Unmet Mental Health Needs and Barriers to Mental Health Treatment Among Persons with Multiple Sclerosis in the NARCOMS Registry

by

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Author’s Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Background – Multiple sclerosis (MS) is a chronic, neurological disease. Mental health comorbidities, such as depression, anxiety and bipolar disorder, are highly prevalent in persons with MS, and their presence is associated with adverse health and economic consequences. Unfortunately, these conditions are frequently underdiagnosed and undertreated. To better meet the mental health needs of MS patients, it is important to identify the correlates, barriers and consequences associated with untreated mental health comorbidities. Previous studies have generally found socioeconomic factors (e.g., inadequate health insurance, low education) to limit access to mental health care; however, the findings for sociodemographic (i.e., age, race, ethnicity) and clinical factors (i.e., severity of mental health symptoms and level of physical impairment) have been less consistent. While qualitative investigations of MS patients have identified common barriers to mental health treatment, these barriers have been poorly investigated in larger samples of MS patients. Further research is needed to identify disparities in the use of mental health services for the treatment of mental health comorbidities in persons with MS.

Research Aims – Cross-sectionally, this thesis aimed to assess the prevalence and correlates of untreated mental health comorbidities in persons with MS. This thesis also explored the prevalence and correlates of treatment barriers (in those not receiving treatment) and treatment modalities (in those receiving treatment). Longitudinally, this thesis aimed to assess the temporal association between baseline mental health non-treatment and depressive symptoms and health-related quality of life outcomes (mental and physical domains) at one-year follow-up.

Methods – To address these aims, this thesis utilized cross-sectional (2011) and longitudinal (2011 to 2012) data captured by the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry. The NARCOMS Spring 2011 Survey had a total of 9765 respondents; 3928 of whom were diagnosed with one or more of depression, anxiety or bipolar disorder. Mental health comorbidities were explored separately for all our analyses, resulting in three non-mutually exclusive baseline samples: depression (n=3589), anxiety (n=1487), and bipolar disorder (n=196). Other than initial descriptive data, statistical analyses were restricted to the depression and anxiety cohorts due to the small number of participants with bipolar disorder. Baseline respondents who responded to key outcomes (depressive symptoms, HRQOL scores) on the NARCOMS Spring 2012 Survey were included in follow-up analyses.

Cross-sectionally, bivariate and logistic regression analyses were conducted to assess the associations between participant characteristics (with a focus on sociodemographic characteristics) and mental health non-treatment. The barriers to mental health treatment were explored in bivariate analyses through the lens of Andersen's Behavioural Model of Health Service Utilization. Longitudinally, bivariate and logistic regression analyses were conducted to assess the temporal association between baseline mental health non-treatment and depressive symptoms (NARCOMS Depression Scale) and HRQOL quality of life outcomes (MCS-12 and PCS-12 scores on the RAND-12) at one-year follow-up. Multivariable regression analyses adjusted for baseline scores (NARCOMS Depression Scale and RAND-12 scores) and relevant baseline sociodemographic and clinical confounders.

Results – In 2011, NARCOMS participants were more commonly untreated for anxiety (26.1%; 95%CI=23.9, 28.3) and bipolar disorder (23.5%; 95%CI=17.5, 29.4), followed by depression (15.2%; 95%CI=14.0, 16.4). In adjusted analyses, participants with younger and older ages (vs. 45 to 64 years; the former significant for depression cohort only), racialized participants (significant for depression cohort only), and those with low SES (health insurance for depression cohort, education for anxiety cohort) had significantly higher odds of mental health non-treatment. Participants with clinically meaningful depressive symptoms and those with more severe levels of disability had significantly lower odds of non-treatment. Of those not receiving treatment, participants were most commonly untreated due to need factors (i.e., "not having symptoms now") (depression cohort: 57.4%, 313/545; anxiety cohort: 65.2%, 253/388), followed by predisposing factors (depression cohort: 43.1%, 235/545; anxiety cohort: 32.5%, 126/388) and enabling factors (depression cohort: 19.5%, 106/545; anxiety cohort: 22.2%, 86/388). Participants with low SES were significantly more likely to report enabling factors but less likely to report need factors as barriers to mental health treatment. Of those receiving treatment, less than one-third of participants were treated with both psychotherapy and medication (depression cohort: 20.1%, 611/3044; anxiety cohort: 27.7%, 304/1099). Participants with low education were less likely to receive the recommended treatment combination of psychotherapy and medication. Approximately two-thirds of treated participants reported clinically meaningful depressive symptoms (depression cohort: 63.3%, 1927/3044; anxiety cohort: 65.1%, 715/1099). After adjusting for key confounders (baseline scores, as well as other sociodemographic and clinical factors), baseline mental health non-treatment was not associated with the presence of clinically meaningful depressive symptoms or a clinically meaningful decline in mental or physical HRQOL at one-year follow-up.

