

# Exploration of Undertreatment and Patterns of Treatment of Depression in Multiple Sclerosis

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**Background:** *Depression is a common comorbid condition with multiple sclerosis (MS). Historically, however, it has been undertreated. Little is known about the characteristics of those who receive, or do not receive, treatment for depression in the MS population. This study evaluated depression treatment in patients with MS, associated patient characteristics, and probable determinants of antidepressant drug use in those with and without depression.*

**Methods:** *A total of 152 patients with MS completed questionnaires and the Structured Clinical Interview for DSM-IV-TR (SCID) to determine depression status. Tabular analyses and a binary regression model were used to identify patient characteristics associated with antidepressant drug use.*

**Results:** *Of participants with major depression according to the SCID, 65% were taking antidepressant medications. With adjustment for successful treatment (antidepressant drug use by those not currently depressed and currently depressed), the prevalence of treated depression increased to 85.7%. Of those receiving treatment for depression, 19% were receiving nonpharmacologic treatment alone, 38% were taking antidepressant drugs only, and 44% were receiving both pharmacologic and nonpharmacologic treatments. Demographic and clinical variables were not statistically significantly associated with antidepressant drug use in those with depression.*

**Conclusions:** *A large proportion of participants with depression in MS are now receiving treatment, a change from previous reports. The adequacy of treatment has become a bigger question because many of the treated patients continued to have depressive symptoms. Further research is needed to identify ways to achieve better outcomes for depression.*  
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**D**epression is commonly associated with multiple sclerosis (MS); estimates of lifetime prevalence are as high as 50%.<sup>1,2</sup> These depression estimates are higher than those usually reported in the general population (eg, 12.2% in the Canadian Community Health Survey: Mental Health and Well-being<sup>3</sup>) and in association with chronic illnesses (eg, 13% in a widely cited report by Wells et al.<sup>4</sup>). The 12-month prevalence of depression has been reported to be 25.7%

in people with MS compared with 8.9% in the general population,<sup>5</sup> although comparative prevalence estimates vary.<sup>6</sup>

Some literature suggests that both antidepressant drugs and psychotherapy are effective for depression in people with MS.<sup>7–9</sup> However, recent American Academy of Neurology guidelines<sup>10</sup> and a Cochrane review<sup>11</sup> have questioned the quality of evidence supporting the efficacy of antidepressant drug treatment in people with MS. Studies of psychotherapy have shown promising results. Psychotherapy assists patients in developing skills to cope with thoughts, emotions, and adjustments to MS diagnosis.<sup>12</sup> Interventions that focus on developing coping skills have been shown to be more effective at reducing depression in MS compared with supportive group interventions.<sup>9</sup> A 16-week study<sup>8</sup> found that individual cognitive-behavioral therapy (CBT) and the selective serotonin reuptake inhibitor sertraline were

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equally effective, with both forms of treatment superior to supportive-expressive group therapy (SEG). Another study by the same group<sup>13</sup> compared 16 weeks of telephone-administered CBT with 16 weeks of telephone-administered SEG. Telephone-administered CBT was again found to be superior to telephone-administered SEG in improving depression in MS, with improvements maintained at the 12-month follow-up.

It is often reported that depression in MS is underdiagnosed and undertreated.<sup>14-16</sup> For example, in 2006, Mohr et al.<sup>16</sup> reported that 65.6% of patients with MS diagnosed as having depression using a structured telephone interview did not receive any medication. Non-pharmacologic forms of treatment were not assessed in this study. Another study conducted in 2007<sup>14</sup> found that 59% of patients with MS and depression were not receiving medication, and the other 41% were receiving inadequate medical management. Understandably, these concerns have led to recommendations for screening for depression in the MS population.<sup>17</sup> However, screening for depression in MS has not yielded the expected results,<sup>18</sup> and only modest improvement in outcomes has been observed when regular screening was incorporated as part of the management of depression in MS. Many individuals with positive screening results were found to be aware of their depression, and many were already receiving treatment. This suggests that screening was not achieving its usual goal of early detection. In another study,<sup>19</sup> even when depressed individuals were prompted to seek treatment, few sought treatment. This may have been related to misguided beliefs regarding the inevitability of depression, practical issues, or the depression itself, which may diminish motivation, energy, and hope.<sup>19</sup> In any case, these studies suggest that quality and acceptance of treatment, rather than mere detection of depression, are key issues.

