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DEPRESSION IN MULTIPLE SCLEROSIS (MS): THE DISTINCTION BETWEEN MS AND DEPRESSIVE SYMPTOMATOLOGY AND UTILITY OF SELF-REPORT INSTRUMENTS

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Abstract

The long-term objective of the present investigation is to improve the detection of depression in primary care, specifically in Multiple sclerosis (MS) patients. Controversy exists regarding whether or not prevalence rates of depression in MS and the medical population in general, are inflated due to poor delineation of depressive symptoms from medical conditions and use of improper assessment tools. In particular, it has been hypothesized that the overlap of MS symptomatology and neurovegetative depression symptoms (e.g., fatigue, sleep disturbance, weight/appetite changes) on self-report questionnaires may lead to an over-diagnosis of depression in MS. Furthermore, assessment of depression in MS, or any medical sample, is problematic given the difficulty in ascertaining what is a suitable reaction and adequate adjustment to receiving a medical diagnosis and also the impact this has on mood and self-evaluation, both domains of depression as well. Self-report measures may not be the most sensitive tools in delineating these factors but are nonetheless widely used. Self-report measures may not be able to elucidate how patients interpret their medical symptoms or reactions to illness as depressive symptoms without being provided additional information beyond item endorsement. The proposed investigation attempts to explore this issue using a modification of the Beck Depression Inventory (BDI) that asks MS patients to further explain their endorsement of depressive symptoms and how their MS symptoms may contribute to such endorsement. Furthermore, the present investigation proposes to examine the utility of three common self-report instruments (Beck Depression Inventory-II, Beck Depression Inventory-Primary Care, Chicago Multiscale Depression Inventory) and resultant prevalence rates and recommended cutoffs when used with a MS sample.

TABLE OF CONTENTS

List of Tables

List of Figures

Acknowledgments

"I have seen that in any great undertaking, it is not enough for a man to depend simply upon himself."

-- Isna-la-wica, Teton Sioux

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Introduction

Individuals suffering from chronic medical illness are amongst the highest at risk to develop some form of depression (Clark, Cook, & Snow, 1998; Katon, 1984; Katon & Sullivan, 1990; Rodin & Voshart, 1986; Wise & Taylor, 1990). However, depression in the medically-ill patient frequently goes unrecognized, and proper treatment is seldom provided. Research has shown that as many as 50% or more of medical patients with diagnosable depression go unrecognized by their primary care provider (see Clark et al., 1998) with a range of 35% to 65% (see Mulrow et al., 1995). More seriously, medical illnesses, or symptoms of such, may be misconstrued as depression, something that can preclude proper care and attention to the underlying medical condition. Despite the knowledge that there are certain medical conditions in which the comorbidity of psychiatric problems is prevalent, difficulty remains in separating the symptoms of medical illness from those of depression. Possible explanations for inaccurate detection of depression in primary medical care include: (a) the overlap of neurovegetative symptoms of depression and somatic symptoms of illness; (b) difficulty in ascertaining adjustment and reaction to illness as separate from depression; (c) somatization by patients; (d) poor recognition by medical professionals; and (e) the use of self-report depression measures designed for the general, non-medically ill population.

The purpose of the present investigation is to improve our understanding and detection of depression in a medically-ill sample, particularly Multiple Sclerosis (MS) patients, given the above mentioned hurdles. By disentangling which symptoms are common to MS and which are common to depression, a better appreciation of how to best conceptualize and assess depression in MS will be obtained. In doing so, comparisons between healthy controls, non-depressed MS, and depressed MS patients' reports on a modified self-report depression measure will be conducted. Utilization of this modified self-report measure (which includes more qualitative items) will allow MS patients to describe their experience of depression and MS, and their attributions for their endorsement of depressive symptoms. It is hoped that such information will

not only shed light on the phenomenological experience of depression in MS, but will result in a purer measure of depression in MS in which neurovegetative depression items are removed by patients' reports. Finally, comparisons of this new measure and three commonly used self-report depression measures will be conducted to determine the maximal utility of these measures. Given these findings, recommended cutoffs for these measures will be provided for their use in research and clinical settings with MS patients. Most importantly, the overarching objective of this study is to improve the care and treatment to those suffering from MS. It is hoped that this information obtained through this investigation will aid in obtaining this goal.

Assessment of Depression in the Medical Population

Proper assessment of depression in primary care has challenged primary care providers and psychologists for several decades. Disentangling symptoms of depression and medical illness is a significant hurdle and may frequently become an etiological conundrum. Symptoms such as fatigue, sleep disturbance, pain, sexual dysfunction, and loss of energy, amongst others plague individuals suffering from depression and various medical illnesses. Depression may precipitate a medical illness and may also amplify medical conditions while medical illnesses are also more common in the mentally-ill population, particularly depression (Katon, 1984). Reactive hypotheses of depression in the medically-ill further renders it difficult to determine what is depression and what is a normal response or adjustment period to being diagnosed with a chronic medical disorder. Additionally, many patients who are medically-ill, depressed, or both may have higher levels of somatization. Patients with major depression have been found to have significantly more somatic complaints (see Katon & Sullivan, 1990; Zich, Attkisson, & Greenfield, 1990) resulting in increased utilization of health care while potential "shopping" for doctors as a result of vegetative complaints of depression misconstrued as a medical illness is also common (Zich et al., 1990). Physicians are frequently left in a position to decipher the two. As mentioned earlier, another complicating factor regarding proper assessment is the poor recognition of the overlap between neurovegetative depressive symptoms and physical illness

symptoms by medical professionals. Assessment of depression in the medically-ill frequently falls on the shoulders of primary care providers with upwards of 50% to 75% of patients presenting to their primary care physician while only 16% to 23% seek services through a mental health care provider (see Arnau, Meagher, Norris, & Bramson, 2001). This places a tremendous burden on primary care physicians as providing both medical and psychological screening and diagnosis. Several studies have shown that the "miss rate" of depression by primary care physicians is great (see Arnau et al., 2001; Katon, 1984; Katon & Sullivan, 1990). For instance, Moffic & Paykel (1975, as cited by Katon, 1984) showed that medical staff members were only capable of recognizing 4% of their medical inpatients as depressed while objective measures found the rate to be 28.3%. Similarly, Schulberg et al. (1985) found that 74% of primary care patients who met criteria through a structured interview and DSM-III criteria were misdiagnosed. The greatest risk of inaccurate diagnosis is the heightened risk of suicide amongst certain medically-ill patients (Hughes & Kleespies, 2001) heightening the necessity and urgency to properly screen for psychiatric disturbances. In fact, Murphy (1979; as cited by Katon, 1984) found that 15% of patients suffering from major depression for more than one month's time were at risk for committing suicide. Moreover, 82% percent of a sample of successful suicides presented to their primary care physician within one month of their death. More striking though, is that 55% of these individuals died of an overdose of medications prescribed by their physician. Such high liability further supports the need for accurate screening and greater awareness of the medical profession, particularly in light of the strikingly high prevalence rates of psychiatric disturbances in primary care.

Prevalence rates of major depression in primary care in particular, range anywhere from 5% to 10% (Katon & Sullivan, 1990; Mulrow et al., 1995; Steer, Cavalieri, Leonard, & Beck, 1999) yet have also been reported to be as high as 23% to 41% (see Arnau et al., 2001; Zich et al., 1990). Uncertainty regarding the prevalence rates has been partly attributed to the use of varying screening measures. For instance, Mulrow et al.'s (1995) review found prevalence rates

ranging from 4% to 17% using various self-report instruments with some potentially biased reports as high as 31% to 42%. Use of self-report measures and varying cutoffs or modifications is the last and potentially greatest hurdle in properly assessing depression in primary care and is a major focus of this investigation, and will be discussed in detail later. For now, a review of the conceptualization of depression in primary care and how we can begin to best delineate depression from medical symptoms will be conducted.

Conceptualization of Depression in the Medically-ill

Depression in the medically-ill has been conceptualized differently than in the general population given the difficulty of separating medical and psychological symptoms. Clark et al. (1998) present a concise discussion of some of the theories and approaches in assessing the clinical presentation of depression in the medically-ill. For instance, some view cognitive symptoms as the best indicators of true expression in medical populations. Such symptoms include self-accusation, suicidal ideation, hopelessness, sense of guilt, sense of failure, and indecisiveness (Cavanaugh, Clark, & Gibbons, 1983; Goldberg, Bridges, Duncan-Jones, & Grayson, 1988; Hawton, Mayou, & Feldman, 1990). In fact, Clark et al. (1983) conducted a latent trait analysis of the Beck Depression Inventory (BDI) and found that six symptoms depicted depression in a medical sample best. These symptoms were sense of failure, suicidal ideation, sense of punishment, loss of social interest, dissatisfaction, and indecisiveness. I have found in my own research that, in an MS sample, pessimism, failure, dissatisfaction, suicidal ideation, irritability, crying, and loss of interest were the best indicators of depression as measured by the BDI-II. Logistic regression of all items from the BDI-I were conducted to determine which items best differentiated depressed and non-depressed MS patients resulting in these seven items as the best determinants (Strober & Arnett, 2005). Parker, Hilton, Hadzi-Pavlovic, & Bains (2001) also contend that a cognitive-based approach to assessment is recommended for assessing depression in primary care. They found that 16 out of 81 items best differentiated depressed from non-depressed in a medical sample. These items included

brooding, vulnerability, tearfulness, pessimism, depressed mood, demoralization, insecurity, anhedonia, negative self-concept, self-criticism, loss of essence, worthlessness, aloneness, guilt, social withdrawal, and hopelessness/helplessness. Items such as sleeping less, inactivity, difficulty concentrating, among others, were not adequate in differentiating the two. These 16 items were compiled after eliminating "ubiquitous" items that were endorsed by both depressed and non-depressed medically-ill, followed by selecting items that were only endorsed by the depressed subsample and using odd ratios to determine "overrepresented" items among the depressed. Finally, an intercorrelation matrix was done to eliminate redundant items. The resultant 16 item measure was found to have superb internal consistency (Chronbach alpha = .95), and with a cutoff of 18, good sensitivity (100%) and specificity (96%). Furthermore, it showed good convergent validity with both the Beck Depression Inventory – Primary Care (BDI-PC) ($r = .80$, $p < .01$) and Hamilton Depression Scale (HDS) ($r = .72$, $p < .01$).

Others view the somatization found in medical populations as indicators of depression, especially if they are elevated above the expected severity of the medical disorder (Arnau et al., 2001; Katon, 1982, 1984). Cavanaugh (1986) similarly suggested that somatic complaints be used in conjunction with affective-cognitive symptoms of depression to make a formal diagnosis. Examining the severity and frequency of affective-cognitive and vegetative symptoms of the BDI, Canavaugh determined that the *frequency* of vegetative items increased minimally as depression worsened. However, the *severity* of the vegetative symptoms increased linearly as the severity of depression increased. She asserted that, if these somatic complaints were not proportionate to the medical illness, and were related to the affective-cognitive symptoms of depression, they might be more representative of depression. This is consistent with findings that, although sleep disturbance was endorsed quite frequently in an MS sample, it was only related to depression when the endorsement was attributed to psychological factors as opposed to physical factors of MS, suggesting that it exceeded the influence that the disease had on the complaint (Strober, Arnett, Polen, & Bruce, 2002). Similarly, Rodin & Voshart (1986) speak to

the importance of identifying "masked depression" in which pain and other physical complaints are presenting features of depression. Katon (1984) also recommends that reports of neurovegetative components of depression in the medically-ill be taken seriously and that consideration be given to the fact that many depressed patients do not recognize the affective or cognitive symptoms of their condition as well as they do the physical symptoms. Such patients may complain that they are not sleeping well, feel tired all the time, and are not eating before recognizing their negative affect or disinterest. Taken together, these studies suggest that attention be given to all physical complaints, especially if the severity exceeds what is typical for the medical condition. Neurovegetative symptoms of depression, as will be referred to throughout, consists of symptoms such as fatigue, sleep disturbance, appetite/weight changes, diminished concentration, and sexual dysfunction. It is conceptualized that such symptoms of depression can have a direct neurological and/or physiological etiology whereas other symptoms such as self-criticism, guilt, negative self-appraisal, or feelings of punishment are more cognitively derived.

Finally, some investigators have examined the extent to which motivation and behavioral changes are indicative of underlying depression in the medically-ill (Emmons, Fetting, & Zonderman, 1987; Van Hemert, Hawton, Bolk, Fagg, 1993). Such aspects of depression include loss of energy, social withdrawal, lack of interest, and dissatisfaction. In review of these theories, it may appear that no domain of depressive symptomatology is less relevant to the diagnosis in a medical population. What appears more pertinent is the extent to which these symptoms exceed what is caused by or expected in the disease.

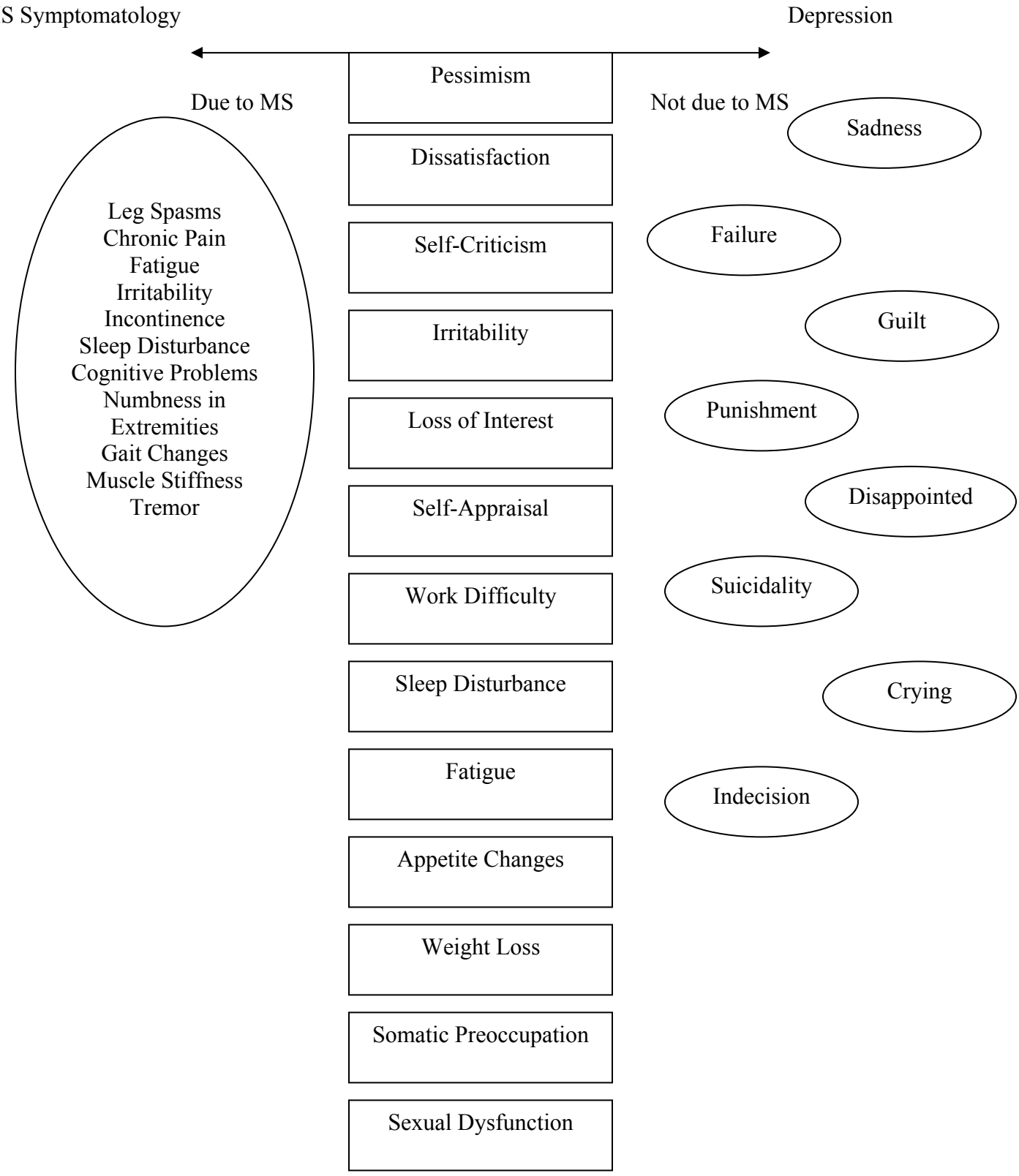
Possible Model for Detection of Depression in Medically-ill Populations

Given the aforementioned theories, inclusion of all items of depression appears warranted in medical populations. However, a re-conceptualization of our assessment models may be needed. Parker et al. (2001) speak to the idea of a "trunk and branch" model when assessing depression

in a medical sample. As will be articulated further below, the proposed investigation involves an adaptation of this model for use with an MS sample (see Figure 1).

Figure 1.

Trunk and branch model of depression



The “trunk” items are thought to be the items commonly found in both depressed and non-depressed MS patients. These items are ones impacted more by MS. The “branch” items are less impacted by the illness, and as such are thought to be endorsed by depressed individuals in this model. Inconsistent with this trunk and branch model, however, was Parker et al.’s study where the depressed individuals reported higher levels of all items, trunk and branch. This may be consistent with Cavanaugh & Katon’s suggestions that not only are the extraneous depressive symptoms endorsed, but that medically related complaints may be disproportionate to the particular medical condition. With a model such as this in place, individual symptoms of depression may be more easily and thoroughly assessed to determine whether they are above the norm for a particular disorder. However, delineating what is a result of the disease, what exceeds expectations for the disease, and what is independent of the disease has not been investigated in the extant literature.

It has been recommended that, in order to determine how much a medical illness contributes to reports of depression, a thorough clinical interview be conducted. However, in both clinical practice and research, interviews are not always practical, or in many cases, even an option. As such, self-report instruments are used more frequently. Nonetheless, the qualitative and diagnostic value inherent in an interview may be lost when patients complete a questionnaire. For instance, someone who endorses sleep disturbance on a depression questionnaire who is in fact depressed may be quite different relative to someone suffering from a medical condition and is sleep disturbed. More specifically, if a patient is subsequently asked about sleep problems in an interview, a diagnostician may find a more precise explanation for the complaint. Patients may report that they are waking for a particular medically related problem or as a result of side effects of medication. Asking patients whether they fall back asleep immediately or stay awake ruminating also sheds light on their complaint and whether it is being driven by medical or psychological factors. Furthermore, for some who endorse both medical

and psychological complaints, erring on the side of caution may be the most prudent course of action. Knowledge of patients' other affective and cognitive symptoms of depression can help determine whether these complaints are due to the psychological complaints. Such information, especially with medical patients, conveys a more specific meaning when examined in its context.

Both the Structured Clinical Interview for DSM-IV (SCID) and the Composite International Diagnostic Interview (CIDI) are designed to follow up with some of the questions outlined above. The CIDI, for example, asks patients how much of their sadness and anhedonia is due to their medical illness or medications. If they report that it is always due to these attributes, a psychiatric diagnosis is not given. Both of these structured interviews emphasize that if an item is mostly due to the medical illness, it should not be weighed as heavily; however, inclusion of the item, if it is not attributable to the illness, is warranted. The inclusion of an "exclusionary criterion" due to a medical condition in the DSM-III-R has in fact shown lower prevalence rates compared to the earlier DSM-III in which this exclusion did not exist. Kathol, Mutgi, Williams, Clamon, & Noyes (1990) found a decrease from a prevalence of depression of 38% using the DSM-III compared to 30% using the DSM-III-R in a sample of cancer patients. The removal of endorsed items that are more attributed to a medical condition is necessary for the assessment of depression in primary care. This approach has yet to be taken with self-report instruments in the assessment of depression in the medically-ill. As such, an additional aim of the proposed investigation is to better understand which items are more related to depression or MS, per se, and to give proportionate weight to such items utilizing a "trunk and branch" model in its assessment on a self-report measure. This brings us to the crux of this investigation – how to best utilize self-report measures of depression in primary care. First, a brief review of some approaches that have been pursued in the literature thus far.

Self-report Measures & the Medical Population

Utilization of self-report measures in the primary care setting has become widespread, given their efficiency and accuracy in assessing depression and other psychiatric complaints in

the general population. Commonly used measures include the Beck Depression Inventory (BDI) Beck, & Steer, 1987), the Center for Epidemiological studies-Depression (CES-D) (Radloff, 1977), and the Zung Self-rating Depression Scale (SDS) (Zung, 1965). Although the above questionnaires have been shown to be valid in the general population, most have not been standardized for use with medical populations and may have limited validity when used in this context. In lieu of this, investigators have made various modifications to existing measures. 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 receives the optimal accuracy. Precision of self-report questionnaires are commonly examined through Receiver Operating Characteristics (ROC) procedures. ROC curves plot the sensitivity (ability to detect) and specificity (ability to rule out noise) of all cutoffs of the measure (Vida, Des Rosiers, Carrier, & Gauthier, 1994). 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 one wants to detect if an individual exhibits any of the attribute under question (i.e. depression), sensitivity is more important in a measure. However, when it is suspected that an individual has the attribute and a diagnosis is to be made, specificity is more important (Streiner, 2003). Under severe consequences, such as suicide, screening measures may employ greater sensitivity, but when trying to determine, or confirm a diagnosis, a measure should contain good specificity. For the purposes of detecting depression in the medically-ill, the distinction should be on what is acceptable for screening and what is advisable for diagnosis. It is suggested by some that a sensitivity greater than 80% and specificity greater than 60% is good for diagnosis while a sensitivity of 90% is acceptable for screening (Lincoln, Nicholl, & Flannaghan, 2003). However, others suggest that that both a high sensitivity and specificity is warranted when differentiating depressed and non-depressed individuals (Weintraub, Oehlberg, Katz, & Stern, 2006). Mulrow et al.'s (1995) review found that the average sensitivity of common measures used in primary care

was 84%, while the average specificity was 72%. Given the risk of missing nearly 30%, many would suggest that an increase in specificity was warranted in primary care, particularly in light of suicide risks in certain populations. Several investigators have taken this approach in determining which measures are presumably useful in primary care and what the modified cutoffs would be, if needed.