Conclusion – The findings of this thesis add to the literature by identifying important sociodemographic and clinical correlates of mental health service use and later health outcomes in MS patients to be considered in future research. Targeting the barriers identified in this thesis may improve access to mental health care for disadvantaged MS patients. To build upon the results of this thesis, future investigations could utilize multiple data sources (administrative, clinical and registry data) to assess the prevalence and correlates of mental health treatment barriers in a more diverse and representative sample of persons with MS.

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List of Abbreviations

CES-D20	20-Item Center for Epidemiologic Studies – Depression Scale
CI	Confidence Interval
DMT	Disease-Modifying Therapies
DSM	Diagnostic and Statistical Manual of Mental Disorders
HRQOL	Health-Related Quality of Life
GED	General Educational Development
MCS	Mental Component Score
MDD	Major Depressive Disorder
MHC	Mental Health Comorbidity
MS	Multiple Sclerosis
NARCOMS	North American Research Committee on Multiple Sclerosis
OR	Odds Ratio
PCS	Physical Component Score
PDDS	Patient Determined Disease Steps
RAND-12	12-Item RAND Health Status Inventory
RR	Relative Risk
SD	Standard Deviation
SES	Socioeconomic Status
SF-12/36	12/36-Item Short-Form Health Survey
Tx	Treatment
USA	United States of America
VIF	Variance Inflation Factor

1.0 Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated neurological condition affecting over 2.9 million people across the globe in 2023 (Atlas of MS, 2023). MS is considered the most common non-traumatic disabling neurological condition among young adults (Murray, 2006). Mental health comorbidities, such as depression and anxiety, are highly prevalent in persons with MS relative to individuals with other immune-mediated inflammatory diseases and within the general population (Marrie et al., 2013, 2017b; Marrie, Fisk, et al., 2015; Marrie, Reingold, et al., 2015). These comorbidities are associated with adverse health and economic consequences for MS patients as well as health systems (Berrigan et al., 2016; Bhattacharjee et al., 2021). For instance, comorbid depression and anxiety in MS patients have been associated with increased healthcare use and expenditures (Bhattacharjee et al., 2021), meaningful reductions in health-related quality of life (Berrigan et al., 2016; Bhattacharjee et al., 2021; Hanna & Strober, 2020; Lo et al., 2021; Marrie, Bernstein, et al., 2023; Marrie et al., 2012; Marrie, Patten, et al., 2018), and increased mortality (Marrie, Elliott, et al., 2015; Marrie, Walld, et al., 2018).

Despite these consequences, depression and anxiety are often underdiagnosed and undertreated in MS patients (Korostil & Feinstein, 2007; Marrie et al., 2009; Marrie, Patten, et al., 2018; Mohr et al., 2006; Orr et al., 2018; Raissi et al., 2015). Unmet mental health needs adversely affect health behaviours and the quality of life of MS patients (Ploughman et al., 2020; Ponzio et al., 2020). To better meet the mental health needs of MS patients, it is important to identify the correlates, barriers and consequences associated with untreated mental health comorbidities.

To date, there are limited quantitative investigations of the factors and barriers associated with unmet mental health needs in persons with MS. Previous quantitative studies have explored the correlates of untreated mental health comorbidities in MS, as well as the use of mental health services by persons with MS (Beatty et al., 2003; Buchanan et al., 2006, 2009, 2010; Garcia & Finlayson, 2009; Korostil & Feinstein, 2007; Marrie et al., 2009; Minden et al., 2007, 2013; Orr et al., 2018; Stepleman et al., 2014; Wu et al., 2007); however, the associations between sociodemographic (i.e., age, race, ethnicity) and clinical factors (i.e., severity of mental health symptoms and level of physical impairment) and untreated mental health comorbidities have been inconsistent across studies. Qualitative studies have also explored the perspectives of MS patients and providers (A. Hunter et al., 2021; Marck et al., 2022; Methley, Campbell, et al., 2017; Methley, Chew-Graham, et al., 2017; Rintell et al., 2012); however, few quantitative studies have explored both the correlates and the barriers associated with mental health treatment in MS patients (Buchanan et al., 2006; Minden et al., 2007, 2013; Pimentel Maldonado et al., 2022; Wu et al., 2007). While the results of these studies provide insights into MS patient experiences, findings have varied across investigations due in part to variability in sample populations and study methodologies. Further investigation is needed to more clearly identify the correlates and barriers associated with untreated depression and anxiety among persons with MS.