Recommendations for screening are predicated on the idea that underdetection of depression is the major challenge. However, there have been very large increases in the use of antidepressant agents in the general population<sup>20</sup> such that the extent of undertreatment of depression in general may be diminishing over time. Although this trend has not been reported specifically in the MS population, antidepressant drug use may also have increased in people with MS. To develop strategies for priority setting, improving access, and ensuring appropriate treatment, it is necessary to understand the char-

acteristics of people with MS who receive and do not receive treatment.

In this study, we examined the prevalence of depression and the use of antidepressant agents and psychotherapy in a clinical sample of adults with MS. Our specific aims were to 1) evaluate the frequency of depression and antidepressant drug use in patients with MS, 2) describe the treatment patterns of depression, and 3) identify the characteristics and predictors of antidepressant drug use.

## Methods

### Participants

This project used data collected for the Neurological Disease and Depression Study (NEEDS). Outpatients attending the Calgary Multiple Sclerosis Clinic (Calgary, AB, Canada) for their follow-up appointments were recruited consecutively. The eligibility criteria were 1) age 18 years or older, 2) province of Alberta resident, 3) proficient in English, 4) no severe hearing impairment (interviews were administered by telephone), and 5) absence of neurologist-diagnosed dementia, severe developmental delay, or aphasia. Study participants were further restricted to those who met the diagnostic criteria for MS as determined by an MS neurologist. Eligibility was determined by the attending neurologist before arrival of the patient in the clinic. Patients who presented with possible MS or a clinically isolated syndrome were excluded. The study protocol and consent forms were approved by the Conjoint Health Research Ethics Board at the University of Calgary.

### Procedures

The recruitment process involved a two-stage consent procedure. Initially, preliminary consent was obtained that allowed the research staff to discuss the study with potentially eligible patients. Once preliminary consent was obtained, the study staff explained the study and obtained written informed consent. Consent was required for the completion of a questionnaire, medical record review, and a telephone call within 2 weeks for telephone administration of the Structured Clinical Interview for *DSM-IV-TR* (SCID), the reference standard for psychiatric diagnoses used in this study.<sup>21</sup>

The questionnaire package included a detailed demographic section, several questions related to depression and treatment (Have you been diagnosed with depression by a health professional? Who is currently managing [treating] your depression? Are you currently taking

any antidepressant medications? Are you currently receiving other forms of treatment for your depression?), and three depression scales (the Patient Health Questionnaire-9 [PHQ-9],<sup>22</sup> the Hospital Anxiety and Depression Scale [HADS],<sup>23</sup> and the Center for Epidemiologic Studies-Depression [CES-D] scale<sup>24</sup>). Participants were asked whether they had ever been diagnosed as having depression by a health professional and whether they were currently taking medication or receiving nonpharmacologic treatment for depression. Nonpharmacologic treatment included visits with psychiatrists, counselors, psychologists, or other specialists. These variables were assessed with single items from field-tested questionnaires used in Canadian national surveys.<sup>25</sup> Trained senior graduate psychology students masked to depression status on the questionnaires administered the SCID over the telephone within 2 weeks of each participant's clinic appointment. The questionnaire package also included a disease severity scale and a quality of life questionnaire, namely, the 12-item Short Form Health Status Survey (SF-12)<sup>26</sup> (an abbreviated version of the SF-36<sup>27</sup>). Additional information, such as MS course, medication use, and a neurologist-rated Expanded Disability Status Scale (EDSS) score,<sup>28</sup> was gathered through medical record review after recruitment.

## Measures

### The PHQ-9

The PHQ-9 consists of nine questions designed to align with the nine diagnostic criteria for major depression in the *DSM-IV-TR*.<sup>22</sup> Each item is rated from 0 (not at all) to 3 (nearly every day), with a possible total score ranging from 0 to 27. One way of scoring the PHQ-9 is through the cut-point method. This method suggests major depression with a total score of 10 or higher of 27. A cut-point of 10 yields sensitivity of 88% and specificity of 88% compared with a structured psychiatric interview in the general population.<sup>22</sup>

