01)	$t(79) = -4.63$, $p = .001$
MS-BDI	10.18 (4.24)	3.24 (2.31)	$t(79) = -5.31$, $p < .001$
STAI Trait	47.64 (8.08)	35.96 (5.18)	$t(79) = -5.86$, $p < .001$
STAI State	47.82 (6.63)	45.97 (4.34)	$t(79) = -1.15$, $p = .253$

Note. MS = multiple sclerosis; BDI–II = Beck Depression Inventory–Second Edition; BDI–FS = Beck Depression Inventory–Fast Screen; CMDI Mood, Eval, Veg, Total = Chicago Multiscale Depression Inventory Mood, Evaluative, and Vegetative subscales, and total; MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory, STAI Trait = State Trait Anxiety Inventory Trait Scale; STAI State = State Trait Anxiety Inventory State Scale.

TABLE 2
Participant demographics

Variable	*Depressed MS (N = 11) Mean (SD)*	*Nondepressed MS (N = 70) Mean (SD)*	*t-test or χ^2*
Age	43.82 (6.18)	47.59 (9.47)	$t(79) = 1.27$, $p = .206$
Education	14.09 (1.87)	14.37 (1.97)	$t(79) = 0.44$, $p = .659$
WAIS–R IQ estimate	101.09 (7.60)	105.86 (9.14)	$t(79) = 1.64$, $p = .105$
Gender (F/M)	9F/2M	58F/12M	$\chi^2 = .007$, $p = .932$

Note. MS = multiple sclerosis; WAIS–R = Wechsler Adult Intelligence Scale–Revised; F = female; M = male.

TABLE 3
Differences between depressed and nondepressed MS on disease variables

Disease variable	*Depressed (N = 11) Mean (SD)*	*Nondepressed (N = 70) Mean (SD)*	*t, sig.*
EDSS	5.41 (1.45)	4.31 (1.52)	$t(79) = -2.25$, $p = .027$
Diagnosis duration	10.84 (8.61)	12.27 (6.42)	$t(79) = -.527$, $p = .600$

Note. MS = multiple sclerosis; EDSS = Expanded Disability Status Scale.

TABLE 4
Correlations of modified depression measures, common self-report depression measures, and depression proneness among the entire MS sample

Measure	*DPRS*	*BDI–II*	*BDI–FS*	*CMDI*	*MS-BDI*
DPRS		.49**	.49**	.48**	.58**
BDI–II			.83**	.80**	.79**
BDI–FS				.77**	.82**
CMDI					.75**

Note. MS = multiple sclerosis; DPRS = Depression Proneness Scale; BDI–II = Beck Depression Inventory–Second Edition; BDI–FS = Beck Depression Inventory–Fast Screen; CMDI = Chicago Multiscale Depression Inventory; MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory.
**$p < .01$.

To assess the sensitivity, specificity, positive predictive power, and negative predictive power of this new measure (MS-BDI) and the three commonly used measures (BDI–II; BDI–FS; CMDI, full scale and subscales), receiver operating characteristic (ROC) analyses were conducted (see Table 5). ROC procedures also provide information regarding the predictive values of the measure or, more precisely, the number of false positives and false negatives that would result from the use of particular cutoffs. For screening purposes, in which detecting whether an individual exhibits any of the attribute under question (i.e. depression) is central, sensitivity is most important. However, when it is suspected that an individual

TABLE 5
Area under the curve, sensitivity, specificity, negative predictive value, positive predictive value, positive likelihood ratio, and overall correct classification using the Beck Depression Inventory–Second Edition, Beck Depression Inventory–Fast Screen, Chicago Multiscale Depression Inventory, and Multiple Sclerosis Specific Beck Depression Inventory

Measure	*Cutoff*	*AUC*	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*PLR*	*OCC (%)*
BDI–II	13	.93	.909	.771	.385	.982	3.98	79
	14	.93	.909	.814	.435	.983	4.90	83
BDI–II	19	.93	.727	.957	.727	.957	16.97	93
BDI–FS	4	.96	1.00	.786	.423	1.00	4.67	82
CMDI Total	81	.92	.818	.857	.474	.968	5.73	85
CMDI Mood	27	.93	.545	.857	.375	.923	3.82	82
	23	.93	1.00	.814	.458	1.00	5.39	84
CMDI Evaluative	24	.89	.636	.957	.700	.944	14.85	91
	22	.89	.727	.900	.533	.955	7.27	88
CMDI Vegetative	35	.79	.818	.629	.257	.957	2.20	65
MS-BDI	8	.91	.727	.957	.727	.957	16.97	93