To address the knowledge and methodological gaps in the literature, this project used comprehensive sociodemographic, clinical, and mental health data (2011 to 2012) collected by the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry. The main objectives of this study were two-fold. First, this project examined the prevalence and correlates of untreated depression and anxiety (with a focus on sociodemographic factors) using data from the NARCOMS Spring 2011 survey. As part of this objective, we examined the prevalence and correlates of mental health treatment barriers captured by the NARCOMS Spring 2011 survey informed by the framework of Anderson's Behavioural Model of Health Service Use (Andersen, 1995). Second, this project examined the temporal association between unmet mental health needs (i.e., not receiving treatment for depression or anxiety in 2011) and depressive symptomology and health-related quality of life (HRQOL) outcomes at one-year follow-up.

The results of regression analyses identified key sociodemographic correlates of untreated mental health comorbidities, as well as potential predictors of clinically meaningful depressive symptomology and decline in HRQOL, to be considered in future research. The results of descriptive analyses highlighted common barriers to mental health treatment in MS patients diagnosed with depression and/or anxiety. The findings of this study may inform future clinical and public health initiatives to reduce disparities in the treatment of mental health comorbidities among MS patients with socioeconomic disadvantages. As the global prevalence of MS continues to rise (Walton et al., 2020), it is critical to ensure that MS patients are receiving adequate mental health support to reduce the adverse health and economic consequences associated with comorbid depression and anxiety (Bhattacharjee et al., 2021; Ponzio et al., 2020).

2.0 Literature Review

2.1 Overview of Multiple Sclerosis

Multiple Sclerosis (MS) is a complex neurological disease that has been thought to occur from a combination of genetic predisposition and exposure to environmental and behavioural risk factors (McKay & Tremlett, 2021; Schriger, 2008). Established risk factors for MS (notably in White populations from Northern European ancestry) include Epstein-Barr Virus (Bjornevik et al., 2022; Disanto et al., 2013; Handel et al., 2010; Levin et al., 2010; Munger et al., 2011), vitamin-D deficiency (Munger et al., 2004; Pierrot-Deseilligny & Souberbielle, 2017), cigarette smoking (Ascherio & Munger, 2007; Handel et al., 2011; Paz-Ballesteros et al., 2017), and obesity (Gianfrancesco et al., 2014; Munger et al., 2009, 2013).

MS typically begins with a relapsing-remitting pattern, which is characterized by periods of neurological deterioration (relapses) followed by symptomatic recovery (remission) (Lublin et al., 2014). Relapsing-remitting MS can later progress into secondary progressive MS, in which individuals experience a steady, progressive neurological deterioration without remission (Lublin et al., 2014). In primary progressive phenotypes, patients experience progressive deterioration from onset without periods of remission (Lublin et al., 2014). While there is no cure for MS, disease-modifying therapies (DMT) may prevent or reduce the severity of relapses and reduce disability progression (Goodin et al., 2002; Wingerchuk & Carter, 2014).

MS is a debilitating condition associated with adverse physical, psychological, and economic consequences (Adelman et al., 2013; Janssens et al., 2003; Julian et al., 2008; Kister et al., 2013; Marrie, Fisk, et al., 2015). The following sections highlight the epidemiology of MS and its demographic correlates, as well as the factors associated with poor mental and physical health-related quality of life (HRQOL) outcomes among persons with MS.

2.1.1 Epidemiology of Multiple Sclerosis

The global prevalence of MS is on the rise, with Canada and the United States reporting among the highest estimates worldwide (Browne et al., 2014; Walton et al., 2020). The global prevalence of MS in 2020 was estimated to be 35.9 cases per 100,000 people, which was 30% higher than 2013 estimates (33 cases per 100,000 people) (Browne et al., 2014; Walton et al., 2020). In 2022, the prevalence of MS in the United States and Canada was estimated to be 290 and 288 cases per 100,000 people, respectively (Atlas of MS, 2023). Increases in the prevalence of MS are thought to be due to earlier diagnosis, improved treatment and support, and reduced disease mortality (Marrie, Cutter, Tyry, Hadjimichael, Campagnolo, et al., 2005; Roh et al., 2011; Rotstein et al., 2018; Walton et al., 2020).