### The HADS

The HADS is a 14-item self-report questionnaire that includes a depression subscale (7 items) and an anxiety subscale (7 items).<sup>23</sup> This instrument has been designed to disentangle symptoms associated with depression from somatic symptoms that may be better explained by MS.<sup>23</sup> Symptoms of anxiety and depression related to physical disorders, such as dizziness, headaches, insomnia, anergia, and fatigue, are excluded.<sup>23</sup> Each item is scored from 0 to 3 depending on the severity of difficul-

ty experienced, for a total possible score of 21. The most frequently used cut-point score of 8 results in sensitivity of 90% and specificity of 87% in patients with MS.<sup>29</sup>

### The CES-D Scale

The CES-D scale is a 20-item instrument that measures depressive symptoms with an emphasis on the cognitive and affective components of depression.<sup>24</sup> Each item is rated from 0 to 3, with a total score ranging from 0 to 60. This scale includes six components: depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. The standard cut-point score for the CES-D scale is 16, with no available data on the sensitivity and specificity in patients with MS.

### The SCID

The SCID is a semistructured diagnostic interview considered the gold standard for the diagnosis of psychiatric conditions.<sup>21</sup> It was developed to represent the *DSM-IV-TR*<sup>30</sup> criteria for mental disorders. This instrument is administered by a trained health professional with the ability to follow up on the required symptoms and seek clarification when needed. Depression was diagnosed if the appropriate number and level of symptoms were present for 2 weeks during the previous month according to *DSM-IV-TR* criteria.<sup>21</sup> Major depressive disorder was defined in this study in the same way that it is defined in *DSM-IV*: the occurrence of one or more major depressive episodes. Hence, the analysis includes both currently active and lifetime cases.

### The SF-12

The SF-12<sup>26</sup> is a shortened version of the SF-36 quality of life instrument<sup>27</sup> containing 12 items that measure health-related quality of life. It encompasses domains of general health, physical functioning, social functioning, role limitations caused by physical problems, role limitations caused by emotional problems, mental health, vitality, and bodily pain. This instrument contains two subscales, a physical component summary and a mental component summary.

### Disease Severity Scale

The disease severity scale is an ad hoc–designed scale for the NEEDS. This scale is a self-reported measure of the perceived severity of MS. Participants rated their perceived disease severity from extremely severe to not at all severe. For analyses, the disease severity scores were categorized into mild (not at all severe, a little severe,

and somewhat severe), moderate (moderately severe), and severe (quite severe, very severe, and extremely severe).

### The EDSS

The EDSS was used to measure neurologic impairment in MS.<sup>28</sup> This scale rates neurologic impairment in MS from 0 (normal neurologic examination) to 10 (death due to MS) in 20 steps.<sup>28</sup> For the analyses, the EDSS scores were categorized into mild (<3.5), moderate ( $\geq 3.5$ –<5.5), and severe ( $\geq 5.5$ ).

Medical record review and patient self-report data were used to examine treatment of depression. If the medical record review indicated the use of psychotropic medication for any indication or receiving treatment from a mental health professional (psychiatrist, psychologist, counselor, or therapist) for depression, they were also considered treated. The adequacy of the medication dosage, the quality of psychotherapy, and the use of adjunctive depression treatments, such as medication or exercise, could not be assessed due to a lack of availability of this information in patients' medical records.

### Assessment of the Frequency of Treatment

In addition to calculating a conventional antidepressant drug–treated frequency, the proportion of depressed individuals receiving antidepressant drug treatment for depression was adjusted for successful treatment in individuals with remitted depression by using the algorithm created by Beck and Patten,<sup>31</sup> further described as adjusted antidepressant drug–treated prevalence or proportion. This adjustment took into account antidepressant drug–treated individuals without depression. When the antidepressant drug–treated proportion is calculated as the frequency of treatment in those with active depression, the treatment frequency is typically underestimated because participants who have been successfully treated with antidepressant agents (those taking the medication and no longer depressed) are neglected. The “liberal adjusted” method was used to calculate the adjusted proportion of treatment ( $P$ ). The adjustment is liberal in the sense that all of those taking antidepressant agents and not depressed are assumed to represent successful outcomes. These participants are added to both the numerator and denominator of the estimated treatment frequency:

$$P = (a + c)/(a + b + c)$$

where  $a$  is the number of individuals with depression taking antidepressant agents,  $b$  is the number of indi-

viduals with depression not taking antidepressant agents, and  $c$  is the number of individuals without depression taking antidepressant agents.