Note. AUC = area under the curve; NPV = negative predictive value; PPV = positive predictive value; PLR = positive likelihood ratio; OCC = overall correct classification; BDI–II = Beck Depression Inventory–Second Edition; BDI–FS = Beck Depression Inventory–Fast Screen; CMDI = Chicago Multiscale Depression Inventory; MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory. Based on a prevalence of 14%.

has the attribute, and a diagnosis needs to be made, specificity is more important (Streiner, 2003).

All measures except the CMDI Vegetative scale were considered to have good to excellent test accuracy as measured by the area under the curve (AUC) index (See Table 5). The previously suggested cutoffs of the BDI–II, BDI–FS, and CMDI (total and subscale scores) were first examined. The suggested cutoff of 13 on the BDI–II was found to have a sensitivity of 91% and specificity of 77%, while the recommended cutoff of the BDI–FS of 4 had a sensitivity of 100% and specificity of 79%, suggesting that these cutoffs are acceptable for distinguishing depressed from nondepressed MS. The previously recommended cutoff of 1.5 standard deviations above the mean of controls (see Strober & Arnett, 2010, for description of healthy control sample) on the CMDI total score resulted in a sensitivity of 82% and a specificity of 86%. However, the CMDI Evaluative and Mood scale recommended cutoffs of 1.5 standard deviations above the mean (24 and 27, respectively) demonstrated excellent to good specificity of 96% and 86%, respectively, but poor sensitivity of 64% and 55%, suggesting a significant sacrifice of sensitivity for specificity. Finally, the Vegetative scale of the CMDI performed the worst, with a sensitivity of 82% and specificity of 63%.

By utilizing the ROC curves, the present recommended cutoffs of the BDI–FS remained at 4. However, an increase in 1 point on the BDI–II (cutoff of 14) resulted in an improved specificity of 81%. Moreover, when increasing the cutoff to 19, the BDI–II performed even better as a diagnostic tool with specificity increased to 96%. However, this did come at a cost of sensitivity (73%). With regard to the CMDI, a lower cutoff of 23 for the CMDI Mood scale (sensitivity = 100%, specificity = 82%), and 22 on the CMDI Evaluative scale (sensitivity = 73%, specificity = 90%) were found to improve their utility as screening and diagnostic tools, respectively. Given its novelty, there were no existing cutoffs for the MS-BDI. Review of the AUC coordinates suggested that a cutoff of 8 was most accurate (sensitivity = 73%, specificity = 96%) and approximates what has previously been found by Sullivan et al. (1995) with regard to sensitivity when using a cutoff of 13 on the BDI (sensitivity = 71%). However, the specificity was much improved (79% compared with 96%). Review of the PLRs was also conducted as the PLR is one of the best known determinants on a test's diagnostic accuracy. The PLR assists practitioners in knowing the increase in odds that an individual has the disease when obtaining a positive test result. In general, a PLR of 1–2 indicates an unlikely chance that the individual has the condition. A PLR of 2–5 indicates a small chance; 5–10 suggests a moderate chance; and a PLR >10 indicates a large chance and is almost conclusive that the condition is present. When examining the PLR of all of these measures, the MS-BDI was found to be the best tool for determining the presence of or diagnosis of depression, with a PLR of 16.97. This suggests that the likelihood of an individual being depressed is increased by nearly 17-fold given a positive test result on this measure. Another alternative is to examine the overall correct