For instance, Zich et al. (1990) evaluated the CES-D and BDI for use in primary care and found a prevalence of 41% using standard cutoffs of both instruments; 10 on the BDI and 16 on the CES-D. However, utilizing a more stringent cutoff of 16 on the BDI and 27 on the CES-D resulted in a lower prevalence of 19% and 23%, respectively. Furthermore, despite all four cutoffs having 100% sensitivity, the specificity was greatly improved when raising these cutoffs. More specifically, a cutoff of 10 on the BDI had a specificity of 75% while a cutoff of 16 resulted in a specificity of 89%. Similarly, raising the cutoff on the CES-D from 16 to 27 improved its specificity from a low 53% to 81%. This raised cutoff of 27 on the CES-D for use in primary care has been recommended previously by Schulberg et al (1985) (see Zich et al., 1990). Similar to these findings, Arnau et al. (2001) found a prevalence of 23% when employing a cutoff of 15 on the BDI-II. They also showed that lowering the cutoff to 10 on the BDI-II resulted in a sensitivity of 100% and specificity of 70% while a strict cutoff of 25 yielded a sensitivity of only 58%, but specificity of 97%. They suggested that a cutoff of 18 be used as it acquired a sensitivity of 94% and specificity of 92%. From such reviews, it is apparent that modifications of cutoffs is one solution to improving our ability to accurately assess depression in primary care, but may also be responsible for the inconsistencies found in prevalence rates in the literature, further complicating our understanding of depression in the medically-ill. Additionally, raising or lowering a total score tells us very little about the symptoms endorsed and which are more indicative of depression in the medically-ill.

Others have suggested removing items that are thought to be more related to the medical condition. Somatic complaints for instance may be inflating the total score and may only be

reflective of the medical condition and not depression. Thus, someone could potentially meet criteria based solely on their total score, but have endorsed mostly, or only, somatic complaints that may be due to their medical condition. Given this, the necessity of including somatic items on depression measures in primary care has also been reviewed. Some contend that somatic items should be removed (Beck et al., 1999; Mohr, Goodkin, Gatto, & Van der Wende, 1997) while others caution that removal of such items is not warranted as long as the integrity of the measure remains the same (i.e. factor structure). Arnau et al. (2001) argue that neurovegetative items be included in assessment of depression in the medically-ill given their contribution on second order factorial structures of self-report instruments which suggests that they are reflective of a general construct of depression. Furthermore, their support for including neurovegetative items was accompanied by their findings that the item-total correlations for neurovegetative items of the BDI-II were equivalent to other items while all items retained good sensitivity and specificity, on the whole, as a measure. Similarly, Clark, Cavanaugh, & Gibbons (1983) found that the BDI measures a single dimension of depression in both a psychiatric and medical sample suggesting comparable validity. However, they also found that irritability and work inhibition were not associated with depression in the medical sample while other items were more indicative of depression in the two samples. Despite these contentions, certain measures have been designed specifically for medically-ill populations (i.e. Hospital Anxiety & Depression Scale [HADS][Zigmond & Snaith, 1983] and the Beck Depression Inventory for Primary Care [BDI-PC] [Beck, Guth, Steer, & Ball, 1997]) that are thought to be less reliant on somatic symptoms of depression. The Hospital Depression Subscale (HDS) of the HADS consists of seven items thought to be more indicative of depression in a medical population. Items include enjoyment of things, having a sense of humor, cheerfulness, feeling slowed down, loss of interest in appearance, looking forward to enjoyment of things, and enjoyment of books, radio, or television. The BDI-PC is Beck et al.'s (1997) adaptation of the BDI-II in which only seven non-somatic items (sadness, loss of pleasure, pessimism, past failure, self-dislike, self-criticalness,

and suicidal ideation) are included in the measure. Beck et al (1997) found that using a measure consisting only of these items demonstrated good convergent validity with the HDS ($r = .62$, $p<.001$) while it was significantly more associated with a diagnosis of major depression ($r = .66$, $p<.001$) than the HDS ($r = .37$) suggesting greater utility of these seven non-somatic items.

Another measure, the Chicago Multiscale Depression Inventory (CMDI), was developed for use with medical populations (Nyenhuis, et al., 1998). The CMDI consists of three scales delineating mood, evaluative, and vegetative symptoms. These scales can be used in combination or separately when it is hypothesized that a certain domain is inflated by a particular medical illness. Despite advances in measures such as the CMDI, HADS, and BDI-PC, there remains uncertainty as to whether or not depression is being accurately assessed in the medically-ill.

With the aforementioned factors in mind: a high prevalence of depression in primary care, poor detection of depression by physicians, increased risk for suicide amongst other detriments in overall functioning of medically-ill individuals with depression, and the widespread use of screening tools that are not designed specifically for this population, it is clear that efforts need to be made to assure that we are doing a better job at recognizing the hurdles in assessment in this population and to generate more appropriate means to conquer these hurdles.

Multiple sclerosis (MS), in particular, is a medical condition for which there has been ongoing controversy over the ability to accurately assess depression. 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. The proposed investigation described hereafter examines depression in MS as measured by common self-report instruments (BDI-II, BDI-PC, CMDI). An evaluation of the prevalence rates and accuracy of each of these measures will be conducted to determine which, if any, is ideal for use with MS patients. However, the unique aspect of this investigation is that, unlike any other, it looks beyond item endorsement. By giving MS patients an instrument on which they are provided with options for attribution when they endorse depression items, a

more accurate characterization of the nature of their symptoms may be possible. Additionally, a second aim of this investigation is to determine whether assessment of depression in MS is improved when one can distinguish whether endorsement is due to medical/physical or cognitive difficulties associated with MS versus psychological processes. Finally, it is hoped that the qualitative information provided by patients regarding their endorsement of items will shed some light on the phenomenological experience of depression and MS symptoms.

Multiple Sclerosis & Depression

It is well recognized that there is a high comorbidity of depression in MS. Point prevalence rates reported in the literature range from 27% to 54% (for a full review, see Minden & Schiffer, 1990, 1991). Multiyear prevalence rates have also been found to be as high as 42% to 62% (see Nyenhuis et al., 1995) while lifetime prevalence ranging from 22% to 54% (see Patten, Fridhandler, Beck & Metz, 2003). MS patients have a higher suicide rate than the general population or in other individuals with chronic medical illness (Sadovnick, Eisen, Ebers, & Paty, 1991). Depression in MS also occurs more frequently than in other similar neurological disorders (Schiffer & Babigan, 1984; Whitlock & Siskind, 1980). In fact, Patten, Beck, Williams, Barbui, & Metz (2003) recently found the annual prevalence of major depression in MS to be 15.7% compared to 9.1% in those with other chronic medical conditions. This difference was even greater for MS patients aged 18-45 in which the prevalence was 25.7% in the MS sample compared to 8.9% without MS. This is consistent with the suggestion that individuals with MS are three times more likely to experience depression in their lifetime than those without MS (see Butt & Demaree, 2004). Dalton & Heinrichs' (2005) meta-analysis also found that more than half of their 1,817 MS patients had higher levels of depression than the 2,704 healthy controls. However, they also found comparable rates for depression in MS compared to non-neurological medical conditions but greater likelihood of depression when compared to other neurological conditions. Given the high prevalence of depression in MS, many have investigated the possible etiologies to explain the disproportionate representation of depression in this population. Possible

theories tend to err on the side of a psychological/psychosocial theory, biological theory, or a combination of both.

Support for a psychological and/or psychosocial theory includes the finding that depression in MS tends to be unrelated to disease severity (Huber, Rammohan, Bornstein, & Christy, 1993, Shnek, Foley, LaRocca, Smith, & Halper, 1995) and that other psychosocial factors contribute significantly in predicting depression or emotional distress in MS patients. For instance, Mullin et al. (2001) found that illness intrusiveness and uncertainty regarding one's illness explained 24% of the variance above and beyond other demographic (age and education) and disease related variables (cognitive status and ambulation). The suggestion that unpredictability and unforeseen prognosis in MS can lend itself to depression has been theorized for some time, and seems intuitively easily applied to a disorder such as MS. In fact, Shnek et al. (1995) found that learned helplessness was the greatest predictor of depression in MS, above and beyond other psychological factors (i.e., cognitive distortions, self-efficacy) and biological factors (i.e., disease activity, disability). Nearly a decade later, Zabad, Patten, & Metz (2005) found that depression was lower in individuals with a progressive course compared with a relapsing remitting course of MS. They suggested that despite the more progressive disease, the later onset, absence of unpredictable attacks, and potentially greater levels of support, protected these patients from depression. The suggestion that unpredictability of disease in relapsing remitting patients may be associated with depression in MS was confirmed by Randolph & Arnett (2005). They found that symptom variability as measured by patients' and informants' ratings of the best, worst, and current periods of functioning was related to depression, even when controlling for disability as measured by the EDSS. Additionally, findings that adjustment in MS is related to the patient's perception of support while being inversely related to functional disability and perceptions of a lack of support (Wineman, 1990) further supports Zabad et al.'s assertion. Similarly, Mohr, et al. (1997) found that individuals with a greater level of disability (as measured by the EDSS) were more likely to be depressed, but were also less likely to utilize

adaptive coping, suggesting that coping may mediate this relationship. Such findings render little conviction in determining whether there is a direct relationship between disease severity and depression in MS. It has been speculated that illness duration and coping may mediate this relationship in which individuals with a greater level of disability (and/or longer duration) have learned to adjust, or cope, with their disease and are thus, less prone to depression. In fact, it has been shown that individuals with MS who utilize more adaptive, active coping and less avoidance coping over time show a decrease in their depressed mood while those who showed increases in their depressed mood demonstrated a decrease in their use of active coping (Arnett & Randolph, 2006). This is also consistent with the finding that depression may be greatest at initial stages of the disease. Chwastiak et al. (2002) found a greater risk of depression early on in the disease (i.e. first year) as opposed to later on in the disease process (i.e. 5 to 10 years post disease onset). More specifically, it was found that, although 32.1% of their sample diagnosed within a year were depressed, only 21.8% of those diagnosed within one to five years were depressed while even less (10.3%) of those diagnosed over ten years prior were depressed. Moreover, cross-sectional studies have found that age may play a factor in depression in MS as well, suggesting that the impact of the disease at certain stages of one's life may vary. Patten, Metz, & Reimer (2000) evaluated the influence that various biosocial factors contributed to depression in MS. Age less than 35 years of age was a significant predictor of depression in their sample, with an odds ratio of 4.62, the highest of all the variables investigated. Others have also found that illness intrusiveness may be moderated by age and that higher levels of emotional distress were found in younger individuals with MS (see Mullins et al., 2001). Taken together, this may suggest that depression may be more pronounced in younger individuals in an early stage of MS with inadequate coping. In sum, the existence of a direct relationship between disability and depression is unclear, with some finding that there is a direct relationship (see Lynch, Kroencke, & Denney, 2001; McIvor, Riklan, & Reznikoff, 1984), an inverse relationship (see Dalton & Heinrichs, 2005), or, no relationship at all (Rabins et al., 1986). Uncertainty as to

whether it is disability, duration of illness, or disease course, accompanied by a host of mediating and moderating variables (e.g., coping, age) has plagued this area of research. However, the findings that depression in MS is unrelated to disease severity, is moderated by variables such as social support, coping, and perceived stress, is greater in initial stages of the disease and less at advanced stages, and, is greater in individuals of a younger age, suggest, in part, that depression in MS may be result of an aggregate of psychosocial factors opposed to biological.

Despite convincing support for extraneous, psychosocial factors influencing depression in MS, some investigators contend that depression is a cardinal symptom of MS. In Charcot's (1877) early descriptions of MS, depression was considered characteristic of the disease. Charcot noted that "it is not rare to see them… melt into tears without reason" (1879 cited by Minden & Schiffer, 1993 from Dalton & Heinrichs, 2005). Many individuals with MS have also been initially misdiagnosed as having primary affective disorders and other psychiatric disorders, despite obvious neurological symptomatology (Shnek et al., 1995). Furthermore, some investigators have found that depression may actually be an initial symptom (Scott, Allen, Price, McConnell, & Lang, 1996) and may precipitate a formal diagnosis of MS. Such findings are further supported by the frequency of emotional or stressful events that occur simultaneously with the diagnosis, or exacerbation, of the disease (Grant et al., 1989). Given these observations, possible biological causes of depression in MS have been investigated. Depression in MS has been shown to be associated with lesions in the left arcuate fasciculus (Pujol, Bello, Deus, et al., 2000), temporal lobe lesions (Honer, Hurwitz, Li, Palmer, & Paty, 1987; Ron & Logsdail, 1989) and right temporal regions (Berg et al., 2000; Zorzon et al., 2002), as well as those in the periventricular region and the frontal lobes (Reischies, Baum, Brau, Hedde, & Schwindt, 1988). Furthermore, depression has been found to be more severe in those with lesions of cerebral involvement versus spinal cord involvement (Rabins et al., 1986; Schiffer & Babigian, 1984). More recent investigations have found that a higher lesion load in the left inferior medial frontal

region and greater atrophy of the left anterior temporal region in depressed patients explained 42% of the variance predicting major depression (Feinstein, Roy, Lobaugh, et al., 2004).

With these findings in mind, many speculate that depression in MS is a result of a host of psychosocial and biological factors. Disentangling the two has proven difficult and it has been suggested that depression in MS be conceptualized as an interaction of biological, psychological and social factors (Minden & Schiffer, 1990; 1991). Employing such a conceptualization also guides our investigations and understanding of the risk factors for depression in MS. Risk factors for depression in MS include female gender, age less than 35, family history of depression, high levels of stress, lower education, lack of social support, and cognitive difficulties (see Chwastiak et al., 2002). Again, findings are mixed concerning whether illness duration, MS course type, and disease severity are related to depression in MS. This raises the issue raised earlier regarding how to properly assess depression when adjustment processes may play a role earlier in the disease. It also highlights the importance of coping and social support in possibly ameliorating depression over time.

Understanding the types of individuals who are afflicted with MS and its impact on them is vital to the depiction of depression in MS as well. MS affects women twice as often as men (Smith, Samkoff, & Scheinberg, 1993). Multiple sclerosis is the number one cause of neurological disability among young and middle-aged adults (Feinstein, 1995; Shnek et al., 1995), with a peak onset of about 33 years of age (Shnek et al., 1995). Given that the onset of MS occurs at such an early age, the effects of this disease may be more devastating and detrimental than other neurological conditions. Individuals who are stricken with the disease are usually highly functioning, young individuals who are adjusting to a disease that is unpredictable and varying in its course. Furthermore, many are just beginning to make decisions regarding employment, children, and so on that are now hindered by their disease. In fact, it has been found that men and women with MS aged 25-44, an age at which one is making such decisions, experienced more depression than their age matched, healthy counterparts. In particular,

depression in healthy men in this age group was 5% compared to 13.3% with MS. Women, who were more likely to suffer from depression whether healthy or not, were found to have a prevalence of 11.4% and 22.2%, respectively (Patten, Svenson, & Metz, 2005). A diagnosis of a medical condition can also affect body image, self-esteem, sense of identity, capacity to work, and maintenance of social, family, and marital relationships (Rodin & Voshart, 1986). With these considerations in mind, it is clear why depression is so common in MS. However, despite the powerful psychosocial impact of the disease and the contribution of psychosocial factors to depression in MS, dispute remains regarding its etiology, and relatedly, its assessment.

Detection of depression in MS is difficult given the overlap with physical complaints, the nature of the disease, and the demographics of the people afflicted. In fact, it has been suggested that upwards of 40% of MS patients with depression do not receive appropriate treatment (see Butt & Demaree, 2004) and that two-thirds of MS patients with major depression received no treatment for their depression while only 3% of those treated with medication were above a therapeutic threshold (Mohr, Hart, Fonareva, & Tasch, 2006). To meet criteria for a mood disorder, according to the *DSM-IV* (American Psychiatric Association), an individual must endorse at least five of the nine following symptoms: depressed mood, loss of interest or pleasure, weight/appetite changes, sleep disturbance, loss of energy/fatigue, psychomotor retardation or agitation, feelings of worthlessness/guilt, diminished concentration, or recurrent thoughts of death. As will be described in detail later, MS patients, depressed or not, may easily endorse six of these items (sleep disturbance, fatigue, appetite changes, concentration difficulties, psychomotor slowing, and loss of interest/pleasure) because they are also disease symptoms (Mohr et al., 1997). Given this, MS is recognized in the *DSM-IV* as a common medical disorder associated with depression. The *DSM-IV* criteria allow for an individual with low mood, who does not meet the full criteria listed above, to be diagnosed as depressed. Despite such leniency in the *DSM-IV*, evaluation based solely on mood may not create an accurate picture of depression for all suffering from MS. As suggested by some, care providers and

researchers cannot deny the importance of taking the vegetative, evaluative, and mood components of depression into consideration when making a diagnosis. Again, if such an approach is taken, an understanding of what symptoms are common, excessive, or independent of the disease must be developed.

Somatic complaints: Depression or MS?

Common physical symptoms of MS include difficulties or changes in gait, tremors, visual problems, bladder and bowel incontinence, spasticity, muscle stiffness or spasms, and numbness/tingling in the extremities. Such symptoms are more easily recognizable as being caused by MS. However, frequent symptoms of MS also include a variety of somatic complaints including chronic pain, sexual dysfunction, and numerous neuropsychological difficulties (Shnek et al., 1995). In addition to these symptoms, MS patients suffer from secondary symptoms such as fatigue and sleep disturbance at a strikingly high rate (e.g. Saunders, Whitman, & Schaumann, 1991). Fatigue, for example, is estimated to affect anywhere from 53% to 87% of MS patients (Colosimo et al., 1995; Ford, Trigwell, & Johnson, 1998; Freal, Kraft, Coryell, 1984; Krupp, Alvarez, LaRocca, & Scheinberg, 1988; van der Werf et al., 1998). Additionally, Clark et al. (1992) showed that MS patients are three times more likely to experience sleep difficulties relative to healthy controls. Furthermore, in a recent study our research group found that 62% of an MS sample complained of some sort of difficulty with sleep (Strober, Arnett, Polen, & Bruce, 2002). Appetite changes may also be found in MS due to medications, difficulty swallowing, or effort in preparing meals. Finally, sexual dysfunction in MS occurs quite frequently. McCabe, McKern, McDonald, & Vowels (2003) showed that men with MS are much more likely to experience sexual dysfunction relative to the general population. Men with MS attributed their dysfunction to erectile problems and lack of sensation/numbness. Further, although women in the general public as well as those with MS reported sexual dysfunction, women with MS were significantly different in that they reported lack of sensation/numbness in the genitals. This is consistent with previous reports showing that the prevalence of sexual dysfunction for women

with MS ranges from 10.6% to 59.6% (Hulter & Lundberg, 1995) and that women most often attribute it to lack of sensation/numbness (McCabe, 2002). Despite this high prevalence and potential contribution of MS, it has also been found that disinterest in sex may be a good indicator of depression in an MS sample and given even more weight than other neurovegetative symptoms (Randolph, Arnett, Higginson, & Voss, 2000). These findings show that fatigue, sleep disturbance, appetite changes, and sexual dysfunction are common MS symptoms. However, a distinction must be made regarding whether these symptoms exceed what is expected for the disease or relate to underlying depression. Without following up on these items in an interview or self-report instrument, this distinction may be easily overlooked.

My preliminary research has in fact shown that MS patients attribute many of the neurovegetative items they endorse on the BDI-I to physical complaints caused by MS. In particular, of the 62% of the sample that complained of sleep disturbance on the BDI-I, 53% reported that their difficulty with sleep was primarily due to disease consequences (i.e., bladder incontinence, muscle stiffness, leg spasms) versus psychological processes like worry (Strober et al., 2002). Furthermore, of the 91% of our MS sample who reported fatigue on the BDI-I, 64% attributed it primarily to physical exertion or related physical problems (Strober & Arnett, 2004).

Others have also examined whether MS patients endorse neurovegetative items on self-report instruments differently than controls or depressed individuals. Chang et al. (2003) found that, after closer examination of individual items on the CMDI using differential item analysis, the "sluggish" and "fatigued" items on the vegetative scale were amongst the "easiest" items to endorse for MS patients. They suggest that MS patients were responding to the fatigue items differently than the standardization group and that their endorsement of these fatigue items may be more reflective of their medical condition. In addition, Verdier-Taillefer, Gourlet, Fuhrer, & Alperovitch (2001) cautioned that, although the somatic complaints of the CES-D are not as specific to MS and may therefore be less influenced by MS symptomatology, there were only two individual items of the somatic scale on which MS patients scored significantly higher.

These items, “Unable to get going” and “Feeling as if everything is an effort” may be more representative of the enduring fatigue in MS and may explain their differentially high endorsement.

Beyond the Physical: How are Evaluative Depression Symptoms Influenced by MS?