### Statistical Analysis

Descriptive statistics were used to characterize the study population, and comparisons were made using exact tests of proportions. Because the analysis combined current and lifetime cases, stratified analysis techniques were used to assess the heterogeneity of associations depending on past versus current use. The Cochran-Mantel-Haenszel test of heterogeneity was used to assess effect measure modification, and the pooled Cochran-Mantel-Haenszel estimate was used to identify confounding in situations in which effect measure modification was not evident. Variables for inclusion in the stratified analysis included sex, age, functional status, severity of disease, marital status, highest level of education, and income. Because age is a continuous variable, a binary regression model was used rather than stratification, with heterogeneity assessed by a cross-product interaction term. This was fit as a generalized linear model of the binomial family using a log link function. Results are presented as prevalence ratios with 95% confidence intervals (CIs). Statistical analysis was performed using Stata release 11.0 (StataCorp LP, College Station, TX).

### Results

During the study, 554 patients booked visits to the MS clinic; 299 patients were presented with preliminary consent forms, and 281 (94.0%) provided their informed consent for participation. Of those who provided consent, 152 (54.1%) completed the questionnaire and the SCID. This is the final sample used in the present analysis. The demographic characteristics of the study sample are listed in Table 1. According to the SCID, 20 participants were currently depressed, for an estimated prevalence of 13.2% (95% CI, 7.7%–18.5%). Lifetime prevalence, as defined by current depression or past episodes, was 38.8% (95% CI, 31.0%–46.7%). Some statistically significantly different characteristics were identified between those with and without current depression as defined by the SCID (Table 1). Individuals with current depression self-reported higher levels of MS disease severity and had a lower mean mental quality of life score on the SF-12 (28.1,  $P < .001$ ). Of the individuals with depression according to the SCID ( $n = 20$ ),

**Table 1. Characteristics of individuals with multiple sclerosis by depression status**

Characteristic	Overall (N = 152)	With depression (n = 20) <sup>a</sup>	Without depression (n = 132) <sup>a</sup>
Sex, %			
Female	78	70	79
Male	22	30	21
Age, %			
<50 y	46	60	44
≥50 y	54	40	56
EDSS score, %			
<3.5 (mild)	59	42	61
≥3.5 to <5.5 (moderate)	16	26	15
≥5.5 (severe)	25	32	24
Severity of disease, %			
Mild	69	45 <sup>b</sup>	73 <sup>b</sup>
Moderate	21	25	20
Severe	10	30	7
Marital status, %			
Married or living with someone	72	70	72
Not living with anyone	28	30	28
Educational level, %			
High school diploma and lower	39	30	40
Postsecondary education	61	70	60
Income, %			
Receiving disability	22	35	20
Not receiving disability	78	65	80
Not employed	51	55	50
Employed	49	45	50
Mental quality of life score, mean <sup>c</sup>	38	28 <sup>b</sup>	40 <sup>b</sup>

<sup>a</sup>With/without depression defined as current depressive episode according to the Structured Clinical Interview for DSM.

<sup>b</sup>Significant difference at  $P < .05$ .

<sup>c</sup>Quality of life based on 12-item Short Form Health Status Survey scores. Higher scores indicate greater quality of life.

75% reported that they had been diagnosed as having depression by a health professional.

Characteristics associated with antidepressant drug use and nonuse in participants diagnosed as having current and lifetime depression are shown in Table 2. No interactions between any of these characteristics and current versus lifetime depression were identified (all  $P > .05$ ). The current versus lifetime distinction also did not act as a confounder in the analysis: in all cases, the adjusted and unadjusted prevalence ratios from stratified and model-based analyses were similar to the crude estimates.

Of those receiving pharmacologic or nonpharmacologic treatment for their depression defined by the SCID

**Table 2. Characteristics of individuals with multiple sclerosis and depression<sup>a</sup> by antidepressant drug use status**

Characteristic	Not taking antidepressant drugs (n = 7)	Taking antidepressant drugs (n = 13)
Sex, %		
Female	57	77
Male	43	23
Age, %		
<50 y	86	46
≥50 y	14	54
EDSS score, %		
<3.5 (mild)	33	46
≥3.5 to <5.5 (moderate)	33	23
≥5.5 (severe)	33	31
Severity of disease, %		
Mild	29	54
Moderate	57	8
Severe	14	38
Marital status, %		
Married or living with someone	71	69
Not living with anyone	29	31
Educational level, %		
High school diploma and lower	29	31
Postsecondary education	71	69
Income, %		
Receiving disability	43	31
Not receiving disability	57	69
Not employed	57	54
Employed	43	46
Mental quality of life score, mean <sup>b</sup>	31	26.5

<sup>a</sup>Depression defined as current depressive episode according to the Structured Clinical Interview for DSM.