Globally, the incidence of MS has generally decreased since the early 2000s (Koch-Henriksen & Magyari, 2021). In Canada, the 2022 incidence of MS was estimated to be 14 cases per 100,000 people, respectively (Atlas of MS, 2023). Trends from the Canadian population indicate that the incidence of MS appears to be stabilizing or decreasing slightly (Hader & Yee, 2007; Koch-Henriksen & Magyari, 2021; Public Health Agency of Canada, 2021; Rotstein et al., 2018). In the United States, the 2022 incidence of MS was estimated to be 7.9 cases per 100,000 people (Atlas of MS, 2023), with trends suggesting that the incidence of MS in the United States seems to be stabilizing or increasing (Feigin et al., 2021; Langer-Gould et al., 2013). Both of these trends can be attributed in part to improvements in MS diagnostic criteria, as this may be facilitating the diagnosis of MS in racialized Americans (Amezcua et al., 2021; Langer-Gould et al., 2013, 2022; Wallin et al., 2012), while also reducing the rate of false positives in the general population (Koch-Henriksen & Magyari, 2021; I. S. Mackenzie et al., 2014).

2.1.2 Demographic Characteristics of Persons with Multiple Sclerosis

The sociodemographic characteristics of MS patients, such as their age, gender, race and ethnicity, can influence the onset and progression of MS (Confavreux et al., 2003; Confavreux & Vukusic, 2006; Langer-Gould et al., 2013). The onset of MS symptoms typically occurs in individuals between 20 and 40 years of age, although MS can appear in those younger than 16 (early-onset MS) (Ghezzi et al., 1997; Renoux et al., 2007) and older than 50 years of age (late-onset MS) (Martinelli et al., 2004; Polliack et al., 2001). Late-onset MS is typically associated with more rapid disease progression relative to MS patients with younger ages of onset (Guillemin et al., 2017; Martinelli et al., 2004). Females are, on average, two to three times more likely to develop relapsing-remitting MS than males (Confavreux & Vukusic, 2006; Golden & Voskuhl, 2017; Orton et al., 2006; Walton et al., 2020), though males with relapsing phenotypes typically experience more rapid disease progression compared to females (Confavreux & Vukusic, 2014; Manouchehrinia et al., 2016; Ribbons et al., 2017). There is little to no female preponderance in primary progressive MS (Alonso et al., 2007; Ramagopalan et al., 2010; Tremlett et al., 2005).

For many years, MS was thought to primarily affect White populations, particularly in individuals from northern European backgrounds, and was considered to be rare among racial and minority groups, notably in Black persons (Kurtzke et al., 1979; Rosati, 2001). However, more recent studies have found the incidence and prevalence of MS in Black persons to be similar or higher than in White persons (Amezcua et al., 2018; Hittle et al., 2023; Langer-Gould et al., 2013, 2022; Romanelli et al., 2020; Wallin et al., 2012). While MS is less common in Hispanic persons relative to White persons in the United States (Langer-Gould et al., 2013; Romanelli et al., 2020), Hispanic Americans have reported higher rates of early-onset MS (Amezcua et al., 2011; Langer-Gould et al., 2013, 2022).

Black MS and Hispanic MS patients tend to have a more severe and rapid disease course relative to White MS patients (Amezcua et al., 2018; Amezcua & McCauley, 2020; Cree et al., 2004; Gray-Roncal et al., 2021; Kister et al., 2010, 2021; Marrie et al., 2006; Ventura et al., 2017). Genetic factors and differential exposure to risk factors are thought to contribute to racial differences in MS (Cree et al., 2004; Oksenberg et al., 2004); however, these findings have not been consistent across studies (Beecham et al., 2020; Jacobs et al., 2023; Johnson et al., 2010; Langer-Gould et al., 2013; Oksenberg & Barcellos, 2005). An increasing number of studies have found environmental and clinical care factors to contribute to racial disparities among persons with MS (Amezcua & McCauley, 2020; Buchanan et al., 2010; Geiger et al., 2023; Gray-Roncal et al., 2021; Minden et al., 2007, 2008; Rivera, Repovic, et al., 2021; Saadi et al., 2017; Wang et al., 2020). For instance, relative to White MS patients, Black MS patients are more likely to have a lower socioeconomic status (SES) (Amezcua & McCauley, 2020; Buchanan et al., 2010; Gray-Roncal et al., 2021; Minden et al., 2007; Rivera et al., 2021; Wang et al., 2020), more likely to receive low- or moderate-efficacy DMT as first-line treatment (Geiger et al., 2023), and less likely to be treated by a neurologist (Minden et al., 2008; Saadi et al., 2017). Though racial disparities in MS remain poorly investigated, this area of research is growing rapidly.