Given the high level of functional disability of some patients, the exuberant age at which the disease occurs and its unpredictable course, MS patients may evaluate themselves differently or inconsistently relative to others. Furthermore, not being able to do what one once enjoyed, or as well as one once did, may lead to a negative self-appraisal or withdrawal of activities. This sense of anhedonia or negative appraisal would typically present as depression. However, in MS it may at times simply be a reflection of one’s disability (Nyenhuis et al., 1995). Again, it is the extent to which this loss of pleasure or interest exceeds the disability inherent in the disease that is central. An example often used in our laboratory is of the individual who loved to sail and cannot enjoy this because of his/her disability or uncertainty of attacks. When initially asked if patients no longer enjoy doing what they once enjoyed, they may endorse the item; however, it may not reflect depression but simply the reality of the limitation placed upon them due to their disease. Additionally, when asked about sense of self-appraisal MS patients may truthfully report that they are less capable or feel more self-critical of themselves. In fact, Chang et al. (2003) found that MS patients in their sample were more likely to feel “useless.” Reports of feeling useless may appear to be a significant indicator of depression. However, these investigators also found that these individuals were less likely to endorse “depressed”, “low”, or “resented” in comparison to the normative sample. This suggests that the connotation of feeling “useless” may be more reflective of MS patients’ functional disability despite not having a formal diagnosis of depression. This conceptualization is consistent with Nyenhuis et al. (1995) who caution that the evaluative scale of the CMDI may be ascertaining functional disability as opposed to negative self-appraisal.

Coming Full Circle: Are We Only Left With Mood?

It may appear that mood is the only domain that unambiguously reflects depression in MS. As suggested by the *DSM-IV*, a reasonable approach to the diagnosis of depression in the medically-ill could involve examining only mood symptoms. In fact, Nyenhuis et al. (1995) suggested that the mood scale on the CMDI was the best indicator of depression in MS. These investigators found that rates of depression were significantly lower when only the mood scale was used to diagnosis depression compared to the full scale that included all mood, evaluative, and vegetative symptoms of depression (17.7% vs. 26.6%). When matched with healthy controls based on BDI scores, MS patients did not differ on mood, but displayed significantly higher vegetative and evaluative scales, suggesting that these scales may be the cause of inflated prevalence rates of depression in MS. Similarly, Feinstein & Feinsten (2001) showed that, although 73% of their sample endorsed some emotional dyscontrol, only 17% met criteria for depression when more stringent criteria (*DSM-IV*) were used. Such findings suggest that if attention is only given to mood, we may find lower and more accurate prevalence rates of depression in MS. That said, 48%, which is closer to the higher estimates of depression in MS, of Feinstein and Feinstein's sample had some sort of emotional difficulty. The most common symptoms in the sample were irritability (57%), crying (40%), and sadness (36%). Feinstein & Feinstein caution that only employing the "low mood" criterion of the *DSM-IV* in medical populations may result in overlooking the nearly 50% reporting significant distress. However, others have cautioned that the irritability and crying seen in MS patients may be more indicative of the emotional lability in MS and not diagnosable depression. Furthermore, irritability, crying, sadness, discouragement, and dissatisfaction are commonly associated with medical illnesses (Cavanaugh, 1986). Despite this, endorsement of such items should not be taken for granted or overlooked.

From this review, it may appear that few items of depression are exempt from the infiltration of MS symptomatology. Past approaches to rectify this problem have involved the

removal of somatic items, or heightened priority given to few mood or evaluative items hypothesized to be relatively independent of MS. It is here proposed that, rather than allocating greater relative importance to the few remaining depression items, or eliminating potentially crucial somatic items, further exploration of all symptom clusters of depression in MS is necessary. Again, following suggestions from previous research and the inconsistencies in past theories regarding the accurate assessment of depression in the medically-ill, the proposed investigation will involve the inclusion of items encompassing all depression symptoms, but with further exploration of the attributions made regarding their endorsement. If an item is considered to be mostly or completely due to MS for an individual, the item may be weighed less. However, if the item is endorsed, and the patient continues to describe its endorsement as emanating from psychological factors, it should be included in that patient's report of depression. It should be noted that this investigation does not assume that psychological and biological/physical factors are separate entities, as in a mind and body dualism. It is quite reasonable to assume that endorsement attributions are both physically and psychologically interconnected, rendering it difficult to discern which symptom(s) are most likely to be the cause of patients' reports. This investigator does not assume that these factors are easily distinguishable or, more importantly, that they are not intertwined. However, for the sake of this investigation, patients were asked to separate these factors to the best of their ability in their reports. It was hoped that by providing an option of physical and psychological factors, patients would be allowed to determine for themselves if their perceptions of their MS symptoms were more likely to be a factor than psychological causes. The differentiation between physical MS symptoms and psychological factors is conceptualized only at this relatively simplistic level for the purpose of this investigation and development of this new measure. Before describing the proposed measure, I turn now to some of the studies that have examined depression measures in MS thus far.

Investigations of Self-report Measures in MS

To date, investigations of the BDI (Aikens et al., 1998; Avasarala, Cross, & Trinkaus, 2003; Moran & Mohr, 2005; Mohr et al., 1997; Sullivan, Weinshenker, Mikail, & Bishop, 1995), BDI-PC (Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003), CES-D (Chwastiak et al., 2002; Pandya, Metz, & Patten, 2005; Patten, Lavorato, & Metz, 2005;Verdier-Taillefer et al., 2001), and CMDI (Chang et al., 2003; Nyenhuis et al., 1995) for use with MS have been conducted.

Beck Depression Inventory (BDI). Investigators of the BDI have examined the optimal cutoffs as well as the benefit of removing potentially confounded items. 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 a small sample (N=46), Sullivan found that 40% met DSM-III-R depression criteria through a structured interview. In utilizing ROC analyses they showed that a 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%) suggest that a false-negative rate of nearly 30% still remains. Taking the suggestion to use a cutoff of 13, Avasarala et al. (2003) found the point prevalence rate of depression to be 40.8% in their sample. Although this prevalence rate is within the range of what is typical of depression in MS, this number is on the higher end and may be an overestimation. Mohr et al. (1997) examined the BDI and suggested that three items be removed when used in MS (BDI-18). Items to be removed from the measure were based on the extent to which the item contributed to the overall BDI score. If one of the original 21 item's contribution on MS reports exceeded that of normal controls and individuals with major depression, the endorsement of the item was thought to be inflated due to MS symptomatology. The three items on the BDI that met this criterion were: fatigue, work difficulty, and concerns about health. However, these investigators did not compare the items between non-depressed and depressed MS. These items

may be likely to be endorsed by MS patients regardless of whether or not they are depressed. Furthermore, as mentioned earlier, more severe complaints on somatic items that exceed what is expected of the disease may in fact be indicative of depression.

Questions have also been raised about the validity of removing items from the BDI. Aikens et al. (1998) conducted a study suggesting that removal of such items was not warranted. They found that exclusion of such items did not enhance the reliability of the BDI in MS in comparison to controls, depressed, and medically-ill comparison groups and suggested that the BDI was a valid measure for diagnosing depression in MS. McGuigan & Hutchinson (2006) also found that removing confounding items (fatigue and lack of energy) had negligible effects, resulting only in the placement of four individuals (out of a total sample of 176) into the mild range from the moderate/severe range.

Moran & 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 but these reductions cannot be interpreted as not being confounded by MS. Moreover, it is possible that the somatic complaints were truly reflective of depression and not MS, and thus ameliorated by treatment, as the sample consisted of individuals who had only been diagnosed with MS for approximately six years, on average. Furthermore, the authors did not report the level of disability of the sample. It is plausible that this was a minimally disabled group in which their neurovegetative complaints were not as yet influenced by their MS.

Given the number of recent studies on the topic, it appears that the BDI is still under scrutiny for use with MS. However, the BDI has been recognized as a gold standard for self-reported depression and involves less reliance on somatic items (although does not exclude them entirely), making it relatively more applicable to medical populations. In the present investigation, the BDI-I will be modified for use with an MS sample. Additionally, modifications

made of the BDI-I will allow for further questioning of the etiology of the symptoms to determine if in fact they are confounded by MS symptoms or more related to depression, an issue that Moran & Mohr, amongst others, suggest we begin to explore.

Beck Depression Inventory-Primary Care (BDI-PC). The BDI-PC was recently developed and has begun being used within MS samples (Benedict et al. 2003). Benedict et al. (2003) found that a cutoff of 4 in a MS sample differentiated depressed from non-depressed MS and showed good concurrent validity with the BDI (r = .85) and CES-D (r = .86). It was suggested that future research examine the sensitivity and specificity of the BDI-PC employing a structured clinical interview for more stringent criteria. Benedict et al.'s results were very similar to what has been reported for in primary care clinics, where a cutoff of 4 was determined to be the optimal cutoff. In a primary care sample, a cutoff of 4 was found to have a sensitivity of .97 and specificity of .99 (Steer et al., 1999). Given its novelty to the field and likely applicability to individuals with MS, an additional goal of the proposed investigation is to explore the validity of the BDI-PC in MS.

Center for Epidemiological Studies – Depression (CES-D). Despite some of their cautionary notes, as mentioned earlier, Verdier-Taillefer et al (2001) compared a MS sample to two groups: a group of general practice patients and a healthy control group and found the CES-D to be reliable and valid in an MS population. Factor analyses were conducted confirming the integrity and validity of this measure. However, some have questioned the validity of these findings, particularly in regards to how the factors were extracted (see Butt & Demaree, 2004). Having used principal component analyses, Verdier-Taillefer et al (2001) confined their data to a four factor model as is found in previous studies of the CES-D and only considered an item as belonging to a factor if its loading was greater than .50. Furthermore, there were items that loaded differently on two of the four factors between MS patients, general practice, and healthy controls, suggesting there was not an exact comparable replication. More recently, Pandya et al (2005) found that, despite the contention that the structural validity of the CES-D was sound,

using the suggested cutoff of 16 only accurately identified 75% of their depressed MS sample who were evaluated by a psychiatrist and met DSM-IV criteria for a depressive disorder. These investigators suggested raising the cutoff on the CES-D, but lacked any data regarding the utility of scores below 16. The CES-D has been examined in other medical samples and has had mixed results. For instance, Jones et al (2005) found a lowering of the cutoff to 14 was optimal (sensitivity = .89, specificity = .79) when used with an epileptic population. Schein & Koenig (1997) examined three cutoffs of the CES-D (16, 20, and 27) for use with a medically-ill elderly population and found varying levels of accuracy. A cutoff of 16 resulted in a sensitivity of .73 and specificity of .84. Raising the cutoff to 20 (sensitivity = .62, specificity = .94) and 27 (sensitivity = .23, specificity = .98) resulted in improved specificity, but compromised the sensitivity of the measure. In sum, these investigators cautioned that using the standard cutoff of 16 resulted in a large number of false positives and suggested that a cutoff of 20 resulted in the greatest hit rate. Patten, Lavorato, & Metz (2005) examined the utility of raising the cutoff on the CES-D in MS, suggesting that a reduction in prevalence rates would be an indicator of a more stringent and accurate cutoff. They found that raising the cutoff altered the point prevalence from 32.8% (using a cutoff of 15) to 24.5% (using a cutoff of 21). They also found a slight lowering of the prevalence when removing items that may be confounded by MS. In particular, removal of the cognitive difficulties item resulted in a prevalence rate of 31%; removal of the fatigue item (30%) and finally, removal of both (30.4%) resulted in comparable prevalence rates. Scores were prorated for each exclusionary analysis while a cutoff of 15 was still used. It was suggested that removal of these items on the CES-D did not play an influential role on reports of depression in MS. Finally, Chwastiak et al (2002) found that the point prevalence of depression in a MS community sample was 41.8% when utilizing a cutoff of 16, but that this prevalence dropped to 29.1% when the cutoff was raised to 21. Additionally, they suggested that those suffering from depression were in the more severe range, as 69.6% of the sample that met criteria

using a cutoff of 16 still met criteria with a cutoff of 21. However, it is important to note that 30% of patients who still have significant symptoms were not detected using such a cutoff.

Chicago Multiscale Depression Inventory (CMDI). 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 to assess its utility for use with MS. They were able to replicate the same five factor structure with the MS group as Nyenhuis et al (1998) found which included mood, evaluative, fatigue, sleep disturbance, and cognitive inefficiency and found that few items were endorsed differently by the MS group, as mentioned earlier. 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 scales and the total CMDI were significantly higher in a depressed sample compared to a MS community sample, while all but the mood scale were higher in MS compared to a healthy control sample. Matched on the BDI, depressed and MS patients were also not found to be significantly different on the total MDI nor have any main effects for scale (mood, evaluative, or vegetative), yet MS patients were still significantly lower on the mood scale but similar on the evaluative and vegetative. Nyenhuis et al. (1995) suggested that assessing depression using the mood scale may be best practice and may result in more accurate prevalence rates that are not inflated due to the inclusion of non-mood 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 scale alone compared to 26.6% when using the total CMDI. This prevalence of 17% is closer to the prevalence found when employing more stringent criteria such as structured clinical interviews (Feinstein & Feinstein, 2001; Patten, Beck et al., 2003) which found prevalence rates of 17% and 16%, respectively. These findings may suggest that utilizing only the mood scale of the CMDI may be a more accurate reflection of the prevalence of depression in MS when neurovegetative symptoms are not inflating reports.

Varying Prevalence Rates in MS

In the same sample, Nyenhuis et al. (1995) reported varying prevalence rates of depression using the BDI and subscales of the CMDI using a cutoff of one and a half standard deviations above the means of controls (approximately 14 on the BDI and 93 on the total CMDI). In fact, both the BDI and CMDI total score did not yield different rates, 30.5% and 26.6%, respectively. However, using only the vegetative scale increased the prevalence to 34.6% while using the evaluative and mood scales resulted in lower prevalence rates, 22.2% and 17.7%, correspondingly. The varying rates found in the same sample raise the question as to which measure (or scale) is most accurate. Furthermore, prevalence rates fluctuate between samples. Although recent estimates of hospital based populations of MS suggest a point prevalence of depression between 14% and 57%, McGuigan & Hutchinson's (2006) epidemiological study of 211 MS patients residing in Ireland found a point prevalence rate of moderate to severe depression to be 23.3% as rated by the BDI-II using a cutoff of 20. Patten, Svenson, & Metz's (2005) most recent study of a community based sample consisting of 8,999 MS patients found 17% to suffer from a current affective disorder diagnosed using the ICD-9-CM codes received from physicians and psychiatrists compared to 7.7% of the 178,612 patients visiting their primary care physician, neurologist, or psychiatrist.

After conducting a phone interview of the major depression module of the SCID, Mohr et al. (2006) found the current prevalence to be 25.8%. Similarly, Patten, Fridhandler, et al. (2003) found a point prevalence of 25.2% using a cutoff of 15 on the CES-D among a MS sample being treated with disease-modifying treatments. It should be noted that this was a minimally disabled group with a mean level of disability measured by the Expanded Disability Status Scale (EDSS) of 2.0. However, Patten and colleagues have conducted several investigations of population based samples of MS using the Composite International Diagnostic Interview (CIDI) and have found the prevalence to be between 23% (lifetime) and 25.7% (annual; in MS patients aged 18-45 for this study) (Patten et al., 2000; Patten, Beck et al., 2003). Given the varying prevalence

rates amongst measures used within the same sample, between samples, and varying cutoffs, a brief synopsis of some of the prevalence rates found in the literature is warranted for future comparison. See Table 1.

Table 1.

Varying prevalence rates of depression in MS per measure used, sample, and cutoffs

Measure	Sample	Cutoff	Removed Items	Prevalence
BDI	Avasarala et al (2003)	13		41%
	McGuigan & Hutchinson (2006)	**20**		**28%**
	Nyenhuis (1995)	1½ SD above mean of controls		31%
CES-D	Verdier-Taillefer et al (2001)	17♀23♂		51%
	Patten, Fridhandler et al (2003)	15		25%
	Patten, Lavorato et al (2005)	15		33%
	Patten, Lavorato et al (2005)	21		25%
	Patten, Lavorato et al (2005)		Fatigue	30%
	Patten, Lavorato et al (2005)		Cognitive problems	31%
	Patten, Lavorato et al (2005)		Both fatigue & cognitive	30%
	Chwastiak et al (2002)	**16**		**42%**
	Chwastiak et al (2002)	**21**		**29%**
CMDI				
Full	Nyenhuis (1995)	**1**½ SD above mean of controls		27%
Vegetative	Nyenhuis (1995)	**1**½ SD above mean of controls		35%
Evaluative	Nyenhuis (1995)	**1**½ SD above mean of controls		22%
Mood	Nyenhuis (1995)	**1**½ SD above mean of controls		18%
CIDI	**Patten et al (2000)**			**23%**
CIDI Short Form	**Patten, Beck et al (2003)**			**16%**
SCID	Mohr et al. (2006)			26%
	Feinstein & Feinstein (2001)			17%
ICD-9 CM	**Patten, Svenson & Metz (2005)**			**17%**

Note. **Bold** = Epidemiological study sample. BDI = Beck Depression Inventory; BDI-PC = Beck Depression Inventory-Primary Care; CES-D = Center for Epidemiological Studies

Depression Scale; CMDI = Chicago Multiscale Depression Inventory; CIDI = Composite International Diagnostic Interview; SCID = Structured Clinical Interview for DSM-IV; ICD-9-CM = International Classification of Disease, Ninth Edition – Clinical Modification.

From this brief review of the prevalence rates reported within, it can be seen that among clinically based samples, prevalence rates of depression vary depending on which measure and cutoff is utilized. When using a cutoff of 13 or 14 on the BDI, the prevalence ranges from 31% to 41%. Similarly, using a cutoff anywhere from 15 to 21 on the CES-D resulted in a prevalence of 25% to 33%, with the exception of Chwastiak et al's (2002) cutoff of 16 and Verdier-Tailliffer et al's (2001) French cutoffs of 17 for women and 23 for men which resulted in higher rates, 42% and 51%, respectively. Finally, using a cutoff of one-and-one-half standard deviations above the mean on the CMDI, Nyenhuis et al (1995) found a prevalence rate of 27% using the full scale and varying rates of 18% to 35% depending on which scale of the CMDI was used. Overall, the range of depression prevalence in MS when utilizing self-report measures in clinical samples appears to cluster around 25% to 33% with some exceptions. When a structured clinical interview is used, however, it appears that the prevalence is lowered to a range of 17% to 26% in clinical samples.

Using a clinical sample instead of a community-based sample can result in selection bias which can also influence prevalence rates. However, review of the few epidemiological studies mentioned within found that there was little difference. On the BDI and CES-D, prevalence rates remained between 28% and 42%, with a rate of 28% to 29% when using more stringent cutoffs (20 on the BDI and 21 on the CES-D). Similarly, structured clinical interviews or physician/psychologist diagnoses revealed an almost identical range of 16% to 23% in community versus clinical samples. Such findings suggest that the prevalence of depression on self-report measures lingers somewhere around 25% to 33% with some exceptions in the 40% to 50% range, while clinical interviews and diagnoses are lower, in the 16% to 26% range. Another aim of the current investigation is to compare the derived point prevalence rates of three

common measures (the BDI-II, BDI-PC, and CMDI) and the modified BDI-I within the same sample to assess their concurrent validity as well as to examine the best cutoff for each measure through ROC analyses. A comparison can then also be made of the prevalence rates when utilizing the optimal cutoffs of these measures. Similarly, the removal of items thought to inflate prevalence rates in MS will also be examined. It can be seen in Table 1 and within this review, that the removal of items thus far has had negligible effects. However, the theory surrounding removal of items has also been guided by post-hoc hypotheses that suggest the particular items *should* be inflated due to MS, rather than a priori as in knowing that items *are* due to MS and are described as such by patients. This brings us to the last component of the proposed investigation, modification of the BDI-I.

Modification of the BDI-I

The modified BDI (see Appendix) was formulated based upon previous research in MS and clinical experience. The "trunk and branch" model highlights which items on the BDI-I are thought to be confounded by MS symptomatology and should include follow-up questions. In particular, the proposed modification of the BDI-I consists of follow-up questions to the following "truncal" items hypothesized to be related to the experience of MS: discouragement/pessimism, satisfaction in activities, self-criticism, irritability, loss of interest, self-appraisal, work difficulty, sleep disturbance, fatigue, appetite changes, somatic preoccupation, and sexual dysfunction (See Figure 1).

Upon endorsement of each of these items, patients are asked to make attributions regarding the extent to which their physical or cognitive symptoms of MS contributed to their response. For some questions, more specific follow-up questions are asked. For instance, if patients report that sleep complaints are due to their MS, they are subsequently asked to rank order the greatest contributors from a list provided. This list includes physical complaints (bladder incontinence, muscle stiffness, chronic pain, leg spasms), psychological complaints (worrying about your MS or worrying in general), medications, as well as a place to describe

other factors not listed. For other items, the questions are simpler. In asking about loss of interest in others, for example, patients are asked how much their MS limits social activity, or how much they take their MS into account when making plans with others. By examining attributions patients make when they endorse these items, a more accurate distinction can be made between which symptoms are due to MS symptomatology, which exceed the symptoms of MS, and which are independent of MS.

Beyond Endorsement

Preliminary data from my research have shown that such exploration beyond endorsement does in fact depict a different picture at times and suggests possible improvement in detecting depression in MS. First, on endorsement alone, our findings have been similar to what is described above regarding which items MS patients endorse on the BDI. In comparison to healthy controls, our MS patients endorsed significantly more physical complaints (sleep disturbance, fatigue, sexual dysfunction, and somatic preoccupation) on the modified BDI-I. MS patients were more likely than controls to endorse evaluative items that pertained to performance (work difficulty, negative self-appraisal, indecisiveness) and some cognitive items (sense of failure). Finally, MS patients endorsed affective items (irritability, crying, loss of interest) more often than controls. However, our MS group has not been found to endorse many of the affective or cognitive distortion items found on the BDI-I (sense of disappointment, negative self-appraisal, sadness, pessimism, sense of guilt, sense of punishment, satisfaction, or suicidal ideation).