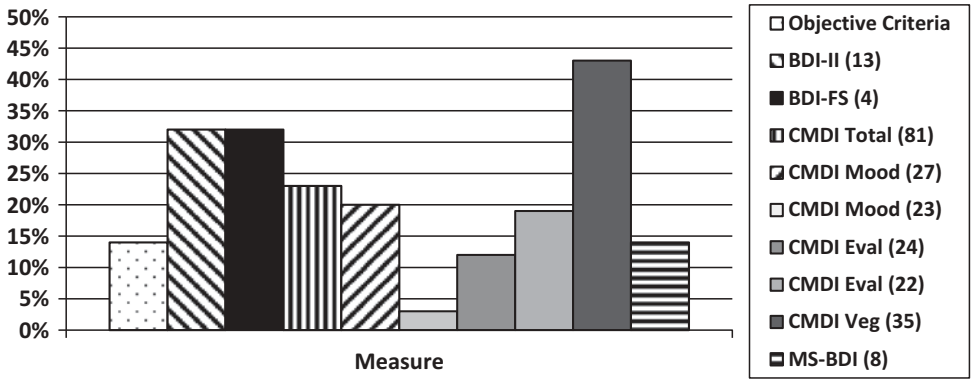

Figure 2. Varying derived prevalence rates of depression per self-report measure. Objective criteria = diagnosis of depression on structured clinical interview. BDI–II = Beck Depression Inventory–Second Edition; BDI–FS = Beck Depression Inventory–Fast Screen; CMDI Mood, Eval, Veg, Total = Chicago Multiscale Depression Inventory Mood, Evaluative, and Vegetative subscales, and total; MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory.

Note. Objective criteria = Diagnosis of depression on structured clinical interview. BDI-II = Beck Depression Inventory-II, BDI-FS = Beck Depression Inventory-Primary Care, CMDI Total = Chicago Multiscale Depression Inventory, CMDI Mood = Chicago Multiscale Depression Inventory Mood subscale, CMDI Eval = Chicago Multiscale Depression Inventory Evaluative Subscale, CMDI Veg = Chicago Multiscale Depression Inventory Vegetative subscale, MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory

classification of the measure. While all but the CMDI Vegetative scale obtained an overall accuracy greater than 79%, the MS-BDI and adjusted score of 19 on the BDI–II were found to have the highest classification accuracy at 93% (see Table 5).

Finally, to further examine the characteristics of the new measure and assess whether or not the MS-BDI would generate more accurate depression prevalence rates, comparisons were made between the prevalence rates resulting from use of this measure and the prevalence rates resulting from use of the BDI–II, BDI–FS, and CMDI. All prevalence rates were then compared to the prevalence rates determined by a diagnostic interview to determine which measure was most accurate (see Figure 2).

As shown, variable prevalence rates were obtained depending on the measure and cutoff, with many cutoffs resulting in prevalence rates higher than those found with our objective criteria. Compared to diagnosis through a structured clinical interview, which resulted in a rate of 14% in the sample, the following measures and cutoffs were most consistent, with rates of 14 to 19%: MS-BDI (cutoff of 8), BDI–II (cutoff of 19), and CMDI Evaluative (cutoff of 22).

Ecological validity of the MS-BDI

To further explore the utility of the MS-BDI, we examined two factors purported to be associated with depression in MS. Namely, we inquired whether individuals had current or past difficulties with depression and whether or not they were employed. Of the 11 identified as depressed by a cutoff of 8 on the MS-BDI, 9 (82%) reported present or past difficulties with depression. Of the 70 who were identified as not depressed per the MS-BDI, only 27 (39%) acknowledged past or present difficulties with depression. This difference was significant, $\chi^2 = 7.20$, $p = .007$. We found no difference in employment status between those identified as depressed and those identified as not depressed on the MS-BDI.

DISCUSSION

This investigation sought to (a) examine the accuracy and derived prevalence rates of commonly used self-report depression measures with an MS sample in comparison to a proposed modified self-report measure; and (b) provide recommendations to assist practitioners in assessing depression in MS by providing suggested cutoffs when using common self-report depression measures in screening or diagnosing depression in MS.