2.1.3 Factors Associated with Poor Health-Related Quality of Life in Persons with Multiple Sclerosis

As a degenerative neurological condition, MS has massive implications for the current and future health-related quality of life (HRQOL) of those affected (Janzen et al., 2013; Wu et al., 2007). Individuals with MS have been shown to experience worse mental and physical HRQOL when compared to the general population (Amtmann et al., 2018; Hopman et al., 2007; McCabe et al., 2009; Wu et al., 2007) and those with other chronic conditions (Hermann et al., 1996; Riazi et al., 2003; Sprangers et al., 2000; Wu et al., 2007).

While findings may vary across studies, worse physical HRQOL in MS has generally been associated with older age, marital status (unmarried), unemployment, and lower levels of education and annual income (Buhse et al., 2014; Gil-González et al., 2021; Hopman et al., 2007; Janzen et al., 2013; O'Mahony et al., 2022; Turpin et al., 2007; Wu et al., 2007). In addition, the presence of depressive symptoms, more severe levels of fatigue and disability, and longer disease duration have also been associated with poorer physical HRQOL in MS patients (Buhse et al., 2014; Gil-González et al., 2021; Hopman et al., 2007; Janzen et al., 2013; Marrie, Bernstein, et al., 2023; Turpin et al., 2007; Wu et al., 2007).

Poor mental HRQOL has been associated with younger age, the female sex, marital status (unmarried), unemployment, lower levels of education and annual income, and being uninsured (Buhse et al., 2014; Hopman et al., 2007; Janzen et al., 2013; O'Mahony et al., 2022; Wu et al., 2007). Symptoms of depression and anxiety, more severe disability, and longer disease duration have generally been associated with poor mental HRQOL outcomes in MS patients (Gil-González et al., 2021; Hopman et al., 2007; Marrie, Bernstein, et al., 2023; Wu et al., 2007).

The presence of mental and physical comorbidities in MS can lead to substantial decreases in HRQOL (Berrigan et al., 2016; Bhattacharjee et al., 2021; Fruewald et al., 2001; Janssens et al., 2003; Lo et al., 2021; Marrie, Bernstein, et al., 2023; Marrie et al., 2012; Marrie, Patten, et al., 2018). In particular, the presence of a comorbid mental health condition, such as depression, bipolar disorder and anxiety, in persons with MS has been associated with delays in initial MS diagnosis (Marrie, Horwitz, et al., 2008), reduced adherence to DMT (Mohr, 1997; Tarrants et al., 2011), worsening of MS symptoms (Alschuler et al., 2013; Fiest et al., 2015; Valentine et al., 2022) and disability progression (Berrigan et al., 2016; Fruewald et al., 2001; Hanna & Strober, 2020; Marrie, Horwitz, et al., 2008; Marrie, Patten, et al., 2018; McKay, Tremlett, et al., 2018). Comorbid depression has also been associated with an increased risk of mortality and suicidality in MS patients (Feinstein, 2002; Marrie, Elliott, et al., 2015; Marrie, Walld, et al., 2018; Turner et al., 2006).

Together, these findings suggest that sociodemographic factors (e.g., low SES, age, race), clinical symptomology (e.g., affective symptoms, disability), and the presence of comorbidities can contribute to worse health outcomes in MS patients. The following sections highlight the prevalence and key sociodemographic, clinical and disease-related factors associated with depression, bipolar disorder, and anxiety in persons with MS.

2.2 Depression in Persons with Multiple Sclerosis

Depression can describe a broad range of emotional symptoms, ranging from regular episodes of low mood to a clinical syndrome (Patten et al., 2017). Major depressive disorder (MDD) is a psychiatric disorder that must be diagnosed by a clinician and is, therefore, distinct from typical sadness (Patten et al., 2017). In the literature, MDD can be assessed using semi-structured diagnostic instruments (e.g., Structured Clinical Interview for DSM [Diagnostic and Statistical Manual of Mental Disorders]), by applying validated case definitions to population-based administrative data, or reviewing the medical records of MS patients (Patten et al., 2017). On the other hand, depressive symptoms can be measured using rating sales to establish the current or recent severity of symptomology (Ayuso-Mateos et al., 2010; Patten et al., 2017). These scales often use validated cut-points to predict symptomology that will likely meet clinical standards (i.e., clinically meaningful depressive symptoms), though scoring above an established cut-point is not equivalent to a clinical diagnosis (Patten et al., 2017).