In light of the ideas set forth by Clark, et al. (1983), such findings suggest that MS patients as a group may not be depressed, but may instead be endorsing what is expected given their disease. However, endorsement differences are not enough to explain what is occurring in MS. For instance, as stated earlier, sleep disturbance was endorsed by 62% of our sample, and 53% attributed it to physical problems. However, what may have been overlooked is that 19% of these patients attributed their sleep problems to worry. Furthermore, sleep disturbance in this

19% was found to be significantly related to depression indexes (CMDI Mood & Evaluative subscales), whereas the individuals who attributed their sleep to physical problems showed no association between their sleep and depression (Strober et al., 2002). These findings suggest that sleep disturbance, for instance, can be reflective of depression in MS when patients attribute their sleep problems to some type of distress. Finally, despite the fact that these endorsement patterns may suggest that these individuals are not depressed, approximately 39% of this sample were found to suffer from mild to severe depression (using a cutoff of 13) as measured by the BDI-II administered at the same time as the modified BDI-I. This has enhanced our understanding and cautioned us in our assessment of depression in MS. The next step is to explore whether patient endorsement of these items is reflective of depression or MS. The contribution of the proposed investigation is potentially ground-breaking for the MS literature. Beyond endorsement of the items described, there may be important information to be gained by merely asking our patients how they are perceiving these items and the influence that their MS has on their endorsement. In theory, if given the opportunity to describe their endorsement as due to MS or depression, a more accurate distinction could be made in deciphering who with MS is depressed, and who is not.

As can be seen in this review, depression in MS can at times become a misnomer as a result of uncertain etiology, improper assessment, and poor understanding of the intricacies of MS and its impact on one's psychological state and expression of such states. In the present investigation it is hoped that we can gain a better understanding of what features of depression are most indicative of depression in MS. In doing so, it is also hoped that the created measure will prove to be more accurate at assessing depression in MS with the knowledge obtained by our patients. Furthermore, it is hoped that we can also provide further support and/or disconfirm the present usage of common measures and provide future recommendations for more accurate use of the measures in the process.

Study Goals & Hypotheses

The long-term objective of the present investigation is to improve the detection of depression in MS. The following study goals were pursued by utilizing a modification of the Beck Depression Inventory (BDI-I) in which patients describe their attributions to their symptoms and exploring the prevalence rates and optimal cutoffs of this new measure as well as three commonly used depression measures in MS (BDI-II, BDI-PC, CMDI) to determine, which, if any, is best for use with MS patients:

Goal 1. Identify the contribution that MS symptomatology makes to reported depression in MS. Modification of the BDI-I will allow for a better understanding of how MS symptomatology might infiltrate self-report measures of depression in MS. The modified BDI takes into account previous research and clinical observations, and asks specific follow-up questions to items on the BDI that are thought to be confounded by MS symptomatology (e.g., sleep disturbance). Endorsement of such items may be inaccurately construed as depression when in fact the items are more reflective of MS. Items thought to be more indicative of depression and not directly influenced by MS do not have such follow-up questions (e.g., sadness). By exploring the endorsement of items among MS patients, insight into how they construe their symptoms and its causes (i.e. whether the complaint is medically related or psychological) will be gained.

> Hypothesis I: MS patients (depressed or non-depressed) will endorse certain items on depression measures that are independent of depression and more related to their MS (e.g., fatigue). If asked if these endorsed symptoms are due to their MS, non-depressed MS patients will report that their endorsement is primarily due to their MS, whereas depressed MS patients will attribute it to psychological factors other than their MS.

Goal 2. Demonstrate further support of a "trunk and branch" model of depression in MS. Comparisons of item endorsement among three groups (healthy controls, non-depressed MS, and depressed MS) will be made to determine which items are more indicative of MS (i.e., "truncal" items that may be present in both non-depressed and depressed MS) and which are more

indicative of depression (i.e., "branch" items that are present only in identified depressed MS). Further, by comparing the frequency and severity of "truncal" complaints between non-depressed MS and depressed MS, an examination can be made as to what extent depressed MS patients' "truncal" symptoms exceed what is typical in MS (i.e., is sleep disturbance more severe in depressed MS than non-depressed MS patients despite both endorsing it?).

> Hypothesis II: Certain "truncal" items will be endorsed by both depressed and non-depressed MS more often than healthy controls. However, if endorsement of these truncal items by depressed MS patients is greater than non-depressed MS, this will suggest that the particular item may be more related to depression than MS and exceed what is typical for MS. Further, differential endorsement of these "truncal" items by depressed MS can be determined by their endorsement being consistent with the endorsement of other "branch" items that are more indicative of depression. Non-depressed MS patients may be differentiated from depressed MS as not endorsing such "branch" items.

Goal 3. Assess the accuracy of self-report measures of depression in MS. If, from goal 1 and 2, it is found that certain items on the modified BDI-I (MBDI-I) are more related to MS than to depression per se, a prorated measure for each individual's responses will be created (MBDI-IM). It is hypothesized that results from this new measure will be less confounded by disease processes and represent a purer assessment of depression for each patient. This modified measure will then be compared to other common depression measures (BDI-II, BDI-PC, CMDI [full scale and subscales]) to determine if the new measure contains superior validity. By using a SCID interview, significant others' reports on the CMDI, and the Depression Proneness Rating Scale (DPRS) as criterion variables, I will explore the case finding ability of all measures. Using Receiver Operating Characteristic (ROC) analysis, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the four measures (MBDI-IM, BDI-II, BDI-PC, CMDI [full scale and subscales]) will be examined to explore the accuracy of currently

suggested cutoffs for the three common measures. Further, analyses will be conducted to determine optimal cutoffs for each of the four measures.

Hypothesis III: The modified BDI-I (minus MS contribution) will have greater sensitivity and specificity than the other depression measures if it is a more valid measure of depression in MS and not confounded by MS symptomatology.

Hypothesis IV: The MBDI-IM will have greater PPV (the proportion of positive test results that correspond or confirm a diagnosis of depression and NPV (the proportion of negative test results that correspond to the absence of depression), taking into account the prevalence of depression in MS, than the other depression measures if it is a purer and superior measure of depression in MS.

Hypothesis V: Based on previous findings, the accuracy of the more common measures will vary, with the CMDI mood subscale being most accurate, followed by the BDI-PC, CMDI evaluative subscale, BDI-II, and finally, the CMDI vegetative subscale.

Goal 4. Explore the varying prevalence rates of depression within a MS sample that may result from the use of varying measures and cutoffs. Prevalence rates derived by each measure (using suggested cutoffs and optimal cutoffs identified within this investigation) will be compared. Furthermore, comparisons of the prevalence rate derived from the MBDI-IM to the other three measures (BDI-II, BDI-PC, CMDI [full scale and subscales]) will be compared to assess whether prevalence rates are in fact inflated due to the intrusion that MS symptoms make on reports of depression. Finally, more detailed comparisons between the MBDI-IM and BDI-II will be conducted to explore the prevalence of mild (total BDI-II [score = 14-19] or MBDI-IM [score = 10-18), moderate (total BDI-II [score = 20-28] or MBDI-IM [score = 19-29]), and severe (total BDI-II [score = 29-63]or MBDI-IM [score = 30-63]) depression to determine if the prevalence of these descriptors are reduced when using a purer measure of depression (i.e. when the total score is not inflated due to item intrusion attributed to MS symptoms).

Hypothesis VI: Prevalence rates of depression derived by the modified BDI-I minus MS contribution (MBDI-IM) will be more accurate than other depression measures (BDI-II, BDI-PC, CMDI), as indicated by the MBDI-IM resulting in a prevalence rate closer to the prevalence rate derived from independent, objective measures (as measured by other's reports, clinician, and depression proneness) than these other measures.

Hypothesis VII: Prevalence rates may vary depending on the cutoff used on each measure. More stringent cutoffs may result in a more accurate prevalence rate derived from the BDI, BDI-PC, and CMDI.

Hypothesis VIII. Given the removal of items attributed to MS symptoms, patients' total scores on the MBDI-IM will be lower (and more accurate) and may result in more patients falling within the range of mild (and/or moderate) depression as opposed to potentially, inaccurately inflated total scores on the BDI-II which may result in more individuals placing in the moderate (and/or severe) depression range.

Goal 5. Creation of a new measure for use with MS. If it is found that the prorated modified measure (MBDI-IM) represents a more accurate measure of depression in MS, future research may be conducted evaluating the validity and reliability of this technique and measure.

Goal 6. Overarching goal. Enhance the detection and treatment of depression in MS in both scientific and clinical domains. Optimal cutoffs will be provided for the new measure as well as the three common self-report depression measures to provide clinicians and researchers further support for the use of modified cutoffs, if needed, in an MS sample in hopes of obtaining greater detection of depression in MS with more valid screening tools.

Research Design & Methods

Participants.

Multiple sclerosis participants were recruited through the Western Pennsylvania chapter of the Multiple Sclerosis Society and local support group meetings for MS. Recruitment of healthy controls was also conducted through the MS chapter and through referral by our MS participants. MS participants were asked if they had a friend of similar age and education who would like to participate. Recruitment of healthy controls in this manner is commonly used in the MS literature and facilitates matching controls to MS participants on important demographics variables. Exclusionary criteria for MS participants included history of alcohol/drug abuse; history or current diagnosis of a neurological disorder besides MS; 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 for the MS patients included a diagnosis of definite or probable MS based on the criteria outlined by Poser et al. (1983). Exclusionary criteria for healthy controls included history of alcohol/drug abuse; history or current diagnosis of a neurological disorder; severe visual or motor impairment that may have impeded cognitive testing; and evidence of a premorbid learning disability.

For the purposes of this investigation, healthy controls were also excluded if they (1) met criteria for depression on the SCID and/or met two of the other criteria for depression (proneness and significant other's report), or (2) their reported anxiety was one and half standard deviations or more above the mean on the State Trait Anxiety Inventory (STAI) state or trait scale. This resulted in the removal of five controls, resulting in a control group of 22 participants. Non-depressed MS patients were also removed if their reported anxiety was one and a half standard

deviations or more above the mean on the STAI. This resulted in the removal of 13 patients, leaving a non-depressed MS sample of 67.

The identification of depressed individuals was based on the following: (1) a score of 1.5 standard deviations or more above the mean of the significant others' report on the CMDI, (2) a score above the median on the DPRS, and (3) a diagnosis of a major depressive disorder on the SCID interview. The mean for the significant other's CMDI was derived from the healthy control sample (Mean = 22.73, S.D. = 9.20). The suggestion to use 1.5 or more standard deviations from the mean as the criterion for selection based on the CMDI was suggested by Nyenhuis, et al. (1995) and this criterion was used for selection for the sake of consistency. A median split of the DPRS (Median = 51) was conducted with the MS sample to separate the groups. Individuals who met at least two out of these three criteria were labeled as suffering from clinically significant depressive symptoms. Seventeen MS patients were found to meet two out of the three criteria for depression. 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. Comparisons of depression and anxiety measures between the depressed and non-depressed MS groups were also conducted (see Table 2).

Reports of depression and trait anxiety were greater for the depressed MS group than the non-depressed groups. There were no significant differences for current anxiety (STAI state scale) between the two groups.

Table 2.

Differences between depressed and non-depressed MS on depression and anxiety measures

Measure	**Depressed (N=17) Mean (SD)**	**Non-Depressed (N=67) Mean (SD)**	**t-test, sig.**
DPRS	62.06 (7.67)	44.58 (13.23)	t (82) = -7.09, p < .001
BDI-II	20.35 (6.49)	8.61 (4.80)	t (82) = -8.36, p < .001
BDI-PC	6.18 (2.24)	1.81 (1.62)	t (82) = -9.16, p < .001
CMDI Mood	32.47 (9.23)	18.63 (5.16)	t (82) = -5.95, p < .001
CMDI Eval	26.53 (10.24)	16.45 (3.56)	t (82) = -4.00, p = .001
CMDI Veg	40.35 (7.50)	33.21 (8.89)	t (82) = 3.05, p = .003
CMDI Total	99.35 (22.81)	68.28 (12.86)	t (82) = -5.40, p <.001
MBDI-I	16.06 (5.96)	7.88 (3.82)	t (82) = -5.38, p <.001
MBDI-IM	12.65 (6.54)	4.77 (2.89)	t (82) = -4.85, p <.001
STAI Trait	50.88 (6.31)	36.03 (6.99)	t (82) = -7.96, p <.001
STAI State	34.94 (9.59)	31.13 (7.16)	t (82) = -1.82, p =.072

Note. DPRS = Depression Proneness Scale; BDI-II = Beck Depression Inventory-II; BDI-PC = Beck Depression Inventory-Primary Care; CMDI Mood, Eval, Veg, Total = Chicago Multiscale Depression Inventory Mood, Evaluative, and Vegetative subscales, Total; Eval MBDI-I = Modified Beck Depression Inventory; MBDI-IM = Modified Beck Depression Inventory Minus MS Contribution, STAI Trait = State Trait Anxiety Inventory Trait Scale; STAI State = State Trait Anxiety Inventory State Scale.

Demographics of the three samples can be found in Table 3. There were no significant differences between the three groups on age, education, or estimated IQ. No significant differences were found between depressed and non-depressed 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 EDSS (see Table 4).

Table 3.

Participant demographics.

Variable	Depressed MS (N=17)	Non-Depressed MS (N=67)	Controls (N=22)
Age	45.24 (8.39)	47.93 (9.30)	46.18 (13.36)
Education	13.76 (1.89)	14.42 (1.99)	15.00 (1.93)
WAIS-R IQ Estimate	99.76 (9.86)	106.09 (9.23)	106.04 (12.17)
Gender (F/M)	14F/3M	56F/11M	18F/4M

Table 4.

Differences between depressed and non-depressed MS on disease variables

Disease Variable	Depressed (N=17) Mean (SD)	Non-Depressed (N=67) Mean (SD)	t- test, sig.
EDSS	5.18 (1.50)	4.32 (1.54)	t (82) = -2.06, p = .043
Symptom Duration	15.71 (8.34)	14.82 (9.22)	t (82) = -.360, ns
Diagnosis Duration	10.59 (6.42)	11.15 (8.66)	t (82) = .250, ns

Note. EDSS = Expanded Disability Status Scale

Procedures.

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 SCID interview was conducted at the completion of the testing session.

Measures.

Modified BDI-I (MBDI-I) and MBDI-I Minus MS Contribution (MBDI-IM). The modified BDI-I takes into account research in MS and clinical observations in adding follow-up

questions to certain BDI-I items thought to be confounded with MS symptomatology. These questions are intended to ascertain if and how much ones' endorsement of particular BDI items is due to MS or depression, per se. This modified BDI-I was designed by this investigator and is the principal instrument in this investigation (See Appendix). The BDI-I was chosen for modification given that it includes items (somatic preoccupation and work difficulty) that have been found to be frequently endorsed by MS patients. It has been suggested that these two items and the fatigue item are endorsed differently by MS patients on the BDI-I and should be removed. Exploration of these items may support or disconfirm these findings. The modified BDI-I was designed to explore not only the contribution of MS symptomatology to self-reported depression questionnaires, but to evaluate whether or not reports of depression are inflated in MS due to such overlap. As such, in the present investigation there is a Modified BDI-I (MBDI-I) used to explore attributions individuals make for their endorsement and more qualitative investigations (e.g., how much does your MS limit social activity?) and a Modified BDI minus MS contribution (MBDI-IM) for use with all other analyses. This MBDI-IM was created by removing any items of the MBDI-I that were found to be more related to MS than depression. Such a new measure should provide a purer representation of depression. Based on hypothesis 1, it was expected that certain items on the BDI-I would be endorsed by MS patients (depressed and non-depressed) independent of their depression. Further, non-depressed MS participants may have attributed these symptoms to their MS while depressed MS patients may not. Given this, data reduction of the MBDI-I to the MBDI-IM was conducted in the following manner. If a participant rated the contribution of MS symptoms (physical or cognitive) as 1 (Not at All) or 2 (A little) the item was considered to be unaffected in a significant way by MS symptomatology. However, if a participant rated the endorsement anywhere from 3 (Moderately) to 5 (Completely), endorsement of that item was interpreted as suggesting that the endorsement is either typical (Moderate) or excessive (Quite a Bit, Completely) and was considered more representative of MS symptomatology than depression. These items were subsequently not

included in the new measure of depression (MBDI-IM). On one item, sleep disturbance, patients were asked to rank order the physical and cognitive symptoms to which they attributed their sleep problems after having endorsed that their MS contributed significantly. Given that the individual was able to rank order "worry" as a contributor, their score on this item was included if they ranked "worrying about their MS" or "worrying in general" as their primary contributor (1^{st} or 2^{nd}). Based on these findings, participants obtained a new prorated score for their MBDI-IM. This new score is thought to be reflective of only the items that were endorsed as depression and not due to MS symptoms according to the above criteria. This prorated score was derived utilizing the following formula:

Prorated Score = Score of Valid Items * (21/Number of Valid Items)

Structure Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID) (First, Spitzer, Gibbon, & Williams, 1995). The SCID was conducted by the same clinician who administered the testing battery. The clinician conducting the interview did so following the five-hour neuropsychological battery and was kept blind to patients' self-report data. It should be noted that because the SCID interview includes only the Major Depressive Episode (MDE) component of the module, the DPRS and significant others' reports was used in conjunction with the clinician's report.

Depression Proneness Rating Scale (DPRS). The DPRS examines an individual's susceptibility to depression and tendency to experience long-lasting depression. It has been shown to be a valid predictor of past (measured by prior treatment, antidepressant prescriptions, suicide attempts, and hospitalizations) and future (as measured by the BDI) depression in the general population (Zemore et al., 1990). The DPRS asks participants about the frequency, severity, and duration of depressive episodes. It also includes depressive symptoms, ie. sense of failure, discouragement, isolation, etc. Participants are asked to rate themselves on these depressive features they have experienced over the past two years in comparisons to other people.

Chicago Multiscale Depression Inventory (CMDI). The CMDI is a 42-item inventory consisting of three subscales: mood (e.g., sadness), evaluative (e.g., feelings of uselessness), and vegetative (e.g., fatigue). Each subscale contains 14 items. These subscales can be used separately or in combination with one another. Patients are asked to rate themselves on a 5-point Likert scale the extent to which each word/phrase describes themselves during the past week, including today with "1" being "Not at All" and "5" being "Extremely." In the present investigation, the full scale of the CMDI (inclusion of mood, evaluative, and vegetative subscales) and all three independent subscales were used. A cutoff of one and half standard deviations above the mean of controls was used for each subscale and the full scale.

Significant Other's Chicago Multiscale Depression Inventory (CMDI-SO). Significant others of the participant also completed the CMDI in order to provide information regarding their views of the participants' current depression symptoms. Other investigators have suggested that reports from significant others be obtained (Aikens et al., 1998), as patients may not be most accurate in their perceptions of depression. Significant others' of patients are asked to rate on a scale of 1 to 5 the extent to which each word/phrase describes the patient during the past week, including today with "1" being "Not at All" and "5" being "Extremely." For the purpose of identifying depressed subjects by other's reports, only the mood subscale was used. A cutoff of one and half standard deviation above the mean of controls was used to differentiate depressed from non-depressed as recommended by Nyenhuis et al. (1995).

Beck Depression Inventory-II (BDI). The BDI-II is a self-report inventory consisting of 21 items. The BDI-II is 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 the extent that

they have experienced the symptom in the past two weeks yielding a total score in the range of 0 to 63.

Beck Depression Inventory – Primary Care (BDI-PC). The BDI-PC 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 the extent that they have experienced the symptom in the past two weeks yielding a total score in the range of 0 to 21.

Results

All statistical analyses were conducted using SPSS 14.0 computer software in conjunction with an algorithmic table designed in accordance with Steiner's (2003) publication regarding the sensitivity, specificity, NPV, and PPV of diagnostic and screening tools.

Initial examination of the relationship between the modified measures (MBDI-I and MBDI-IM), common self-report depression measures, and depression proneness was established using Pearson correlation coefficients (See Table 5).

Table 5.

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

	DPRS	BDI-II	BDI-PC	CMDI	MBDI-I	MBDI-IM
DPRS		.49**	.49**	.48**	.52**	.49**
BDI-II			.83**	.80**	.83**	.72**
BDI-PC				.77**	.78**	.73**
CMDI					.76**	.68**
MBDI-I						.85**

Note. DPRS = Depression Proneness Scale; BDI-II = Beck Depression Inventory-II; BDI-PC = Beck Depression Inventory-Primary Care; CMDI = Chicago Multiscale Depression Inventory; MBDI-I = Modified Beck Depression Inventory; MBDI-IM = Modified Beck Depression Inventory Minus MS Contribution.
** Significant at the .01 level

Both the MBDI-I and MBDI-IM were found to be moderately correlated with depression proneness and other self-report measures. The specific correlations (r =.52 and r =.49) with depression proneness and (r = .68 to r = .73) with other self-report depression measures were consistent with correlations found for the other measures, suggesting that these measures have concurrent validity with other more common measures.

The primary results of the present investigation can be organized into two categories: those findings that explore the phenomenological experience of depression in MS and guide the development of a "trunk and branch" model for assessing depression in MS; and those examining the utility of common self-report depression measures in MS and the proposed new measure. For clarity, study hypotheses I and II pertain to the former, while hypotheses III through VIII pertain to the latter. Finally, more qualitative findings regarding the endorsement patterns of MS patients were also found and will be discussed within.