The proposed, new measure (MS-BDI) was guided by a previously developed model of depression in MS, which includes only the 12 items found to best differentiate depressed from nondepressed individuals with MS and does not include symptoms found to be more related to MS (Strober & Arnett, 2010). Given the significant overlap of depression and MS symptoms, common self-report depression measures that include items more related to MS symptomatology may result in inflated prevalence rates. Thus, removing items that are more

related to MS than depression, per se, may result in more accurate assessment. In fact, the literature has shown a prevalence rate ranging from 16% to 26% when more stringent criteria to assess depression in MS (e.g., SCID interviews) are utilized (Feinstein & Feinstein, 2001; Mohr, Hart, Fonareva, & Tasch, 2006; Patten, Beck, et al., 2003), while varying cutoffs of commonly used self-report measures result in prevalence rates that range anywhere from 25% to 33% with some outlying reports as high as 42% (Avasarala et al., 2003; Chwastiak et al., 2002; Nyenhuis et al., 1995; Patten, Lavorato, & Metz. 2005). Given such varying rates, the accuracy of such measures may be compromised when used in MS. By comparing common self-report measures (BDI–II, BDI–FS, and CMDI) with a new measure that consists only of those items most reflective of depression in MS, it was hoped that this investigation would shed some light regarding the potential overlap of MS on reports of depression and potential misdiagnosis.

Given the noted advantages and disadvantages of current measures and the previous development of the "trunk and branch" model in assessing depression in MS, we hypothesized that the MS-BDI would outperform these other measures, resulting in it having the greatest sensitivity, specificity, PPV, NPV, and PLR as a diagnostic tool in MS, while the CMDI Mood subscale would be the most accurate as a screening measure, followed by the BDI–FS, CMDI Evaluative subscale, BDI–II, and, finally, the CMDI Vegetative subscale. It was also expected that the MS-BDI would result in a prevalence rate most akin to the prevalence rate when utilizing more stringent criteria for depression such as a clinical interview.

Based on the findings of the present investigation, some measures appear best for screening for depression in MS and others optimal for diagnosis. More specifically, the BDI–FS (cutoff of 4) and the CMDI Mood Scale (cutoff of 23) performed as the best *screening* tool in MS (i.e., had the best sensitivity, 100%, and sufficient specificity, 78% and 81%, respectively), followed by the BDI–II (cutoff of 14; sensitivity = 91%, specificity = 81%). Of note, however, these latter measures resulted in depression prevalence rates ranging from 28% to 32%. Although this point prevalence rate is consistent with previous findings involving common self-report screening measures that typically show prevalence rates of depression in MS between 25% and 33%, it is higher than what is typically reported for more rigorous diagnostic interview approaches. The finding that the CMDI Mood subscale performed well as a screening tool confirmed our hypothesis, but required some modification to the previously recommended cutoff (lowering the cutoff of 27 to 23). The BDI–FS reigned as the best screening tool and is consistent with previous suggestions that the BDI–FS was well correlated with other self-reports, informant reports, and treatment for depression, making it a more appropriate measure for use in MS (Benedict et al., 2003). Additionally, the finding that the BDI–II performed slightly worse as a screening tool than these measures was consistent with study hypotheses. However, when raising the recommended cutoff of 13 to 14, the BDI–II demonstrated a specificity comparable to the CMDI Mood cutoff of 23 (81%), while maintaining a sensitivity of 91%, suggesting that it is adequate for screening. With regard to assisting with *diagnosis* of depression, measures obtaining high specificity without compromising sensitivity are optimal. With such criteria in mind, the BDI–II, CMDI Evaluative scale, and MS-BDI performed well. More specifically, they all obtained the highest specificity and PLR (as discussed above). As shown in Table 5, the CMDI Evaluative scale initially performed poorly using the previously suggested cutoff of 24, with a significant sacrifice in sensitivity to specificity. However, using the recommended cutoff derived from the ROC curves in the present study (22) resulted in a significant improvement in its applicability as a diagnostic tool, with a specificity of 90% and improved sensitivity of 64% from 73%. Based on the overall performance of all measures, it is suggested that a lower cutoff on the CMDI Evaluative scale, a higher score on the BDI–II, or the MS-BDI be used for assisting in *diagnosis* of depression in MS.