The 12-month period prevalence of depressive disorders in MS patients typically ranges between 15% and 25% (Boeschoten et al., 2017; Marrie et al., 2017a; Mohr et al., 2006; Patten et al., 2003), with depression affecting up to 50% of MS patients across their lifetimes (Minden et al., 1987; Sadovnick et al., 1996). When using similar measurement approaches, prevalence estimates of depression are consistently two to four times higher in MS relative to the general population (Patten et al., 2017). For instance, using administrative data between 1984 and 2006 in Manitoba, Canada, the age-standardized prevalence of depression in MS was estimated to be 31.7% compared to 20.5% in the general population (matched on sex, age, area of residence) (Marrie et al., 2013). Meanwhile, clinically meaningful depressive symptoms affect between 25% and 60% of MS patients, depending on the study population and methodology (Chwastiak et al., 2002; Marrie et al., 2009; Patten et al., 2005; Sacco et al., 2016)

Though depression is highly prevalent in MS, its pathogenesis is poorly understood (Filser et al., 2023). It has been suggested that psychosocial, environmental, biological, immunological, and genetic factors may mediate the onset of depression among those with MS (Feinstein et al., 2014; Patten et al., 2017); however, the onset of depression can also precede MS (Kowalec et al., 2022; Whitlock & Siskind, 1980). The following sections discuss the primary sociodemographic, clinical and MS factors associated with severe depressive symptoms in people with MS.

2.2.1 Sociodemographic Factors Associated with Depressive Symptoms

Previous studies have explored the sociodemographic correlates (i.e., gender, age, marital status, race and ethnicity, SES) of depressive symptoms in persons with MS. In general, studies have not found sex to be significantly associated with major depressive disorder (Patten et al., 2000, 2003) or depressive symptoms in persons with MS (Beal et al., 2007; Beiske et al., 2008; Chwastiak et al., 2002; Garcia & Finlayson, 2009; Taylor et al., 2014; Théaudin et al., 2015), though it should be noted that many of these study populations had a high proportion of White/Caucasian participants (~92%). In contrast, studies in the general population have found females to have a higher prevalence of MDD (Altemus et al., 2014; Gater et al., 1998; Kessler et al., 1994; Weissman et al., 1996) and depressive symptoms (Altemus et al., 2014; Hankin, 2009; Nolen-Hoeksema et al., 1999) relative to males.

Younger age, typically defined as 20 to 40 years of age, has generally been associated with more severe depressive symptoms among persons with MS (Beal et al., 2007; Briggs et al., 2019; Chwastiak et al., 2002; Marrie et al., 2009; Patten et al., 2000, 2003), while older age has been associated with reduced depressive symptoms (Ensari et al., 2013). Marital status, particularly being unmarried, divorced, or separated, has also been associated with more severe depressive symptomology in MS patients (Beiske et al., 2008; Ensari et al., 2013; Marrie et al., 2009; Patten et al., 2005; Simpson et al., 2019; Taylor et al., 2014).

The association between race and depressive symptoms remains less clear. A previous NARCOMS study found a higher proportion of Black and Latino MS patients to report depressive symptoms relative to White participants (Buchanan et al., 2010). Prior studies have found Black/African American and Latino/Hispanic American MS patients to report more severe depressive symptoms relative to White patients (Chan et al., 2021; Kister et al., 2021); however, this finding has not been consistent (Pimentel Maldonado et al., 2022; Stepleman et al., 2014; Wu et al., 2007).

Measures of SES, such as lower levels of annual family income (Briggs et al., 2019; Marrie et al., 2009), lower educational attainment (Bamer et al., 2008; Chwastiak et al., 2002; Hanna & Strober, 2020; Marrie et al., 2009; Taylor et al., 2014; Wang et al., 2020) and unemployment (Ensari et al., 2013; Simpson et al., 2019; Taylor et al., 2014; Wang et al., 2020), have been more consistently associated with clinically meaningful depressive symptoms. Health insurance coverage has also been associated with depressive symptomology; having private health insurance has been associated with decreased odds of having a lifetime diagnosis of depression (Marrie et al., 2009), while having Medicaid (Briggs et al., 2019; Wang et al., 2020) or being uninsured (Wang et al., 2020) has been associated with more severe depressive symptoms.

In a sample of American persons with MS, Wang et al. (2020) found race to modify the association between measures of low SES (education, insurance, employment status) and severe affective symptoms (depression, anxiety, fatigue). Multiple measures of low SES (lower education, Medicaid or uninsured status, unemployed or disabled status) were associated with severe affective symptoms among White participants. In contrast, only unemployment status was associated with severe affective symptoms among Black/African American participants (Wang et al., 2020). Given that racialized MS patients are significantly more likely to have low SES (Pimentel Maldonado et al., 2022; Wang et al., 2020), environmental factors may contribute to racial disparities in depressive outcomes.

2.2.2 Clinical Factors Associated with Depressive Symptoms

Clinical factors, such as disability, fatigue, cognitive dysfunction, and pain, have been commonly considered when investigating depression in MS. Though structural abnormalities are outside the scope of this investigation, brain lesions and structural damage can contribute to depression in MS (Bakshi, Czarnecki, et al., 2000; Corallo et al., 2019; Feinstein et al., 2004).