Hypothesis I posited that MS patients, depressed or not, will endorse certain items on depression measures independent of depression. However, non-depressed MS patients may report that their endorsement of these items is attributed to their MS, while depressed MS patients will not attribute their endorsement to their MS, and will be more likely to attribute it to psychological factors. To determine if non-depressed MS patients attribute their endorsement of depressive symptoms to their physical and cognitive MS complaints more often than depressed MS patients, frequency and chi-square analyses were conducted of the follow-up questions of certain items thought to be confounded by MS (dissatisfaction, self-appraisal, self-criticism, irritability, work difficulty, sleep disturbance, fatigue, and loss of libido), assessing the contribution that physical and cognitive MS complaints have on patients' endorsement (see Table 6). It was found that depressed and non-depressed MS patients attribute physical MS complaints comparably as contributing to their initial endorsement of items assessing self-appraisal, work difficulty, and loss of libido. Similarly, there were no differences between the groups in how they attributed their cognitive MS complaints to reports of irritability, work difficulty, and fatigue. However, there were significant differences found for a greater number of depressed MS patients attributing their physical MS complaints to reports of dissatisfaction, self-criticism, irritability, and sleep disturbance, with a trend for fatigue. Similarly, a greater number

of depressed MS patients attributed their cognitive complaints to reports of dissatisfaction and self-criticism.

Table 6.

Frequencies of endorsement of questions assessing physical and cognitive MS symptoms contributing to reports of depression among depressed and non-depressed MS patients.

Item & Contributor	**Entire MS Sample**	**Depressed MS (N=17)**	**Non-depressed MS (N=67)**	**X^2, sig**
Dissatisfaction:				
Physical Symptoms	**52%**	**77%**	**46%**	**$X^2(1) = 4.96, p=.032$**
Cognitive Symptoms	**21%**	**41%**	**16%**	**$X^2(1) = 4.94, p=.026$**
Self-Criticism:				
Physical Symptoms	**32%**	**53%**	**27%**	**$X^2(1) = 4.23, p=.040$**
Cognitive Symptoms	**23%**	**47%**	**16%**	**$X^2(1) = 7.27, p=.007$**
Irritability:				
Physical Symptoms	**38%**	**65%**	**31%**	**$X^2(1) = 6.40, p=.023$**
Cognitive Symptoms	26%	41%	22%	$X^2(1) = 2.48$, ns
Self-Appraisal:				
Physical Symptoms	24%	35%	21%	$X^2(1) = 1.55$, ns
Work Difficulty:				
Physical Symptoms	54%	65%	51%	$X^2(1) = 1.06$, ns
Cognitive Symptoms	31%	47%	27%	$X^2(1) = 2.59$, ns
Sleep Disturbance:				
Physical Symptoms	**33%**	**59%**	**27%**	**$X^2(1) = 6.23, p = .013$**
Fatigue:				
Physical Symptoms	**29%**	**47%**	**24%**	**$X^2(1) = 3.57, p=.059$**
Cognitive Symptoms	71%	88%	67%	$X^2(1) = 2.95$, ns
Loss of Libido:				
Physical Symptoms	27%	35%	25%	$X^2(1) = .67$, ns

For certain items (irritability, fatigue, sleep disturbance appetite changes, and pessimism), follow-up questions were given in which patients could rate the contribution that specific MS and psychological symptoms had on their endorsement. It was speculated that depressed MS

patients would reveal a more psychological etiology in their endorsement. Reports revealed some differences between depressed and non-depressed MS patients' perceptions to which they attribute their complaints suggesting that depressed MS patients do in fact endorse psychological factors more often (see Table 7). More specifically, depressed MS patients attributed worrying as a contributor to their irritability more often than non-depressed MS. Depressed MS patients were also more likely to attribute worrying about their MS and bladder incontinence as contributing to their sleep problems. Physical effort was the only significantly different contributor in explaining depressed MS patients' fatigue. Lack of appeal of food and effort required to prepare a meal were endorsed more often by depressed MS patients than non-depressed MS patients in explaining their changes in appetite.

Table 7.

Endorsement patterns of depressed and non-depressed MS on follow-up questions

Item & Contributing Symptom	**Entire Sample**	**Depressed MS (N=17)**	**Non-depressed MS (N=67)**	**X^2, sig.**
IRRITABILITY				
Physical effort	21%	29%	19%	$X^2(1) = .81$, ns
Cognitive effort	10%	12%	9%	$X^2(1) = .12$, ns
Tremor, gait	4%	6%	3%	$X^2(1) = .33$, ns
Chronic Pain	1%	----	2%	$X^2(1) = .26$, ns
Sleep Disturbance	4%	----	5%	$X^2(1) = .79$, ns
Worrying	**4%**	**18%**	**----**	**$X^2(1) = 12.26$, p=.007**
Inability to get going	2%	----	3%	$X^2(1) = .52$, ns
Medications	----	----	----	
SLEEP DISTURBANCE				
Bladder Incontinence	**20%**	**41%**	**15%**	**$X^2(1) = 5.79$, p =.016**
Muscle Stiffness	4%	----	5%	$X^2(1) = .79$, ns
Chronic Pain	1%	----	2%	$X^2(1) = .26$, ns
Leg Spasms	8%	6%	9%	$X^2(1) = .17$, ns
Worrying about MS	**2%**	**12%**	**----**	**$X^2(1) = 8.08$, p = .039**
Worry in general	8%	12%	8%	$X^2(1) = .33$, ns
Medications	2%	----	3%	$X^2(1) = .52$, ns
FATIGUE				
Physical exertion	**44%**	**71%**	**37%**	**$X^2(1) = 6.09$, p =.014**
Mental exertion	6%	6%	6%	$X^2(1) = .00$, ns
Tremor, gait	5%	----	6%	$X^2(1) = 1.07$, ns
Chronic Pain	4%	----	5%	$X^2(1) = .79$, ns
Sleep Disturbance	13%	6%	15%	$X^2(1) = .97$, ns
Worry	2%	6%	2%	$X^2(1) = 1.12$, ns
Inability to get going	4%	6%	3%	$X^2(1) = .33$, ns
Medications	----	----	----	
APPETITE CHANGES				
Difficulty swallowing	4%	6%	3%	$X^2(1) = .33$, ns
Medications	1%	6%	----	$X^2(1) = 3.99$, ns
Tremors	----	-----	----	
Work required	**5%**	**18%**	**2%**	**$X^2(1) = 7.80$, p =.005**
Indigestion, heartburn	----	----	----	
Appeal of food	**8%**	**24%**	**5%**	**$X^2(1) = 6.44$, p =.011**

To test hypothesis II (that certain items will be endorsed more often by MS patients, suggesting, in part, that such items are more reflective of MS symptomatology than depression, but that the endorsement of these items may exceed what is common to MS and/or be related to other depressive symptoms in depressed MS patients), chi-square and correlational analyses were conducted. Initial chi-square analyses were conducted between MS and controls to first identify which symptoms were more prevalent in MS (see Table 8 and Figure 2). It was found that MS patients endorsed the following items at a disparate rate from healthy controls: fatigue, work difficulty, indecision, irritability, loss of libido, loss of interest, crying, dissatisfaction, and self-criticism. It should be noted that MS and controls did not differ in their endorsement of sleep disturbance, but both reported high rates (60% for MS and 46% for controls).

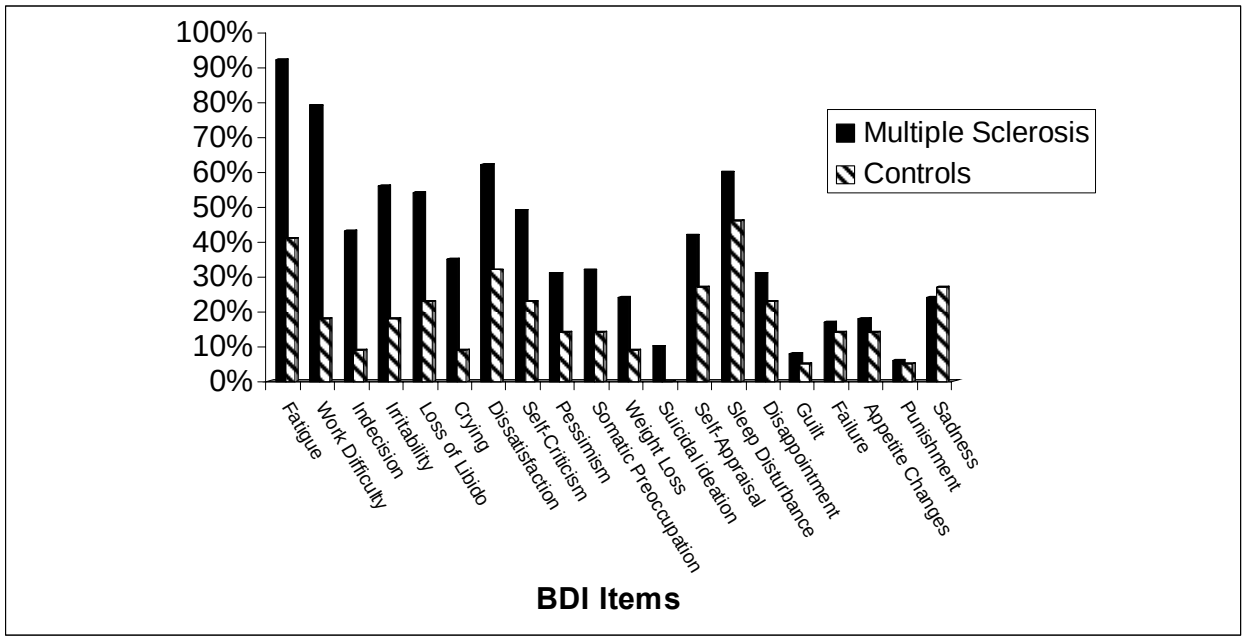
Table 8.

Differences in endorsement of BDI-I items between MS and healthy controls

Item	MS (N=84)	Controls (N=22)	X^2, p-Value
Fatigue	**92%**	**41%**	**$X^2(1) = 28.54$, p <.001**
Work Difficulty	**79%**	**18%**	**$X^2(1) = 27.63$, p <.001**
Indecision	**43%**	**9%**	**$X^2(1) = 8.64$, p = .003**
Irritability	**56%**	**18%**	**$X^2(1) = 9.96$, p = .002**
Loss of Libido	**54%**	**23%**	**$X^2(1) = 6.91$, p = .015**
Loss of Interest	**33%**	**5%**	**$X^2(1) = 6.86$, p = .007**
Crying	**35%**	**9%**	**$X^2(1) = 5.45$, p = .019**
Satisfaction	**62%**	**32%**	**$X^2(1) = 6.39$, p = .016**
Self-criticism	**49%**	**23%**	**$X^2(1) = 4.83$, p = .032**
Pessimism	31%	14%	$X^2(1) = 2.63$, ns
Somatic Preoccupation	32%	14%	$X^2(1) = 2.51$, ns
Weight Loss	24%	9%	$X^2(1) = 2.30$, ns
Suicidal Ideation	10%	----	$X^2(1) = 2.27$, ns
Self-Appraisal	42%	27%	$X^2(1) = 1.52$, ns
Sleep Disturbance	60%	46%	$X^2(1) = 1.41$, ns
Disappointment	31%	23%	$X^2(1) = .57$, ns
Guilt	8%	5%	$X^2(1) = .36$, ns
Failure	17%	14%	$X^2(1) = .12$, ns
Appetite Changes	18%	14%	$X^2(1) = .22$, ns
Punishment	6%	5%	$X^2(1) = .07$, ns
Sadness	24%	27%	$X^2(1) = .11$, ns

Figure 2

Differences in endorsement of BDI-I items between MS and healthy controls



The next step was to determine which symptoms were more indicative of depression in MS. In doing so, further examination of the endorsement patterns of depressed and non-depressed MS was warranted. Chi-square analyses were conducted between these two groups (see Table 9 and Figure 3). It was found that depressed MS patients endorsed the following items significantly more often than non-depressed MS patients: sense of failure, appetite changes, pessimism, loss of interest, sadness, crying, feelings of guilt, less satisfaction, disappointment, irritability, weight loss, and self-criticism. It should be noted that both depressed and non-depressed MS patients endorsed a high level of indecision (59% depressed, 39% non-depressed), somatic preoccupation (44% depressed, 29% non-depressed), work difficulty (87% depressed, 77% non-depressed), negative self-appraisal (47% depressed, 40% non-depressed), sleep disturbance (65% depressed, 58% non-depressed), and loss of libido (59% depressed, 53% non-depressed). Fatigue was found to be the most prevalent symptom with 91% of non-depressed MS and 94% of depressed MS patients.

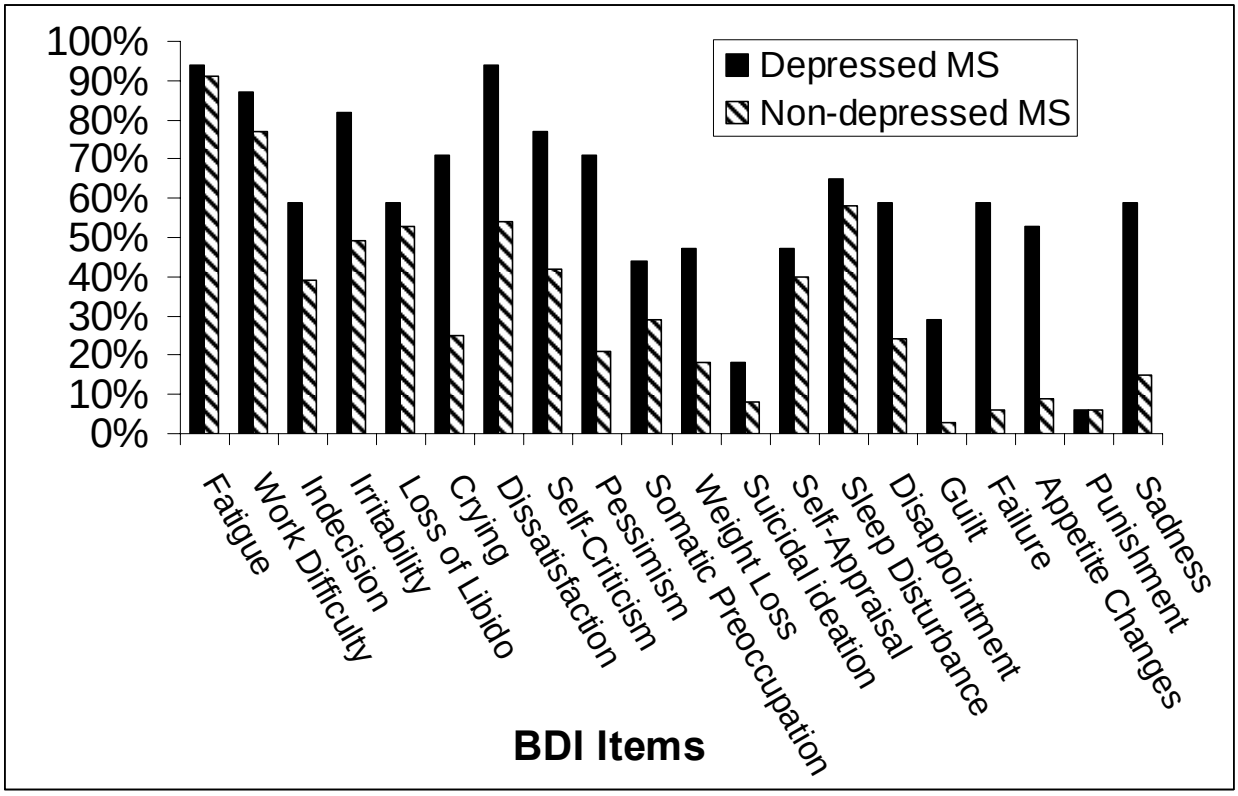
Table 9.

Differences in endorsement of BDI-I items between depressed MS and non-depressed MS

Item	Depressed MS (N=17)	Non-depressed MS (N=67)	X^2, sig.
Failure	**59%**	**6%**	**$X^2(1) = 27.27, p < .001$**
Appetite Changes	**53%**	**9%**	**$X^2(1) = 17.89, p < .001$**
Pessimism	**71%**	**21%**	**$X^2(1) = 15.67, p < .001$**
Loss of Interest	**71%**	**24%**	**$X^2(1) = 13.31, p = .001$**
Sadness	**59%**	**15%**	**$X^2(1) = 14.40, p < .001$**
Guilt	**29%**	**3%**	**$X^2(1) = 12.40, p < .001$**
Crying	**71%**	**25%**	**$X^2(1) = 12.26, p = .001$**
Satisfaction	**94%**	**54%**	**$X^2(1) = 9.39, p = .002$**
Disappointment	**59%**	**24%**	**$X^2(1) = 7.75, p = .005$**
Irritability	**82%**	**49%**	**$X^2(1) = 6.03, p = .015$**
Weight Loss	**47%**	**18%**	**$X^2(1) = 6.35, p = .012$**
Self-criticism	**77%**	**42%**	**$X^2(1) = 6.53, p = .014$**
Indecision	59%	39%	$X^2(1) = 2.22$, ns
Suicidal Ideation	18%	8%	$X^2(1) = 1.63$, ns
Somatic Preoccupation	44%	29%	$X^2(1) = 1.33$, ns
Work Difficulty	87%	77%	$X^2(1) = .74$, ns
Self-Appraisal	47%	40%	$X^2(1) = .26$, ns
Sleep Disturbance	65%	58%	$X^2(1) = .24$, ns
Loss of Libido	59%	53%	$X^2(1) = .18$, ns
Fatigue	94%	91%	$X^2(1) = .13$, ns
Punishment	6%	6%	$X^2(1) = .00$, ns

Figure 3

Differences in endorsement of BDI-I items between depressed MS and non-depressed MS



With the delineation of which symptoms are more common in MS and which are more prevalent in depressed MS patients, the final steps were to determine (1) which symptoms are more severe in the depressed MS and (2) which of these common MS symptoms are also associated with depression. To determine whether or not endorsement of depressive symptoms were more severe in the depressed MS group, Mann-Whitney U tests were conducted between depressed and non-depressed MS groups (see Table 10 and Figure 4).

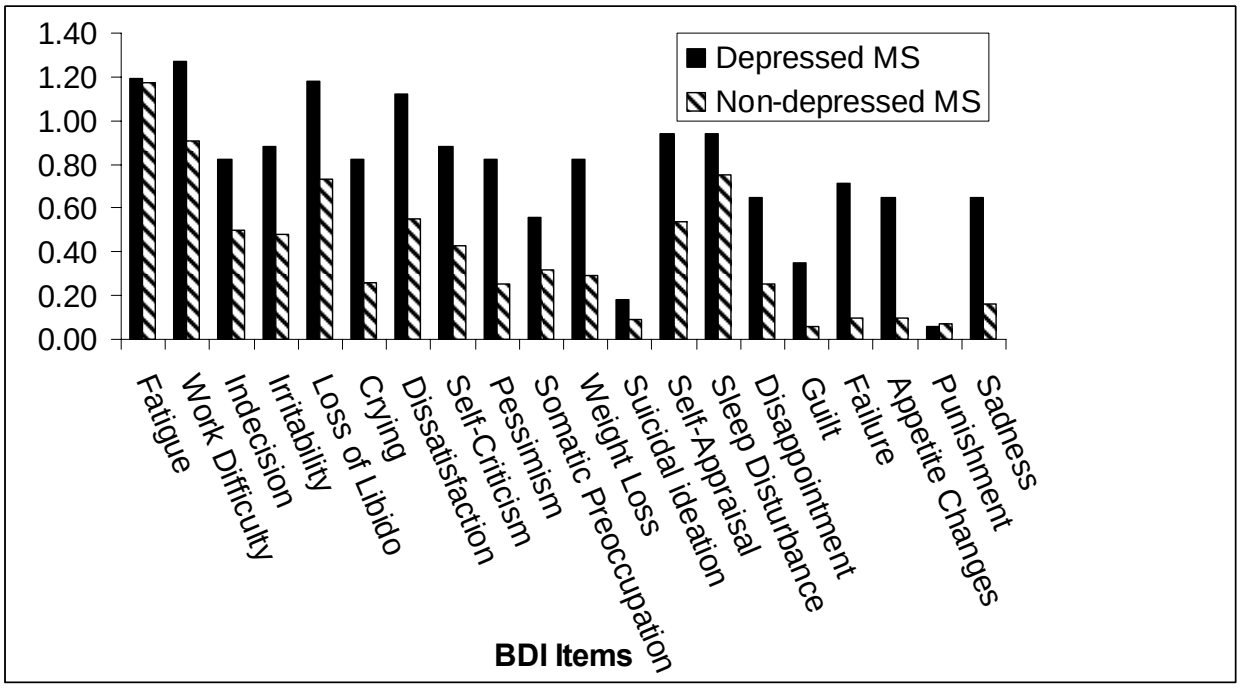
Table 10.