In congruence with the exploration of the accuracy of these measures, the present investigation explored prevalence rates found with each measure. The issue has been raised that varying reports of prevalence rates of depression in MS may be an artifact of the measure used in previous investigations (Nyenhuis et al., 1995). If "all measures are created equal," differences in prevalence rates should not be found in one sample. In fact, in the present sample alone, the prevalence rate varied widely from 13% when using the original suggested cutoffs from the CMDI Evaluative scale, to 44% when using the CMDI Vegetative scale. On more conservative measures and cutoffs, the range was smaller, from 12% to 20%, while the more objective, stringent prevalence (based on the structured clinical interview) was 14%. We theorized in this investigation not only that there would be varying prevalence rates within this sample when using various measures, but that the more accurate measures would derive a prevalence rate similar to the

rate found when using stringent criteria. This was substantiated by the finding that the prevalence rates derived by the CMDI Mood and Evaluative scales and MS-BDI (12% to 20%) were the closest approximation found when using the stringent criteria employed in this investigation as well as others.

Based on the accuracy and derived prevalence rates of the studied measures, it appears that the BDI–FS (cutoff of 4), BDI–II (cutoff of 14), and the CMDI Mood scale (cutoff of 23) are the best available tools to detect or screen for depression in MS. In attempts to obtain a more accurate assessment, in cases where increased certainty of actual diagnosis is needed (i.e., high specificity), a cutoff of 8 on the MS-BDI, as well as a cutoff of 22 on the CMDI Evaluative scale and cutoff of 19 on the BDI–II is recommended. Taken together, we offer guidelines to assist researchers and clinicians in properly identifying symptoms of depression in MS (see Table 6).

Finally, while this investigation provides valuable information and recommendations to guide the assessment of depression in MS, there are several limitations that temper our conclusions. First, the omission of a structured clinical assessment of comorbid anxiety disorders that may have influenced patients' endorsement patterns was problematic. We found that, despite removing individuals whose anxiety was significant from the nondepressed MS sample, depressed MS patients were still significantly higher in trait anxiety than their nondepressed counterparts, something that may have resulted in their overall "over reporting" of symptoms. Future investigations should more systematically examine the influence of anxiety and ways in which it may pervade reports of depression and MS symptoms in MS patients, overall. Another limitation of this investigation was the absence of a depressed healthy control sample. The significance of this investigation would have been improved if there were final comparisons between depressed MS and depressed healthy controls to substantiate the findings that certain symptoms are more representative of depression rather than MS symptoms. A third limitation was the exclusion of participants with a significant present or past use of substances and those with severe visual or motor impairment. We did this because our larger study focused on cognitive functioning. However, given the comorbidity of depression and substance use and the possibility that individuals with more physical impairments are more likely to be depressed, this likely limited our range in enrolling more individuals experiencing significant depression. Related to this, another limitation of this study was the sample size, particularly with regard to our depressed MS sample. In examining the psychometric properties of any new measure or the properties of existing measures, a large sample is ideal and ideally, and the sample will have an equal number of the construct of interest. Subsequent investigations of our new measure using a larger sample size are warranted. In particular, future investigations in both a clinical and community-based samples are needed to determine its utility and aid in the development of this approach and measure. Additionally, replication of the present investigation may show that the CMDI has more utility as both a screening and diagnostic tool if using different cutoffs than what was previously suggested, while replication is also warranted for the BDI–FS as this is the first investigation exploring its sensitivity and specificity in a MS sample. Despite these limitations, our investigation provides clinicians and researchers a better understanding and appreciation of the intricacies involved in assessing depression in individuals with MS. Future work is needed to expand upon these comparative findings to provide convergent validity so that these depression measures in MS can be used with confidence in clinical settings.

TABLE 6
Guidelines for assessing depression in MS

Measure	*Suggested Cutoff*	*Screening*	*Diagnosis*
BDI–II	14	X	
BDI–II	19		X (superior)
BDI–FS	4	X (superior)	
CMDI Total	81		X
CMDI Mood	27		X
	23	X (superior)	
CMDI Evaluative	X		24
	22		X
MS-BDI	8		X (superior)

Note. MS = multiple sclerosis; BDI–II = Beck Depression Inventory–Second Edition; BDI–FS = Beck Depression Inventory–Fast Screen; CMDI = Chicago Multiscale Depression Inventory; MS-BDI = Multiple Sclerosis Specific Beck Depression Inventory.

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