Previous studies have reported a positive association between disability and depressive symptoms in MS patients (Chwastiak et al., 2002; Lynch et al., 2001; Patten et al., 2005). Disability and depression are closely linked in MS; higher levels of disability are associated with an increased risk of depression (Bamer et al., 2008; Berzins et al., 2017), while the presence of comorbid depression is associated with an increased risk of disability progression (Binzer et al., 2019; McKay, Tremlett, et al., 2018).

Fatigue is one of the most common symptoms associated with MS; up to 88% of MS patients have reported being bothered by their fatigue (Krupp et al., 1988, 2010). A positive association between fatigue and depression in MS has been consistently reported throughout the literature (Bakshi, Shaikh, et al., 2000; Beiske et al., 2008; Corallo et al., 2019; Koch et al., 2008; Kroencke et al., 2000; Vercoulen et al., 1996). While MS patients can experience fatigue without depressive symptoms (Chwastiak et al., 2005), fatigue can also predict depression in those with MS (Beiske et al., 2008; Berzins et al., 2017; Brown et al., 2009; Simpson et al., 2019). Fatigue has been associated with depression independently of disability, suggesting common underlying mechanisms (Bakshi, Shaikh, et al., 2000; Koch et al., 2008).

The association between depression and cognitive impairment is less clear. Approximately 50% of MS patients experience substantial cognitive impairments (Brassington & Marsh, 1998; Rao, 1986; Rao et al., 1991). Studies have found that depression can contribute to impairments in cognitive functioning in MS (Arnett, 2005; Arnett et al., 2001; Arnett, Higginson, Voss, Bender, et al., 1999; Arnett, Higginson, Voss, Wright, et al., 1999; Heesen et al., 2010; Landrø et al., 2004); however, MS patients can experience cognitive impairment independently of depressive symptoms (Minden et al., 1990; Rao et al., 1989). Rabinowitz & Arnett (2009) suggested that coping strategies may moderate and mediate the association between cognitive impairment and depression in MS.

Pain is also a common symptom of MS, with a 2013 study estimating the pooled prevalence of pain to be 63% in MS populations (Foley et al., 2013). While pain and depression can co-occur in MS (Alschuler et al., 2013; Drulovic et al., 2015; Fiest et al., 2015; Valentine et al., 2022), pain is not a consistent predictor of depression in MS (Beiske et al., 2008; Hanna & Strober, 2020), nor is depression a consistent predictor of pain (Drulovic et al., 2015; Shahrbanian et al., 2018). Alschuler et al. (2013) found that MS patients with depression reported pain more commonly than MS patients with pain reported depression. Meanwhile, Amtmann et al. (2015) found the association between pain and depression in MS to be mediated by fatigue, anxiety, and sleep disturbances.

2.2.3 Disease-Related Factors Associated with Depressive Symptoms

Characteristics of the MS disease course, such as MS type, age of symptom onset, and disease duration, may also be associated with depressive symptoms. Progressive forms of MS have been associated with elevated depressive symptoms at the time of study or early in the disease course (Beal et al., 2007; Jones et al., 2012; Sarisoy et al., 2013; Taylor et al., 2014). While Zabad et al. (2005) found that MS patients with relapsing-remitting MS had higher odds of a lifetime diagnosis of major depression compared to those with a progressive disease course, other studies have not found the clinical course to influence depression over time after controlling for other variables (Beal et al., 2007; Simpson et al., 2019). Younger age of MS onset and shorter disease duration have also been associated with elevated depressive symptoms among MS patients (Bamer et al., 2008; Beiske et al., 2008; Chwastiak et al., 2002; Garcia & Finlayson, 2009; Patten et al., 2003; Simpson et al., 2019).

2.3 Bipolar Disorder in Persons with Multiple Sclerosis

Bipolar disorders can be defined as disturbances of emotions, thoughts and energy (Vieta et al., 2018). They are characterized by distinct and recurring phases of mania and depression (Vieta et al., 2018). The DSM-V classifies bipolar disorders as distinct from depressive disorders (American Psychiatric Association, 2013); however, they are considered to be mood disorders under the International Classification of Diseases, 10th revision (World Health Organization, 1993).