Differences in severity of depressive symptoms between depressed MS and non-depressed MS

Item	Depressed (N=17) Mean (S.D.)	Non-Depressed (N=67) Mean (S.D.)	Mann-Whitney U, sig.
Loss of Interest	**.82 (.64)**	**.24 (.43)**	**U = 287.500, p<.001**
Satisfaction	**1.12 (.49)**	**.55 (.50)**	**U = 285.500, p<.001**
Sadness	**.65 (.61)**	**.16 (.37)**	**U = 314.500, p<.001**
Crying	**.82 (.73)**	**.26 (.44)**	**U = 303.500, p<.001**
Pessimism	**.82 (.73)**	**.25 (.50)**	**U = 285.500, p<.001**
Failure	**.71 (.69)**	**.10 (.43)**	**U = 267.000, p<.001**
Appetite Changes	**.65 (.70)**	**.10 (.35)**	**U = 317.500, p<.001**
Guilt	**.35 (.61)**	**.06 (.29)**	**U = 420.500, p=.001**
Disappointment	**.65 (.61)**	**.25 (.44)**	**U = 362.500, p=.004**
Self-criticism	**.88 (.70)**	**.43 (.50)**	**U = 358.000, p=.007**
Irritability	**.88 (.49)**	**.48 (.50)**	**U = 364.500, p=.008**
Weight Loss	**.82 (1.07)**	**.29 (.73)**	**U = 400.500, p=.012**
Work Difficulty	1.27 (.70)	.91 (.61)	U = 467.500, ns
Somatic Preoccupation	.56 (.81)	.32 (.50)	U = 504.000, ns
Loss of Libido	1.18 (1.24)	.73 (.85)	U = 462.500, ns
Self-Appraisal	.94 (1.14)	.54 (.70)	U = 471.000, ns
Sleep Disturbance	.94 (.90)	.75 (.75)	U = 498.500, ns
Suicidal Ideation	.18 (.39)	.09 (.29)	U = 511.500, ns
Indecisiveness	.82 (.88)	.50 (.70)	U = 457.000, ns
Punishment	.06 (.24)	.07 (.26)	U = 569.000, ns
Fatigue	1.19 (.54)	1.17 (.57)	U = 559.500, ns

Figure 4

Differences in severity of depressive symptoms between depressed MS and non-depressed MS



Symptoms that were common to MS, regardless of depression, but were greater in depressed MS patients consisted of loss of interest, less satisfaction, crying, irritability, and self-criticalness. Other symptoms commonly reported by MS patients (fatigue, indecision, work difficulty, and loss of libido) were not found to be more severe in depressed MS patients. Symptoms that were found to be more representative of depression in MS were all more severe in the depressed MS sample.

Finally, to determine whether certain somatic symptoms may be reflective of depression if associated with symptoms more indicative of depression, a closer examination of the associations between "common" symptoms of MS and symptoms indicative of depression in this sample was conducted with both the depressed and non-depressed MS samples (See Table 11).

Table 11.

Correlations of common symptoms of MS and common symptoms of depression in depressed and non-depressed MS

Depressed MS (N=17)

	Symptoms Common to Depression						
Symptoms Common to MS	Sadness	Pessimism	Failure	Guilt	Disappointment	Appetite Changes	Weight loss
Dissatisfaction	-.05	-.12	**.49***	-.18	.40	.16	.30
Self-criticism	.18	.09	**.50***	-.08	**.62****	.06	.17
Crying	**.61****	-.18	**.50***	-.06	**.51***	.03	.10
Irritability	.42	-.35	**.50***	.41	**.53***	.15	-.11
Loss of Interest	.23	**-.64****	.30	.18	.21	-.12	.06
Indecision	-.15	-.13	.01	.40	.26	.24	-.01
Work Difficulty	-.05	**.50***	-.06	**.60***	.20	.33	-.10
Fatigue	-.07	.14	-.16	.15	-.14	.41	.17
Loss of Libido	.10	-.10	-.12	-.01	-.19	.04	.39
Sleep Disturbance	**.57***	.01	**.58***	.23	**.54***	.31	-.31

Non-depressed MS (N=67)

	Symptoms Common to Depression						
Symptoms Common to MS	Sadness	Pessimism	Failure	Guilt	Disappointment	Appetite Changes	Weight loss
Dissatisfaction	.05	.11	.15	.16	.24	.08	.06
Self-criticism	.07	**.39****	.19	.21	**.38****	-.06	-.10
Crying	.05	-.05	.16	-.10	.08	.17	.19
Irritability	.01	.00	-.05	.01	.22	.10	.07
Loss of Interest	.16	.14	.03	.10	**.34****	-.06	.00
Indecision	-.15	-.15	.01	.08	.13	-.15	.03
Work Difficulty	-.*32***	.02	-.06	-.09	.12	-.09	.02
Fatigue	.05	.20	**.26***	**.28***	**.30***	.02	-.05
Loss of Libido	-.09	-.00	-.10	-.03	.04	.22	.12
Sleep Disturbance	-.07	-.09	-.10	-.19	-.05	-.00	.22

* Significant at the .05 level
** Significant at the .01 level

Again, common symptoms of MS included crying, work difficulty, loss of interest, self-criticism, irritability, dissatisfaction, fatigue, indecision, and loss of libido. Symptoms most indicative of depression included sadness, pessimism, failure, guilt, disappointment, appetite changes, and weight loss. It was found that although crying was common to MS, it was also

significantly related to feelings of sadness, disappointment, and a sense of failure in the depressed MS group, while it was not related to any depressive symptoms in the non-depressed MS sample. Similarly, while reports of work difficulty are common in MS, these reports were also associated with feelings of pessimism and guilt in the depressed sample, while not being associated with any depressive symptoms in the non-depressed MS sample. Loss of interest, another symptom common to MS, was associated with feelings of pessimism in the depressed MS sample and with feelings of disappointment in the non-depressed MS sample. Feelings of self-criticism were also associated with feelings of disappointment in both the depressed and non-depressed MS sample and with feelings of pessimism in the non-depressed MS sample and failure in the depressed MS sample. Additionally, irritability and dissatisfaction, though common to MS, were both related to feelings and failure in the depressed MS sample. Irritability was also found to be related to feelings of disappointment in the depressed MS sample. Fatigue, an extremely common symptom in MS, was not related to any depressive symptoms in the depressed MS sample. However, in the non-depressed MS sample, fatigue was related to feelings of failure, guilt, and disappointment. Indecision and loss of libido were not found to be related to depressive symptoms in either group. Finally, although sleep disturbance was not an overtly discriminating symptom, it was found to be related to other significant symptoms of depression (sadness, sense of failure, disappointment) in the depressed sample, while showing no association with such symptoms in the non-depressed sample.

Based on these findings, a delineation of two sets of symptom clusters was revealed: (1) items endorsed by MS regardless of depression, so called “common” symptoms of MS and (2) items commonly endorsed by depressed individuals with MS but not non-depressed MS patients. Moreover, an appreciation of which common MS symptoms are more severe and/or associated with depression in the depressed sample was obtained. (See Table 12).

Table 12.

Delineation of symptom clusters found to be common to MS, common to depression, symptoms more severe in depressed MS, and symptoms associated with depression.

Symptom	**Common to MS**	**Common to Depression**	**Excessive in Depressed MS**
Fatigue	Fatigue‡	----------	----------
Indecision	Indecision	----------	----------
Loss of Libido	Loss of Libido	----------	----------
Work Difficulty†	Work Difficulty	----------	----------
Irritability†‡	Irritability	Irritability	Irritability
Loss of Interest†‡	Loss of Interest	Loss of Interest	Loss of Interest
Crying†	Crying	Crying	Crying
Dissatisfaction†	Dissatisfaction	Dissatisfaction	Dissatisfaction
Self-Criticism †‡	Self-Criticism	Self-Criticism	Self-Criticism
Sadness	----------	Sadness	
Pessimism	----------	Pessimism	
Failure	----------	Failure	
Guilt	----------	Guilt	
Appetite Changes	----------	Appetite	
Disappointment	----------	Disappointment	
Weight Loss	----------	Weight Loss	
Punishment	----------	----------	----------
Self-Appraisal	----------	----------	----------
Somatic Preoccupation	----------	----------	----------
Sleep Disturbance†	----------	----------	----------
Suicidal Ideation	----------	----------	----------

† Related to depressive symptoms in depressed MS group
‡ Related to depressive symptoms in non-depressed MS group

For certain symptoms an exploration of specific qualitative items was conducted. For example, the question, "How much do you take your MS into consideration when making plans with others (e.g., bladder urgency or inability to get around)" may elucidate the mechanisms by which MS patients experience a loss of interest in others (where "loss of interest in others" is an item on the BDI-I). Such items may have little utility *per se* in distinguishing depression from MS symptomatology, but could shed light on some of the idiosyncrasies in MS and quality of life, particularly in light of the finding that loss of interest was a symptom common to MS and may be more severe in those suffering from depression. It was found that depressed MS patients

were more likely to report that their MS influences their perception of their future, limits the plans they make with others, and is taken into account when making such plans, than non-depressed MS, while also impacting all MS patients at a relatively high rate of 24%, 19%, and 21%, respectively. Another important qualitative question was regarding how sleep disturbance may influence patients' fatigue. Given the high prevalence of fatigue in MS, any contributing factors should be examined. Regardless of whether or not they were depressed, MS patients reported that their sleep disturbance influences their fatigue (41% of the entire sample), and that once awake it was hard for them to fall back asleep (41% of the entire sample). Such findings are important given the impact that fatigue in MS has on overall quality of life and functioning. These findings suggest that more attention should be given to sleep problems in MS.

The second aim of this investigation was to improve the assessment of depression in MS by exploring the utility of common self-report depression measures and a modified self-report depression measure. To assess the sensitivity, specificity, positive predictive power, and negative predictive power of this new technique and measure (Modified Beck Depression Inventory –I – Minus MS Contributions [MBDI-IM]) and the three common measures (BDI-II, BDI-PC, CMDI [full scale and subscales]), Receiver Operating Characteristic (ROC) analyses were conducted (see Table 13). Based on hypotheses III and IV, it was speculated that the MBDI-IM would demonstrate the greatest sensitivity, specificity, PPV, and NPV, while the more common measures would vary in their accuracy. More specifically, hypothesis V postulated that the CMDI mood subscale would be the most accurate, followed by the BDI-PC, CMDI evaluative subscale, BDI-II, and finally, the CMDI vegetative subscale.

Table 13.

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and prevalence rate of depression using the BDI-II, BDI-PC, CMDI, MBDI-I, and MBDI-IM (based on a prevalence of 20%)

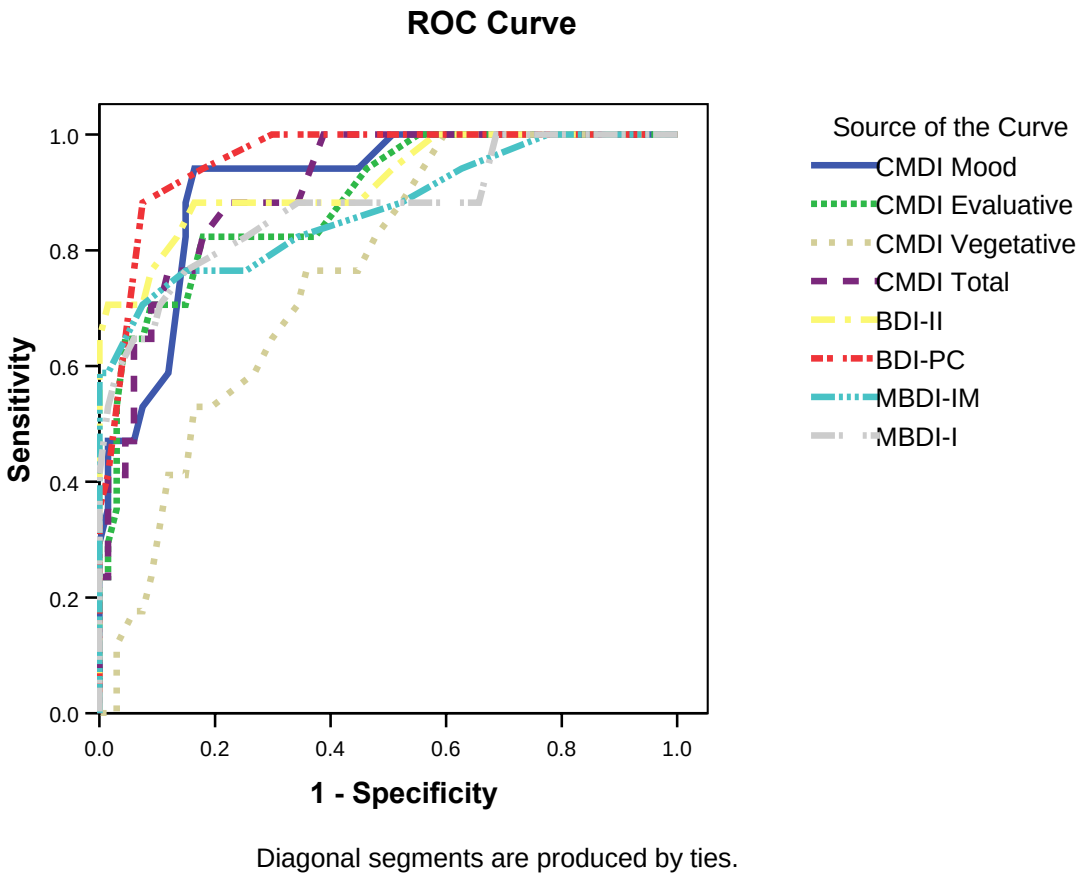
Measure	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Prevalence
BDI-II	13	.92	.882	.791	.517	.964	35%
BDI-PC	4	.96	.941	.821	.571	.982	33%
CMDI Total	81	.91	.765	.881	.619	.937	25%
CMDI Mood	27	.91	.588	.881	.556	.894	21%
	23	.91	.941	.836	.593	.982	32%
CMDI Evaluative	24	.89	.529	.970	.818	.890	13%
	21	.89	.706	.910	.667	.924	21%
CMDI Vegetative	35	.76	.765	.642	.351	.915	44%
MBDI-I	12	.87	.765	.851	.565	.934	27%
MBDI-IM	8	.87	.765	.851	.565	.934	27%
	10	.87	.706	.925	.706	.925	20%

It was found that 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 Figure 5). The previously suggested cutoffs of the BDI-II, BDI-PC, 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 88% and specificity of 79%, while the recommended cutoff of the BDI-PC of 4 had a sensitivity of 94% and specificity of 82%, suggesting that these cutoffs are acceptable for distinguishing depressed from non-depressed MS. The previously recommended cutoff of one-a-half standard deviations above the mean of controls (81) on the CMDI total score resulted in a sensitivity of 77% and a specificity of 88%, suggesting that this measure does not perform as well as the BDI-II and BDI-PC**,** but may be considered as a diagnostic tool. However, the CMDI evaluative and mood scale recommended cutoffs of one-a-half standard deviations above the mean (24 and 27, respectively) demonstrated improved specificity of and 96% and 88%, but poor sensitivity of 53% and 59%, suggesting a significant sacrifice of sensitivity for specificity. Finally, the vegetative scale of the CMDI performed the worst, with a poor sensitivity and

specificity (77% and 64%, respectively) suggesting minimal utility in distinguishing depressed from non-depressed MS.

Figure 5.

ROC curves of all depression measures



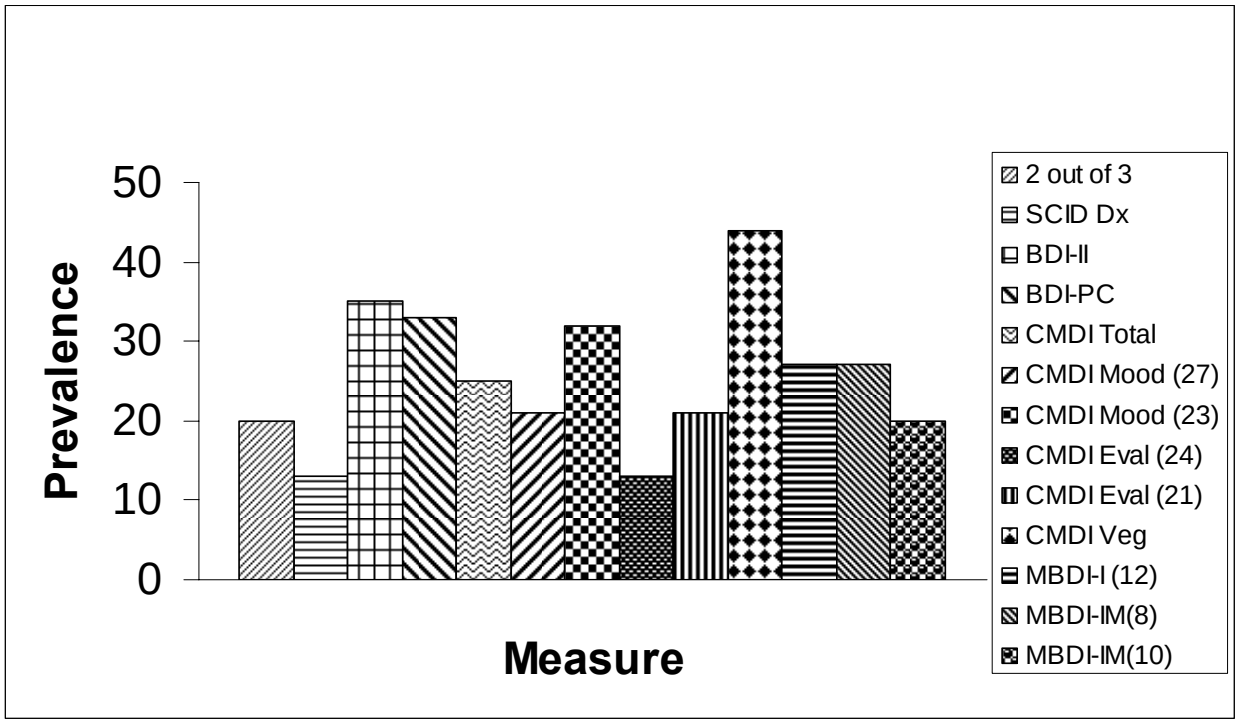
Note. MBDI-I = Modified Beck Depression Inventory-I, MBDI-IM = Modified Beck Depression Inventory-I (Minus MS Contribution), BDI-II = Beck Depression Inventory-II, BDI-PC = Beck Depression Inventory-Primary Care, CMDI Total = Full scale Chicago Multiscale Depression Inventory, CMDI Mood = Chicago Multiscale Depression Inventory Mood subscale, CMDI-Eval = Chicago Multiscale Depression Inventory Evaluative Subscale, CMDI Veg = Chicago Multiscale Depression Inventory Vegetative subscale.

By utilizing the ROC curves, the present recommended cutoffs of these measures remained 13 for the BDI-II and 4 for the BDI-PC, with a lower cutoff of 23 for the CMDI mood scale (sensitivity = 94%, specificity = 84%), and 21 on the CMDI evaluative scale (sensitivity = 71%, specificity = 91%). Given their novelty, there were no existing cutoffs for the MBDI-I and MBDI-IM, though it was speculated that the cutoff might be similar to the original cutoff of 10 on the BDI-I. It was found that a cutoff of 12 on the MBDI-I and a cutoff of 8 on the MBDI-IM were most accurate and exactly comparable (sensitivity = 77%, specificity = 85%). Raising the cutoff on the MBDI-IM to 10 improved the specificity (93%) while lowering the sensitivity (71%). All scores above this cutoff also showed superior specificity as is also found in examining the coordinates of the BDI-PC curve.

Finally, to further examine the characteristics of the new measure and assess whether hypothesis VI (that the MBDI-IM will generate more accurate depression prevalence rates), and hypothesis VII (that prevalence rates would differ depending on the cutoff used), comparisons were made between the prevalence rates resulting from use of this measure contrasted with prevalence rates resulting from use of the BDI-II, BDI-PC, and CMDI [full scale and subscales] (see Figure 6). Comparable prevalence rates were found for the BDI-II and BDI-PC using the recommended cutoffs of 13 (prevalence = 35%) and 4 (prevalence = 33%). Similarly, a prevalence of 27% was found for a cutoff of 8 on the MBDI-IM and 12 on the MBDI-I. A lower prevalence (20%) was found using a cutoff of 10 on the MBDI-IM. Consistent with previous findings of using a cutoff of one and a half standard deviation above the means for the CMDI, prevalence rates of 44%, 25%, 21%, and 13% were found using the vegetative, total score, mood, and evaluative scales, respectively. Using the modified cutoff of 21 on the evaluative scale and 23 on the mood scale resulted in almost the same prevalence found previously (21%) for the evaluative, and a higher, more consistent prevalence to other screening measures of 32% on the mood scale.

Figure 6.

Varying prevalence rates determined by measure and cutoff.



Note. 2 out of 3 = met two out of the three objective criteria (SCID-IV diagnosis, significant other's report, depression proneness), SCID Dx = Met criteria for depression on the DSM-IV, BDI-II = Beck Depression Inventory-II, BDI-PC = 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. MBDI-I = Modified Beck Depression Inventory-I, MBDI-IM = Modified Beck Depression Inventory-I (Minus MS Contribution),

Lastly, comparisons between the BDI-II and MBDI-IM were conducted to test hypothesis VIII (that less individuals will be classified as "moderately" depressed using a purer measure of depression). These comparisons found that the number of individuals classified as "moderately" depressed was reduced when using a purer measure of depression. In fact, the number of individuals classified as "moderately" depressed dropped from 10 (12%) on the BDI-II to two (2%) on the MBDI-IM. Moreover, one individual was classified as "severely" depressed on the

BDI-II (1%), while no one was classified as "severely" depressed on the MBDI-IM. However, both the BDI-II and MBDI-IM found 15 individuals (18%) to suffer from "mild" depression.

Discussion

The intent of the present investigation was to develop a better understanding and appreciation of the intricacies involved in assessing and treating depression in the medically-ill, particularly with a MS population. More specifically, this investigation sought to (1) determine which symptoms best differentiated depressed from non-depressed MS on self-report depression measures in hopes of developing a "trunk and branch" model for use with MS, (2) examine the accuracy and derived prevalence rates of commonly used self-report depression measures with a MS sample in comparison to a proposed modified self-report measure, and (3) provide recommendations to assist practitioners in assessing depression in MS by developing a better understanding of the phenomenological experience of depression in MS while also providing suggested cutoffs when using common self-report depression measures in screening or diagnosing depression in MS.