<sup>b</sup>Quality of life based on 12-item Short Form Health Status Survey component scores. Higher scores indicate greater quality of life.

(n = 16), 19% were receiving nonpharmacologic treatment alone (n = 3), 38% were taking medication only (n = 6), and 44% were receiving both pharmacologic and nonpharmacologic treatments (n = 7). The antidepressant agents used by those depressed according to the SCID and recorded in patient medical records were duloxetine (n = 1), venlafaxine (n = 2), bupropion (n = 1), trazodone (n = 1), and escitalopram (n = 1). Individuals receiving nonpharmacologic treatment visited psychiatrists (n = 2), counselors (n = 3), and psychologists (n = 3). Using the Beck and Patten method, the adjusted antidepressant drug–treated proportion was 85.7% compared with 65% with the conventional method.

Characteristics of antidepressant drug use and non-use in individuals without depression according to the SCID are shown in Table 3. None of the characteristics assessed were statistically significantly different between those using and not using antidepressant agents. Approximately 22% of those without depression according to the SCID (n = 29) were receiving pharmacologic or nonpharmacologic treatment. Of the 29 individuals receiving treatment, 82.8% (n = 24) were taking medication alone and 17.2% (n = 5) were receiving both pharmacologic and nonpharmacologic treatment. The antidepressant agents used by those not depressed according to the SCID and recorded in patient medical records were amitriptyline (n = 3), desipramine (n = 1),

**Table 3. Characteristics of individuals with multiple sclerosis without depression<sup>a</sup> by antidepressant drug use status**

Characteristic	Not taking antidepressant drugs (n = 103)	Taking antidepressant drugs (n = 29)
Sex, %		
Female	78	83
Male	22	17
Age, %		
<50 y	47	34
≥50 y	53	66
EDSS score, %		
<3.5 (mild)	64	54
≥3.5 to <5.5 (moderate)	15	14
≥5.5 (severe)	21	32
Severity of disease, %		
Mild	76	62
Moderate	19	24
Severe	5	14
Marital status, %		
Married or living with someone	69	83
Not living with anyone	31	17
Education level, %		
High school diploma and lower	39	45
Postsecondary education	61	55
Income, %		
Receiving disability	17	31
Not receiving disability	83	69
Not employed	46	66
Employed	54	34
Mental quality of life score, mean <sup>b</sup>	40	38

<sup>a</sup>Depression defined as current depressive episode according to the Structured Clinical Interview for DSM.

<sup>b</sup>Quality of life based on 12-item Short Form Health Status Survey component scores. Higher scores indicate greater quality of life.

venlafaxine (n = 2), citalopram (n = 3), escitalopram (n = 3), paroxetine (n = 3), fluoxetine (n = 2), and trazodone (n = 1). Individuals receiving nonpharmacologic treatment visited psychiatrists (n = 4), other specialists (n = 2), and psychologists (n = 3). Of the individuals determined to have no depression by the SCID (n = 132), 25.0% (n = 33) reported that they had been diagnosed as depressed by a health professional.

Table 4 reports the treated (pharmacologic, nonpharmacologic, or both) prevalence of depression according to various cut-point scores on three depression questionnaires (PHQ-9, HADS, and CES-D scale). The unadjusted frequency of treatment in those with current depression as determined by the SCID was 75%, and the unadjusted frequency of treatment in those with lifetime depression as determined by the SCID was 47%. Of those with clinically significant depressive symptoms on the PHQ-9 (PHQ-9 score ≥10), HADS (HADS score ≥8), and CES-D scale (CES-D scale score ≥16), 68%, 55%, and 49%, respectively, reported currently using any form of treatment for depression.