The first goal of this investigation was to develop a "trunk and branch" model for use in MS. The conceptualization of a "trunk and branch" model is that certain "trunk" symptoms (e.g., sleep disturbance), which are common in the medically-ill, may not be the most representative of depression while certain "branch" symptoms (e.g., sadness) may be more indicative. However, these "trunk" symptoms *may* be reflective of depression if the endorsement of the symptom exceeds what is typical for the disorder and/or if the symptom is related to other identified "branch" symptoms of depression.

Development of a disease-specific "trunk and branch" model was outlined specifically in the present investigation. It was hypothesized that certain items will be endorsed by both depressed and non-depressed MS patients more often than healthy controls, suggesting that these may be "trunk" symptoms of MS. However, the endorsement of these "truncal" symptoms may be greater in depressed MS patients and/or consistent with the endorsement of "branch" items, suggesting that although common to MS, they may be indicative of depression. It was also hypothesized that non-depressed MS patients' endorsement of "truncal" items would be

unrelated to their endorsement of "branch" items, while depressed MS patients would not only be more likely to endorse these "branch" items but their endorsement of "truncal" items would be related to them.

In order to develop such a model, this investigation examined the symptom endorsement of healthy controls, non-depressed MS patients, and depressed MS patients and distinguished symptoms into the following four categories: "branch" symptoms indicative of depression in MS, "trunk" symptoms common in MS, symptoms that exceed what is common in MS, and common MS symptoms associated with "depressive" symptoms in MS.

"Branch" symptoms indicative of depression in MS. Previously, in a general medical sample, Clark et al. (1983) found that sense of failure, suicidal ideation, sense of punishment, loss of social interest, dissatisfaction, and indecisiveness were the best indicators of depression in the medically-ill. More recently, feelings of pessimism, failure, dissatisfaction, suicidal ideation, irritability, crying, and loss of interest were found to be the best indicators of depression in a MS sample (Strober & Arnett, 2005). In the present investigation it was initially hypothesized that sadness, failure, guilt, punishment, disappointment, suicidal ideation, crying, and indecision were symptoms most likely to represent depression in MS, while loss of interest, pessimism, and dissatisfaction were also likely candidates, but could also be influenced by MS. In the present sample, symptoms most indicative of depression in MS were sadness, pessimism, sense of failure, guilt, disappointment, and changes in appetite and/or weight.

Consistent with the findings of Clark and this investigator, feelings of failure and pessimism continued to reign as significant symptoms of depression. Moreover, these findings confirmed the hypothesis of this study that sadness, disappointment, and guilt are important in assessing depression in MS. Surprisingly, dissatisfaction, suicidal ideation, and feelings of punishment, symptoms purported by Clark to be indicative of depression, were not. However, closer inspection found that six of the non-depressed MS and three of the depressed MS patients endorsed suicidal ideation, resulting in there not being a statistical difference. Such findings are

alarming given the high risk of suicide in MS and that these six patients were not categorized as depressed. The finding that dissatisfaction was prevalent in MS and perhaps not best at differentiating depression, is consistent with Cavanaugh's contention that dissatisfaction is common in the medically-ill. Patients' reports in this investigation may lend support to this idea as depressed MS patients attributed both their physical and cognitive MS complaints as contributing to their dissatisfaction. Moreover, both depressed and non-depressed MS reported dissatisfaction at a seemingly high rate (59% and 24%, respectively). Punishment, a symptom found by Clark to be indicative of depression, was neither common to MS nor depression and was reported at a seemingly low rate (6%) in both groups. This is a positive finding and may suggest adequate coping in which individuals with MS, depressed or not, do not view their disease as a punishment.

"Trunk" symptoms common in MS. Fatigue, sleep disturbance, appetite changes, concentration difficulties, psychomotor slowing, and sexual dysfunction are symptoms purported to be common to MS which could be misconstrued as depression. Reliance on such symptoms for diagnosing depression in MS may lead to erroneous diagnoses. An aim of this investigation was to determine and/or confirm which symptoms on a self-report depression measure (modified BDI-I) are common to MS. Based on endorsement patterns on this measure, it was found that symptoms of fatigue, work difficulty, indecision, irritability, loss of interest, loss of libido, crying, dissatisfaction, and self-criticism are common symptoms in MS.

Consistent with previous findings (Mohr et al., 1997), fatigue and work difficulty were found to be common in MS and may demonstrate little utility in identifying depression in MS. Given the high prevalence of sexual dysfunction it was not surprising that loss of libido was found to be common in MS. In fact 59% of depressed and 53% of non-depressed MS reported some disturbance in sexual functioning. However, based on previous results, the finding that loss of interest, dissatisfaction, crying, self-criticism, indecision, and irritability were considered to be common in MS and not helpful in differentiating MS patients who are depressed from non-

depressed was, in part, surprising. In previous investigations (Clark et al., 1983) it has been found that loss of social interest, dissatisfaction, and indecisiveness were among the six discriminating symptoms of depression in a medical sample. The presence of these symptoms suggests something of the experience of those suffering from MS. One can suppose that the indecision may be related to the high prevalence of cognitive impairment in MS while irritability and crying may be more related to the emotional lability seen in MS. Similarly, dissatisfaction is thought to be common in the medically-ill, and as stated before, was common to MS. Loss of interest may be a result of limited physical ability in a population which is typically more active. It is possible that these symptoms are experienced differently in MS than other medical conditions. In fact, in the present sample, approximately half of the non-depressed MS patients reported dissatisfaction and irritability while a quarter reported crying and loss of interest. However, further exploration is warranted before assuming that these symptoms have no utility in distinguishing depression in MS. Namely it is important to determine if the presence of the symptom exceeds what is common to MS and if it is related to other symptoms more indicative of depression.

Symptoms that exceed what is common in MS. Cavanaugh (1986) suggested that "trunk" symptoms may be more indicative of depression if the symptoms were disproportionate to the medical illness, and were related to the affective-cognitive symptoms of depression. In the present investigation, it was in fact found that while reports of irritability, loss of interest, crying, dissatisfaction, and self-criticism are common in MS, their endorsement was greater in those who were depressed. These findings confirm previous findings of the investigator that, with the exception of self-criticism, these symptoms depict depression in MS, despite being common to MS. It is therefore recommended that endorsement of these symptoms should be further examined in a MS sample to determine if they are found in conjunction with other symptoms more related to depression and if seemingly more severe than what is expected in MS. Moreover, reports of fatigue, work difficulty, loss of libido, and indecision were not found to be more

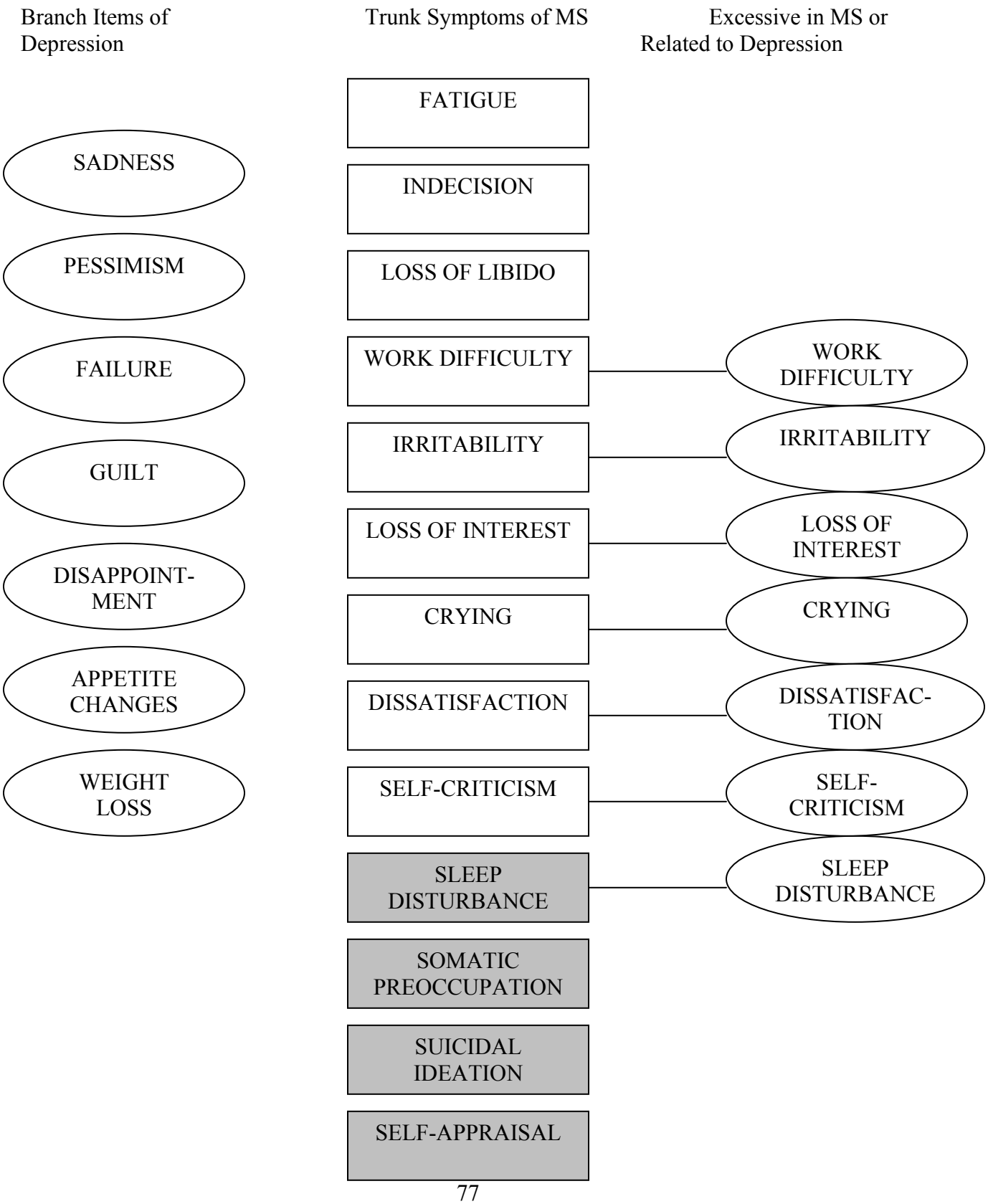
severe in depressed MS, suggesting that these are symptoms common to MS and may have little utility in differentiating depressed from non-depressed MS. In fact, at least a third and upwards of 94% of both depressed and non-depressed MS reported some variation of these symptoms that were not significantly different from one another.

Common MS symptoms associated with "depressive" symptoms in MS. Further support that a symptom may be indicative of depression is if it is found to be associated with symptoms purported to be indicative of depression. Symptoms common to MS that were found to be related to the identified depressive symptoms in the depressed MS group included dissatisfaction, self-criticism, crying, irritability, loss of interest, and work difficulty. With the exception of work difficulty, these symptoms were also found to be more severe in the depressed MS. It is suggested that these symptoms should not be underscored as possible predictors of depression in MS, despite being common to the disease. Similarly, sleep disturbance was found to be related to other significant symptoms of depression in the depressed sample, while showing no association with such symptoms in the non-depressed sample. This is consistent with previous findings of this investigator as well. It has been shown that sleep disturbance may be reflective of depression in MS if it is also found to be associated with other psychological factors (Strober, Arnett, Polen, & Bruce, 2002). Given this, attention should be given to reports of patients who experience sleep problems as well as these other symptoms, despite their being common to MS, in general. The relevance of these symptoms as indicators of depression is supported by the finding that other common symptoms of MS, namely fatigue, loss of libido, and indecision were not related to other depressive symptoms. Finally, fatigue, though regarded as an extremely frequent symptom of MS was found to be related to feelings of failure, guilt, and disappointment in the non-depressed MS sample, suggesting that fatigue may have a more detrimental impact overall on a patient's appraisal of self, even in the absence of clinical depression

Identification of these four symptom clusters aided in the development of a disease-specific "trunk and branch" model of depression in MS. In sum, the current investigation confirmed previous findings that feelings of failure and pessimism are adequate "branch" items. Feelings of sadness, guilt, disappointment, and changes in appetite and/or weight were also found to be useful as "branch" items when assessing depression in MS, and are not common to MS. It was also confirmed that fatigue is a "trunk" item least likely to be influencing reports of depression, while it was discovered that loss of libido and indecision may function similarly. Finally, it was found that loss of interest, crying, dissatisfaction, self-criticalness, and irritability (though "trunk" items common to MS), may be indicators of depression when exceeding what is typical in MS. Similarly, general consideration should be given to reports of crying, self-criticalness, irritability, loss of interest, and work difficulty as they were also found to be associated with other "branch" symptoms of depression. These findings suggest a sort of hierarchy in assessing depression in MS. Namely, reports of sadness, guilt, disappointment, feelings of failure, and pessimism, accompanied with appetite and/or weight changes should be given top priority. Secondly, if loss of interest, crying, dissatisfaction, irritability, and self-criticism are present, further exploration should be conducted to determine whether these symptoms exceed what one may expect in MS. Similarly, consideration should be given to determine the presence of all of these symptoms with the inclusion of work difficulty when other depressive symptoms are apparent, as they were found to be associated with such symptoms. Finally, given these findings, the least amount of merit should be given to reports of fatigue, loss of libido, and indecision when determining the presence of depression in MS. In the present investigation there were no conclusive findings found for the importance of reports of suicidal ideation, somatic preoccupation, punishment, self-appraisal, or sleep disturbance. These symptoms did not prove to be either common to MS or depression, statistically, but it should be noted that self-appraisal, somatic preoccupation, and sleep disturbance were highly prevalent in both non-depressed and depressed MS. Moreover, sleep disturbance was related to depressive

symptoms in the depressed group and is likely to be indicative of depression in the presence of such symptoms. Additionally, suicidal ideation should always be given top priority in the assessment of depression and was found to exist in both depressed and non-depressed MS, raising an alarming concern that 8% of the non-depressed MS who endorsed this item may not have been identified. Further research is warranted, as suicidal ideation and sleep disturbance are typically considered cardinal symptoms in the assessment of depression and may not be understood and properly addressed in MS. Based on these findings, a modified, disease-specific "trunk and branch" model is provided (see Figure 7).

Figure 7.
Modified "trunk and branch" model for use in MS



Another aim of this investigation was to examine the accuracy and derived prevalence rates of commonly used self-report depression measures with a MS sample in comparison to a proposed modified self-report measure. The modified measure was guided by the theory that removal of items on a depression measure found to be confounded by reports of MS complaints would result in a purer measure of depression. Given the significant overlap of depression and MS symptoms, some contend that common self-report depression measures may not be the most accurate in assessing depression in MS and may also result in inflated prevalence rates. In fact, the literature has shown a prevalence rate ranging from 16% to 26% when utilizing more stringent criteria to assess for depression in MS (e.g., SCID interviews), while varying cutoffs of commonly used measures result in prevalence rates that range anywhere from 25% to 33% with some outlying reports as high as 42%. Given such varying rates, it has been speculated that the accuracy of such measures may be compromised when used in MS. One hypothesis for such inflation is the inherent absence of follow-up inquiry on a self-report measure. Structured clinical interviews on the other hand, allow the diagnostician to determine if the report of a particular symptom is more likely to be attributed to MS or whether the presentation of the patient and other symptoms are more indicative of depression. By comparing common self-report measures that inherently have such overlap and a new measure which allowed patients to rate how much their MS contributed to their reports, thus allowing for the removal of items that overlapped, it was hoped that this investigation would shed some light in regards to the controversy surrounding the accuracy of these measures and resultant prevalence rates. Such an investigation of the commonly used measures and obviously, the proposed measure, was warranted at this time and does not exist in the extant literature.

Commonly used self-report depression measures in MS consist of the BDI-II, BDI-PC, and the CMDI. To date, it has been suggested that the CMDI mood scale is one of the most accurate measures in MS as it allows for the removal of both the vegetative and evaluative symptoms that may be more attributed to ones' MS and has resulted in prevalence rates similar

to those of more stringent criteria. The BDI-PC has been found to be useful in general medical populations, and recently recommended for use in MS. The BDI-PC consists only of items thought to reflect mood and evaluative symptoms of depression. The BDI-II, which includes all domains of depression (vegetative, evaluative, and mood), is perhaps the most popular self-report depression measure, but has been under scrutiny for use in medical populations, such as MS, as it includes several neurovegetative items. Given the inclusiveness of the BDI-II, there are at least five of the 21 symptoms (loss of energy, tiredness or fatigue, changes in appetite, changes in sleep pattern, and loss of interest in sex) that may be endorsed simply because they are also consequences of MS.

Given the noted advantages and disadvantages of these measures, it was speculated that the modified BDI-I minus MS contribution (MBDI-IM) would outperform these other measures, resulting in it having the greatest sensitivity, specificity, PPV, and NPV as a diagnostic tool in MS, while the CMDI mood subscale would be the most accurate as a screening measure, followed by the BDI-PC, CMDI evaluative subscale, BDI-II, and finally, the CMDI vegetative subscale. It was also expected that the MBDI-IM would result in a prevalence rate most akin to the prevalence rate when utilizing more stringent criteria for depression, if it were found to be a more specific measure.

Based on the findings of the present investigation, the BDI-PC performed the best as a screening tool in MS, followed by the BDI-II, and CMDI total score. However, closer examination of the CMDI total score suggests that it may be more appropriate as a diagnostic tool given its lower sensitivity than these two measures. These three measures resulted in prevalence rates ranging from 25% to 35%, suggesting that somewhere around 30% of MS patients will be screened as depressed using these measures. This prevalence rate is consistent with previous findings which suggest that the prevalence of depression in MS centers around 25% to 33% when utilizing common self-report screening measures. Both the CMDI mood and evaluative scales performed poorly using the previously suggested cutoffs (27 and 24,

respectively), while the vegetative scale had minimal utility in assessing depression in MS. However, a recommended cutoff of 23 on the mood scale of the CMDI improved its applicability as a screening tool, while a cutoff of 21 on the evaluative scale also improved its use as a diagnostic tool. In fact, the cutoff of 23 on the mood scaled performed as well as the BDI-PC as a screening tool, while the cutoff of 21 on the evaluative scale performed as well as the new measure, MBDI-IM, which was found to have the best utility as a diagnostic tool while not greatly sacrificing its sensitivity. The finding that the CMDI mood scale performed well as a screening tool confirmed the hypothesis, but required some modification to the previously recommended cutoff. The BDI-PC reigned as the best screening tool and is consistent with recent suggestions (Benedict et al., 2003) that the BDI-PC was well correlated with other self-reports, informant reports, and treatment for depression, making it a more appropriate measure for use in MS. Additionally, the finding that the BDI-II performed worse than these measures was consistent with study hypotheses and may be an artifact of its lower specificity. The BDI-II had the second lowest specificity after the vegetative scale of the CMDI and may be due to its reliance on neurovegetative symptoms. A possible explanation for the superior performance of the evaluative scale of the CMDI is the finding that approximately a third of the symptoms most indicative of depression were evaluative in nature (e.g. sense of failure, disappointment, self-criticism, guilt, and pessimism). It is suggested that a lower, potentially less stringent cutoff of the CMDI evaluative scale or the MBDI-IM be used for diagnosis of depression in MS.

In congruence with the exploration of the accuracy of these measures, the present investigation explored the resultant prevalence of these measures. Varying prevalence rates of depression in MS have led to some uncertainty as to whether or not we are accurate in our assessment. 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. If "all measures are created equal," differences in prevalence rates should not be found in one sample. In fact, in this sample alone, the prevalence rate varied widely from 13% when using the CMDI evaluative

scale to 44% when using the CMDI vegetative scale. On more conservative measures, the range was smaller, from 20% to 35%, while the more objective, stringent prevalence was 21%. It was theorized in this investigation that there would not only 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 evaluative and MBDI-IM (21% and 20%, respectively) were the closest approximation found when using the stringent criteria employed in this investigation as well as others. Consistent with this was the finding that fewer individuals were classified as suffering from moderate to severe depression on the MBDI-IM than the BDI-II.

In sum, it is recommended that the BDI-PC (cutoff of 4), BDI-II (cutoff of 13), and the CMDI mood scale (cutoff of 23) may be the best tools at our disposal at this time to screen for depression in MS. In attempts to obtain a more accurate assessment, as in the event of wanting to diagnose, a cutoff of 10 on the MBDI-IM, as well as a cutoff of 21 on the CMDI evaluative scale is recommended. Surprisingly, a cutoff of one and a half standard deviations above the mean on the CMDI total performed comparably to these measures as a diagnostic tool. Finally, the prevalence of depression when attempting to diagnose it was found to be approximately 21%, while positive screens on commonly used measures resulted in a prevalence rate as high as 35%.

Beyond the objective examination of self-report measures and development of a "trunk and branch" model, this investigation also served as a first attempt to better categorize and understand how MS patients construe their symptoms and whether or not their MS symptoms significantly contribute to, and confound their reports of depression. This was accomplished by asking patients to describe how their physical and cognitive complaints of MS contributed to their endorsement of particular symptoms of depression on a self-report measure (dissatisfaction, self-appraisal, self-criticism, irritability, work difficulty, sleep disturbance, fatigue, and loss of libido). It was speculated that non-depressed MS patients may endorse certain symptoms on the

basis of the symptom being a consequence of their MS as opposed to actual depression (e.g., fatigue), while depressed MS patients would not attribute their depressive symptoms to their MS, and may attribute them to more psychological factors. It has been suggested that endorsement of such symptoms by non-depressed MS patients may lead to inflated and inaccurate depictions of depression in MS. In contrast to what was expected, depressed and non-depressed MS patients attributed their MS complaints to their reports of depression symptoms comparably on most symptoms, with the following notable exceptions. Depressed MS patients attributed their physical MS complaints as accounting for their reports of dissatisfaction, self-criticism, irritability, and sleep disturbance and their cognitive MS complaints as contributing to their reports of dissatisfaction and self-criticism on self-report depression measures more often than non-depressed MS patients. These findings are in contrast to what was expected and may suggest that depressed patients may be more likely to endorse MS symptoms as contributing to their reports than non-depressed MS. This may be indicative of an overall bias of depressed individuals to "over report" and may also be a reflection of the greater trait anxiety that was found in the depressed sample. It is questionable whether or not this depressed MS sample was simply more likely to report symptoms. This tendency may also contribute to these patients having a greater level of illness intrusiveness, which may circumvent their reports of depression and anxiety as well.

However, follow-up analyses of the specific symptoms to which they attribute their endorsement of certain items (irritability, sleep disturbance, fatigue, and appetite changes) allowed for a better understanding of the specific nature of their endorsement (e.g., biological versus psychological). Upon reporting that they attributed their physical and cognitive complaints of MS to their symptoms on a depression measure, patients were asked about the specific symptoms that may account for such endorsement. Reports indicated that there may be a greater psychological etiology of the symptoms that depressed MS patients endorse. In particular, depressed MS patients attributed worrying about their MS as influencing their reports

of sleep disturbance and worrying, in general, as contributing to their irritability on a depression measure. Depressed MS patients were also more likely to attribute changes in appetite on a depression measure to a lack of appeal of food and effort required to prepare a meal. In regards to the contribution that physical complaints of MS may have on endorsement of depression symptoms, depressed MS patients were more likely to attribute bladder incontinence as contributing to their endorsement of sleep problems and physical effort as contributing to their fatigue. Unexpectedly, non-depressed MS patients were not more likely to attribute physical complaints to their reports of depressive symptoms. Lastly, it should be noted that MS patients, depressed or not, rated physical MS complaints as influencing their level of dissatisfaction and work difficulty at seemingly high rates, 52% and 54%, respectively. Such findings have significant implications in light of quality of life and overall functioning. Such findings suggest that ameliorating the effects of physical complaints may improve the lives and functioning of MS patients.

Moreover, 71% of MS patients reported that cognitive MS symptoms contributed to their fatigue. There has been a significant discussion in the literature regarding the experience of fatigue in MS and the distinction of physical and cognitive fatigue. In this sample, it appears that there were greater reports of fatigue being experienced through cognitive complaints, not physical. Such findings suggest that more attention be given to the phenomenological experience of fatigue in MS and the potential influence that cognitive complaints and effort have on its report. Using fatigue measures that differentiate cognitive from physical fatigue might be especially illuminating in this regard. The Fatigue Impact Scale (Fisk et al., 1994) would be particularly applicable in that it consists of physical, cognitive, and social fatigue subscales. Related to this, the finding that sleep disturbance was endorsed as contributing to fatigue in 41% of the sample suggests that further investigations are warranted in examining sleep problems in MS. Previous findings by this investigator have in fact found that sleep disturbance is a great predictor of fatigue in MS (Strober, Arnett, Bruce, Polen, & Smith, 2002). From subjective

reports in this sample, this finding appears to be replicated. Other relevant findings are that, dissatisfaction, self-criticism, and irritability (symptoms found to be common to MS, but more severe in depressed) were reported at strikingly high rates. In particular, 94% of depressed MS patients reported dissatisfaction with 82% reporting irritability, and 77% endorsing being more self-critical. However, 54% of non-depressed MS reported dissatisfaction, 49% increased irritability, and 42% self-criticism. These findings suggest that attention be given to these symptoms because, though common to MS, they appear to have a real presence in the lives of those suffering from MS. They may be at a severe level when they reach a threshold to meet criteria, and should be considered in those who do not meet criteria in hopes of improving their quality of life and warding off depression.

Lastly, more qualitative questions found that depressed MS patients were more likely to attribute their MS as contributing to their perceptions of their future, limiting the plans they make with others, and is taken into account when making such plans (see Table 14). In fact, only 18% of non-depressed MS while 47% of depressed MS reported that their MS contributed to their negative views of their future. Given the high risk of suicide in MS and the importance of assessing loss of interest as a cardinal symptom of depression, these findings are important. These findings may suggest that treatment for depression in MS address the importance of reducing the intrusion of MS on one's perceptions and interest in others as they may further exacerbate feelings of depression (e.g., despair and alienation/withdrawal).

Table 14.

Endorsement differences between depressed and non- depressed MS on follow-up qualitative items.

Item	Depressed MS (N=17)	Non-depressed MS (N=67)	X^2, sig.
Perception of future influence by MS	**47%**	**18%**	**$X^2(1) = 6.35, p = .022$**
MS limits social activity	**53%**	**10%**	**$X^2(1) = 15.88, p < .001$**
MS taken into account when making plans	**53%**	**13%**	**$X^2(1) = 12.57, p < .001$**
Sleep disturbance influences fatigue	53%	47%	$X^2(1) = 1.38$, ns
Difficult to fall back asleep when wakened	59%	36%	$X^2(1) = 2.99$, ns

A final relevant finding of this investigation was the lack of group differences between depressed and non-depressed MS patients on various disease variables (disease duration and symptom duration) while there was a difference between the two groups on disease severity (EDSS). Depressed MS patients were slightly more disabled than non-depressed MS. There are mixed findings regarding the relationship between depression and disease severity in the literature, with some studies finding a direct relationship, and others showing no association. It has also been questioned whether differences in duration of illness may impact the development of depression in MS (e.g., shorter duration being associated with greater depression), which was also not found in this sample. However, it should be noted that the mean duration for both groups was around 10 years, a time at which the risk of depression is thought to decline.

Taken together, it is felt that beyond the clear objectives of this investigation, a better appreciation for the subjective and intricate experiences of MS was also found. Having a better

understanding of these experiences should not only improve our treatment of MS and hopefully enhance the lives of MS patients, but also guide further research. In particular, further investigation of this new measure is warranted. Subsequent investigations in both a clinical and community based sample is needed to determine its utility and aid in the development of this approach and measure. Additionally, replication of the present investigation may find 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-PC as this is the first investigation exploring its sensitivity and specificity in a MS sample. Moreover, investigations that continue to examine the symptom representation of MS patients can allow for further development of a disease-specific model for use with MS. By beginning to explore such representation, and symptom clusters, a better appreciation of how to best treat the symptoms can also be obtained.

There were several limitations of this investigation. First, the omission of a structured clinical assessment of comorbid anxiety disorders which may have influenced patients' endorsement patterns was problematic. The finding that, despite removing patients whose anxiety was significant, depressed MS patients were still significantly higher in trait anxiety may have resulted in their overall "over reporting" of symptoms. Future investigations may want to more systematically examine the influence of anxiety, and potential illness intrusiveness and ways in which they may pervade reports of depression and MS symptoms in MS patients, overall. Another noteworthy limitation of this investigation was the absence of a depressed control sample. The significance of this investigation would have been improved if there were final comparisons between depressed MS and depressed controls to substantiate the findings that certain symptoms are more representative of depression. A third limitation of this study was the sample size. In examining the psychometric properties of any new measure or the properties of existing measures, a large sample is ideal. Subsequent investigations of this measure among a larger sample size are still warranted.

Despite these limitations, the present investigation does provide valuable information pertaining to the experiences of those suffering from MS, the accuracy and utility of self-report depression measures in MS, and the beginning of the development of a "trunk and branch" model for use with MS. It is hoped that readers take with them the following information regarding assessing depression in MS. Depression is a frequent complaint of those suffering from MS. Prevalence rates range anywhere from a low of 16% to a high of 42%. Given this, there is a tremendous obligation for clinicians and researchers to do their best to accurately assess depression in their patients. This investigation suggests that, in doing so, consideration should be given that depressed MS patients are likely to report symptoms of sadness, pessimism, feelings of failure, guilt, disappointment, and changes in weight and/or appetite. Despite being common to MS, such patients also may be likely to endorse symptoms of irritability, loss of interest, crying, dissatisfaction, and self-criticism that seem to exceed what one may expect in MS. Finally, although very common, complaints of work difficulty should be given a closer look as it may be more related to depression. With this said, reports of fatigue, loss of libido, and indecision should not be considered as indicative of depression as may be seen in a "healthy" population. Finally, reports of suicidal ideation, sleep disturbance, and somatic preoccupation may need to be further evaluated on an individual basis. Particular attention should be given to sleep problems as they were found to be related to sadness, sense of failure, and disappointment, despite not being reported as an excessive or common symptom of MS or indicative of depression. Moreover, suicidal ideation requires serious consideration given the increased risk of suicide in MS and the finding that six MS patients in this sample endorsed having suicidal thoughts despite not meeting criteria for depression.

When unable to give such individualized attention, as in a clinical interview, self-report measures may be utilized, but caution should be given as to which are used for screening and which are used for a diagnosis. In particular, the BDI-PC, BDI-II, and CMDI mood scale are adequate measures for screening depression in MS. The proposed measure (MBDI-IM), CMDI

evaluative scale, and the total CMDI appear to attain the best accuracy in diagnosing depression in MS. Based on the findings of the investigation, the following guidelines are given in assisting researchers and clinicians in properly identifying and hopefully treating the symptoms of depression in MS (see Table 15).

Table 15.

Guidelines for assessing depression in MS

Measure	Suggested Cutoff	Screening	Diagnosis
BDI-II	13	X	
BDI-PC	4	X (superior)	
CMDI Total	81		X
CMDI Mood	27		X
	23	X	
CMDI Evaluative	24		X
	21		X (superior)
MBDI-IM	10		X (superior)

	Symptoms of Depression	Excessive in Depressed MS	Related to MS (Not likely depression)
Sadness	X		
Pessimism	X		
Failure	X		
Dissatisfaction		X	
Guilt	X		
Punishment			
Disappointment	X		
Self-criticalness		X	
Suicidal Ideation	X (historically)		
Crying		X	
Irritability		X	
Loss of Interest		X	
Indecision			X
Self-appraisal			
Work Difficulty			X
Sleep Disturbance			
Fatigue			X
Appetite Changes	X		
Weight Loss	X		
Somatic Preoccupation			
Loss of Libido			X

In sum, it is hoped that the proposed investigation provides clinicians and researchers a better understanding and appreciation of the intricacies involved in assessing and treating depression in the medically-ill, particularly with a MS population. It is hope that some clarity

was gained in regards to the uncertainty in the current literature regarding prevalence rates of depression in MS while aiding in our selection of the best measure and cutoff for use with MS. Moreover, it is hoped that an exploration of the modified BDI and patients' endorsement will enhance clinicians' understanding of what symptoms can best differentiate depression in MS while potentially providing a new measure and technique for assessing depression in MS in the future. Such information is invaluable when attempting to understand the experience of those suffering from MS and disentangling what is depression and what may be a consequence of their disease. Finally, it is felt that the creation and support of a "trunk and branch" model for use with MS was attained and will hopefully guide further research in developing and applying such models in MS and other medical conditions. Such clarity and specificity may enhance our detection of depression in various medical populations, improve our treatment, and guide theoretical conceptualizations of depression in the medically-ill. However, first and foremost, the aim of this investigation was to improve the lives and care of MS patients. It is hoped that the knowledge gained through this investigation will make a significant contribution to both research and practice in attaining this goal.

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Appendix

MODIFIED BECK INVENTORY

On this questionnaire are groups of statements. Please read each group of statements carefully. Then pick out the one statement in each group which best describes the way you have been feeling the PAST WEEK. INCLUDING TODAY! Circle the number beside the statement you picked. If several statements in the group seem to apply equally well, circle each one.
Be sure to read all the statements in each group before making your choice.

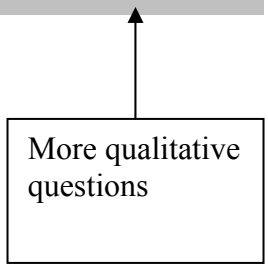
Following some of the numbered statements below are follow-up questions that relate to the immediately preceding numbered question. These statements generally ask you to estimate the extent to which your physical (including fatigue, gait changes, tremor, etc) or cognitive (memory, attention, etc.) MS symptoms contribute to your answer to the numbered question. Please answer these to the best of your ability.

1	0	I do not feel sad.
	1	I feel sad.
	2	I am sad all the time and I can't snap out of it.
	3	I am so sad or unhappy that I can't stand it.
2	0	I am not particularly discouraged about the future.
	1	I feel discouraged about the future.
	2	I feel I have nothing to look forward to.
	3	I feel that the future is hopeless and that things cannot improve.

On a scale of 1 to 5, please rate how much your view of your future, as rated on Q #2 above, has been influenced by your perception of the progression of your MS.

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

3	0	I do not feel like a failure.
	1	I feel I have failed more that the average person.
	2	As I look back on my life, all I can see is a lot of failures.
	3	I feel I am a complete failure as a person.
4	0	I get as much satisfaction out of things as I used to.
	1	I don't enjoy things the way I used to.
	2	I don't get real satisfaction out of anything anymore.
	3	I am dissatisfied or bored with everything.



On a scale of 1 to 5, how much have your ***physical*** symptoms of MS prevented you from doing what you usually enjoy doing?

Not at All	A Little	Moderately	Quite a bit	Completely

1 2 3 4 5

On a scale of 1 to 5, how much have your ***cognitive*** symptoms of MS prevented you from doing what you usually enjoy doing?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

Follow-up questions assessing MS symptom contribution

5 0 I don't feel particularly guilty.
1 I feel guilty a good part of the time.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6 0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7 0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

8 0 I don't feel I am any worse than anybody else.
1 I am critical of myself for my weaknesses or mistakes.
2 I blame myself all the time for my faults.
3 I blame myself for everything bad that happens.

If you rated yourself 1 or above on question # 8 above, on a scale of 1 to 5, to what extent do your ***physical*** symptoms of MS contribute to the things you blame yourself for?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

If you rated yourself 1 or above on question # 8 above, on a scale of 1 to 5, to what extent do your ***cognitive*** symptoms of MS contribute to the things you blame yourself for?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

9 0 I don't have thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10 0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry all the time now.
3 I used to be able to cry, but now I can't cry even though I want to. 11

11 0 I am no more irritated now than I ever am.
1 I get annoyed or irritated more easily than I used to.
2 I feel irritated all the time now.
3 I don't get irritated at all by the things that used to irritate me.

If you rated yourself 1 or above on question # 8, on a scale of 1 to 5, to what extent do your ***physical*** symptoms of MS contribute to your increased irritation?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

If you rated yourself 1 or above on question # 8, on a scale of 1 to 5, to what extent do your ***cognitive*** symptoms of MS contribute to your increased irritation?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

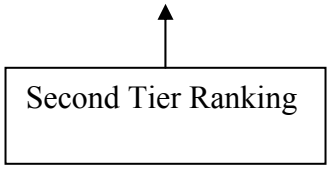
If your rating for either of the 2 questions you just answered was 2 or higher, please

answer the following questions:

What contributes most to your increased irritation? Check those items that apply and then rank those you've checked in order of their contribution, with "1" being the biggest contributor.

____ Increased effort to perform physical tasks
____ Increased effort to perform cognitive tasks
____ Difficulties associated with tremors, gait, etc.
____ Chronic pain
____ Sleep disturbances
____ Constant worrying
____ Inability to get going
____ Medications
____ Others: _____

12 0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.



If you rated yourself 1 or above on question # 12, please answer the following questions to how they may pertain to your reduced interest in others:

On a scale 1 to 5, please rate how much your MS limits your social activity.

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

On a scale of 1 to 5, please rate how much you take your MS into account when making plans with others, such as, getting around in public places, bladder urgency, etc.

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

13
0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions than before.
3 I can't make decisions at all anymore.

14
0 I don't feel I look any worse than I used to.
1 I am worried that I am looking old or unattractive.
2 I feel that there are permanent changes in my appearance that make me look unattractive.
3 I believe that I look ugly.

On a scale of 1 to 5, how much do you attribute how you look, as rated above on Q # 14, to your ***physical*** MS symptoms.

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

15
0 I can work about as well as before.
1 It takes an extra effort to get started at doing something.
2 I have to push myself very hard to do anything.
3 I can't do work at all.

On a scale of 1 to 5, how much have your ***physical*** symptoms of MS interfered with your ability to do things, as rated above on Q #15?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

On a scale of 1 to 5, how much have your ***cognitive*** symptoms of MS interfered with your ability to do things, as rated above on Q #15?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

16
0 I can sleep as well as usual.
1 I don't sleep as well as I used to.
2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep
3 I wake up several hours earlier than I used to and cannot get back to sleep.

If you rated yourself 1 or above on question # 16, how much have your ***physical*** symptoms of MS interfered with your sleep?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

If your rating for the question you just answered was 2 or higher, please answer the

following questions:

What contributes most to your sleep disturbance? Check those items that apply and then rank those you've checked in order of their contribution, with "1" being the biggest contributor.

____ Bladder incontinence
____ Muscle stiffness
____ Chronic pain
____ Leg spasms
____ Worrying about your MS
____ Worrying in general
____ Medications
____ Others: _____

Once you have awakened, how difficult is it for you to fall back asleep?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

How much, on a scale of 1 to 5, do you think your sleep disturbance influences your fatigue during the day?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

17 0 I don't get more tired than usual.
1 I get tired more easily than I used to.
2 I get tired from doing almost anything.
3 I am too tired to do anything.

If you rated yourself 1 or above on question # 17, please answer the following questions:

On a scale of 1 to 5, how much of your tiredness, as rated above, is due to your ***physical*** symptoms of MS?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

If your rating for the question you just answered was 2 or higher, please answer the following questions:

What contributes most to your tiredness? Check those items that apply and then rank those you've checked in order of their contribution, with "1" being the biggest contributor.

____ Typical, daily physical exertion
____ Typical, daily mental exertion
____ Difficulties associated with tremors, gait, etc.
____ Chronic pain
____ Sleep disturbances
____ Constant worrying
____ Inability to get going
____ Medications
____ Others: _____

On a scale of 1 to 5, how much of your tiredness, as rated above, is due to your ***cognitive*** symptoms of MS?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

18 0 My appetite is no worse than usual.
1 My appetite is not as good as it used to be.
2 My appetite is much worse now.
3 I have no appetite at all anymore.

What contributes most to your change in appetite? Check those items that apply and then rank those you've checked in order of their contribution, with "1" being the biggest contributor.

____ Difficulty swallowing
____ Medications
____ Complications/frustrations due to tremors, etc.
____ Work required to prepare a meal
____ Indigestion, heartburn, etc.
____ Lack of appeal of food

19
0 I haven't lost much weight, if any, lately.
1 I have lost more than 5 pounds.
2 I have lost more than 10 pounds.
3 I have lost more than 15 pounds.

* I am purposely trying to lose weight by eating less: Yes_____ No_____

20
0 I am no more worried about my health than usual.
1 I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think about anything else.

On a scale of 1 to 5, how much of your concern for your health is due the symptoms mentioned above that you can attribute solely to your MS?

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

21
0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

On a scale of 1 to 5, please rate how much your interest in sex is affected by your physical symptoms of MS.

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

Vita

Lauren B. Strober

EDUCATION

Doctor of Philosophy, Clinical Psychology
Pennsylvania State University, University Park, PA — August 2007
Dissertation: Depression in Multiple Sclerosis (MS): The distinction between MS and depressive symptomatology and utility of self-report instruments
Advisor: Peter A. Arnett, Ph.D, Associate Professor

Predoctoral Internship, Clinical Psychology, Neuropsychology Specialty Track — August 2007
Veterans Affairs (VA) of Western New York, Buffalo, NY
Supervisor: Kerry Donnelly, Ph.D, ABPP-CN

Master of Science, Psychology — May 2003
Pennsylvania State University, University Park, PA
Thesis: An examination of four models predicting fatigue in Multiple Sclerosis (MS).
Advisor: Peter A. Arnett, Ph.D, Associate Professor

Bachelor of Arts, Major: Psychology, Minor: Biology, pre-med — May 1998
University at Albany, State University of New York

HONORS & AWARDS

Penn State University College of Liberal Arts Graduate Student Excellence in Research Award	2006
Research & Graduate Studies Office (RGSO) award for travel	2006
Don A. Trumbo Psychology Department Student Research Fund	2002, 2004
Bruce V. Moore Graduate Fellowship in Psychology	2001, 2002

PROFESSIONAL AFFILIATIONS

International Neuropsychological Society
National Academy of Neuropsychology

RESEARCH/CLINICAL INTERESTS

Adult and pediatric clinical neuropsychology; phenomenological research of secondary factors associated with multiple sclerosis (e.g., depression, fatigue, personality changes, and sleep disturbance); adjustment and coping with chronic medical illness; and the effects of mood and sleep disturbance on cognitive functioning and overall quality of life.

PUBLICATIONS:

Strober, L.B., & Arnett, P.A. (2005). An examination of four models predicting fatigue in Multiple Sclerosis (MS). *Archives of Clinical Neuropsychology, 20(5*), 631-646.
Strober, L.B. & Arnett, P.A. Assessment and treatment of depression in three medically-ill, elderly populations: Alzheimer's disease, parkinson's disease, and stroke. (Accepted with revisions) *The Clinical Neuropsychologist,* April 10, 2007.

GRANTS APPLIED FOR:

Ruth L. Kirchstein National Research Service Award