Cochran-Mantel-Haenszel analyses and a binary regression model were used to identify factors associated with antidepressant drug use. None of the variables assessed were statistically significantly associated with the use of antidepressant agents. Although no statistically significant associations were seen, there was a trend in the association of age and sex with the use of antidepressant drugs. Higher frequencies of antidepressant drug use were observed in women and older patients: of the 42 individuals using antidepressant agents, 8 (19.0%) were men and 34 (81.0%) were women and 12 (28.6%)

**Table 4. Treated prevalence of depression according to various cut-points on four depression questionnaires**

Questionnaire (cut-point score)	Any treatment, % (95% CI)
PHQ-9 (10)	68 (52-83)
HADS (8)	55 (39-71)
CES-D scale (16)	49 (35-63)
Depression <sup>a</sup>	
Current	75 (54-96)
Lifetime	47 (34-61)

Abbreviations: CES-D, Center for Epidemiologic Studies-Depression; CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire-9.

<sup>a</sup>Current and lifetime depression determined by the Structured Clinical Interview for DSM.

were younger than 45 years and 30 (71.4%) were 45 years and older.

## Discussion

In the present study, 20 participants were currently depressed, for an estimated prevalence of 13.2%, and the lifetime prevalence of depression was 38.8%. Of those depressed as determined by the SCID, 65% were taking antidepressant agents. After adjusting for the antidepressant drug-treated proportion of depression in the MS sample (by taking into account those using antidepressant drugs but not determined to be currently depressed), the adjusted antidepressant drug-treated proportion of depression increased to 85.7%. Of those receiving treatment for their depression, 44% were receiving both pharmacologic and nonpharmacologic forms of treatment, 19% were using nonpharmacologic treatments (psychiatrist, counselors, and psychologists) in the absence of pharmacotherapy, and 38% were using only pharmacotherapy. Finally, a trend toward higher frequency of antidepressant drug use in older individuals and females was seen.

Previous studies have reported lower prevalence estimates of antidepressant drug use in people with MS compared with the findings from this study. Cetin et al.<sup>14</sup> reported that 41% of people with MS presenting with clinically significant levels of depressive symptoms on the CES-D scale were taking antidepressant agents, and Mohr et al.<sup>16</sup> reported a 34.5% frequency of treatment. These previously reported proportions of antidepressant drug use have led to concerns of undertreated depression in MS. However, a more recent study indicates that a large proportion, but not all, of those with depression are receiving antidepressant drug treatment. This may suggest that the extent of undertreatment is diminishing over time. Increased antidepressant drug use has also been observed in the general population.<sup>20</sup> A recent Organization for Economic Cooperation and Development study ranked Canada third in the world after Iceland and Australia in its consumption of antidepressant agents (so the Canadian location of this MS clinic may partially explain the high frequency of use). These recent increases in antidepressant drug use were mainly attributed to an increase in the duration of use rather than increased frequency of use.<sup>32</sup> The suggested increase in the consumption of antidepressant agents in the present study may be due to factors such as increased

awareness, reduced stigma, and decreased threshold for prescribing.

Undertreated depression in MS may no longer be as great a concern as it has been in the past; however, most of those using antidepressant drugs were currently depressed as determined by the SCID in the present study. Some factors that may have contributed to the large number of individuals still depressed while using antidepressant agents are inadequate dose, inadequate duration, and ineffective antidepressant agents. Other researchers have studied the effectiveness of antidepressant drug treatment for depression in MS. A randomized placebo-controlled trial conducted by Ehde et al.<sup>33</sup> evaluated the efficacy of paroxetine in treating major depressive disorder in MS. This study illustrated that 78.6% of those receiving 12 weeks of treatment with paroxetine saw a reduction of at least 50% in depressive symptoms and severity versus 42.1% in the 12-week placebo group. However, the difference in reduction of symptoms and severity did not reach significance. Furthermore, Schiffer and Wineman<sup>34</sup> conducted a double-blind clinical trial of the efficacy of desipramine and found that significant improvement in Beck Depression Inventory scores was not achieved; however, significant improvement in Hamilton depression scores was seen. These studies illustrate the complexity of depression treatment in the MS population. A pooled analysis of these studies found evidence of effectiveness, but with modest differences between the treated and referent groups. Taken together, these results are very consistent with the real-world results suggested herein. There has been progress in the delivery of treatment, but much more progress is needed to achieve better outcomes.<sup>35</sup>

Although the treatment of depression in patients with MS is often complex and needs to be individualized depending on the patient's circumstances and preferences, treatment guidelines have been developed. The most recent reported treatment guidelines by the Canadian Network for Mood and Anxiety Treatments<sup>6</sup> strongly recommends the use of antidepressant agents in conjunction with psychotherapies that emphasize coping strategies. Selective serotonin reuptake inhibitors are considered the first-line treatment in MS, whereas medications with strong anticholinergic adverse effects, such as tricyclic antidepressants, should be avoided.<sup>6</sup> Psychotherapies are also considered an important option for the treatment of depression in MS.<sup>6</sup> Therapies that focus on coping skills are often preferred over insight-oriented

therapies.<sup>9</sup> Psychotherapies using a group format or a CBT approach to depression in MS have also been shown to reduce the severity of depression.<sup>8,13</sup>

Despite Canadian Network for Mood and Anxiety Treatments recommendations of using both antidepressant agents and psychotherapies for the treatment of depression in MS,<sup>6</sup> the present study found that most patients were not receiving psychotherapies. In the general population, combined psychotherapy and antidepressant medication treatment decreased from 39.4% in 1998 to 32.3% in 2007.<sup>36</sup> The frequency of psychotherapy use in the absence of pharmacotherapy decreased from 53.6% in 1998 to 43.1% in 2007.<sup>36</sup> It is not clear whether the declining use of psychotherapy is due to patient preference for pharmacotherapy or to lack of referral and access to therapists, transportation difficulties, and the required time commitments.<sup>37</sup>

Of additional interest are individuals using antidepressant agents in the absence of clinically significant depression according to the SCID. Approximately 22% of those not currently depressed were receiving treatment (pharmacologic or nonpharmacologic), with 83% taking antidepressant medications alone. It is possible that those with atypical depressive symptoms who would benefit from antidepressant agents but do not meet the *DSM-IV-TR* definition or those with remitted depression are reflected in the 22%. In addition, antidepressant drugs may be used for other conditions, such as anxiety disorders, fibromyalgia, migraine, and chronic pain associated with MS.<sup>38</sup> Last, 25% of these individuals had been diagnosed as depressed by a health professional with no depression on the SCID. Given the concerns of undertreated depression in MS, health professionals may be diagnosing depression less stringently. Consequently,

some patients may be using antidepressant drugs unnecessarily. On the other hand, these medications can appropriately be taken in the absence of any depressive symptoms to prevent the recurrence of depressive episodes.

A primary objective of this study was to determine the characteristics and predictors of antidepressant drug use in individuals with MS. This study did not find any patient characteristics associated with antidepressant drug use. This may have been due partly to the small sample size in most groups. However, a trend toward a higher frequency of antidepressant drug use in older individuals and females was seen. Cetin et al.<sup>14</sup> also found that females, those unmarried or not living with a partner, and individuals with health insurance were more likely to use antidepressant agents. In the general population, antidepressant drug use is also more frequent in women compared with men.<sup>39</sup> Beck et al.<sup>39</sup> reported the lowest antidepressant drug use in the youngest age group (15–25 years) in the general population and in those with major depression.

This study was limited by the small sample size of the subgroup with depression, which may have resulted in inadequate power to detect predictors of antidepressant drug use. Furthermore, the generalizability of this study may be limited by the study sample, which was drawn from a clinical population. The sample may represent a more severely affected group compared with a sample of the general population of people with MS. Another limitation is that the frequency of past depression diagnosis was based on self-report, which may be inaccurate. Last, the only nonpharmacologic treatment evaluated in this study was psychotherapy.

## Conclusion

This study demonstrated that most patients with MS and depression are receiving treatment and that the extent of undertreatment may have diminished over time. Furthermore, the form of treatment used by those with depression does not closely follow the clinical guidelines. This study also noted that a large proportion of those with no depression according to the SCID are using antidepressant agents, although the reasons for this pattern of use are not clear. The absence of a strong evidence base supporting the effectiveness of antidepressant medications is problematic but does not provide evidence against the use of depression treatments. In the absence of decisive evidence, clinicians will continue to follow non-disease-specific guidelines and to use both

## Practice Points

- Depression in MS has historically been undertreated and underdiagnosed, despite the fact that it is detrimental to quality of life.
- This study showed that a larger proportion of those with depression in MS are now receiving treatment.
- The extent of undertreatment may have diminished over time. However, many of those receiving treatment continue to be depressed.
- Optimization, rather than introduction, of treatment should now be a priority in clinical settings.



psychotherapy and pharmacotherapy when treating depression. Further research is required to better understand questions of efficacy and barriers to using pharmacotherapy and psychosocial interventions in people with MS and to better understand the reasons for the use of antidepressant agents in people with MS without clinically significant depression. □

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