MS patients have a higher risk of bipolar disorder compared to the general population (Carta, Moro, Lorefice, Trincas, et al., 2014). Using 2005 administrative health data, Marrie et al. (2013) estimated the age-standardized prevalence of bipolar disorder to be 5.8% in people with MS compared to 3.5% in the general population. A 2021 investigation estimated the overall pooled prevalence of bipolar disorder in MS to be 3.0%, with higher prevalence estimates in the Americas versus Europe (4.7% and 2.0%, respectively) (Joseph et al., 2021). Bipolar disorder tends to be more common in women with MS, as studies have found women to have an increased incidence (Marrie et al., 2017b; Marrie, Fisk, et al., 2015) and prevalence (Joseph et al., 2021; Marrie et al., 2016; Marrie, Fisk, et al., 2015) of bipolar disorders relative to men with MS. The incidence of bipolar disorder is higher among younger MS patients (Marrie et al., 2017b).

To date, bipolar disorder has been poorly researched relative to depression in MS patients. An American study found bipolar disorder to exacerbate fatigue, physical and social functioning, and physical health distress in persons with MS (Jun-O'connell et al., 2017). In an investigation of quality of life and mental comorbidity in Italian MS patients, a prior study found bipolar disorder to have an earlier age of onset and to impair HRQOL to a greater degree than MDD (Carta, Moro, Lorefice, Picardi, et al., 2014).

2.4 Anxiety in Persons with Multiple Sclerosis

The prevalence of anxiety disorders and anxiety symptoms is higher among persons with MS relative to the general population (Beiske et al., 2008; Boeschoten et al., 2017; Marrie et al., 2012; Marrie, Fisk, et al., 2015; Marrie, Reingold, et al., 2015). In 2005, the estimated crude prevalence of an anxiety disorder in MS was 8.7% compared to 5.1% in controls matched by age, sex, and geographic location (Marrie, Fisk, et al., 2015). A 2017 review estimated the pooled prevalence of a diagnosed anxiety disorder in the MS population to be 9.8%, while the pooled prevalence of clinically significant anxiety symptoms was much higher (34.2%) (Boeschoten et al., 2017).

Studies have generally found anxiety to be associated with younger age (Beiske et al., 2008; Hanna & Strober, 2020) and the female sex (Korostil & Feinstein, 2007; Marrie et al., 2017b; Marrie, Fisk, et al., 2015; Théaudin et al., 2015). Prior studies have also found racial disparities in anxiety symptoms, showing Black MS patients to have elevated anxiety symptoms relative to White patients (E. Hunter et al., 2023; Kister et al., 2021; Wang et al., 2020). Among Black MS patients, those who reported experiences of racial discrimination have reported even higher levels of anxiety and sleep disturbances (E. Hunter et al., 2023).

Previous studies have found depression to be an independent predictor of anxiety in MS (Brown et al., 2009; Garfield & Lincoln, 2012; Giordano et al., 2011; Hartoonian et al., 2015; Korostil & Feinstein, 2007; McCabe, 2005; Podda et al., 2020). Fatigue, pain, and disability have also been strongly associated with anxiety symptomology in persons with MS (Beiske et al., 2008; Brown et al., 2009; Garfield & Lincoln, 2012; Hanna & Strober, 2020; Marck et al., 2017). Anxiety can contribute to substantial reductions in HRQOL among MS patients (Hanna & Strober, 2020; Marrie, Patten, et al., 2018). MS patients with comorbid depression and anxiety have reported greater stress and worse HRQOL compared to those with depression alone (Hanna & Strober, 2020).

Overall, depression, bipolar disorder and anxiety are highly prevalent in persons with MS relative to the general population, and the presence of these mental health comorbidities can contribute to significantly poorer HRQOL and MS-related outcomes. Sociodemographic factors (e.g., age, race, SES), clinical symptomology (e.g., disability, fatigue, psychiatric symptoms), and characteristics of the MS disease course (e.g., age of symptom onset, disease duration) should be considered when investigating mental health comorbidities in MS.

2.5 Treatment of Mental Health Comorbidities in Persons with Multiple Sclerosis

A combination of psychotherapy and medication (antidepressants) has generally been recommended for the treatment of depression in persons with MS (Fiest et al., 2016; Minden et al., 2014). Ideally, diagnoses of bipolar disorders should excluded be in MS patients with depressive episodes prior to prescribing antidepressants (Carta, Moro, Lorefice, Trincas, et al., 2014). Otherwise, MS patients should be monitored for hypomanic or manic symptoms while taking antidepressants (McIntyre et al., 2012). While there is currently very limited evidence on the treatment of bipolar disorder in MS, anecdotal evidence suggests that bipolar disorder can be managed in MS with medication (notably mood stabilizers and anti-psychotic medication) (Paparrigopoulos et al., 2010).

The treatment of anxiety has been understudied in persons with MS (Fiest et al., 2016; Kidd et al., 2017). Clinical trials have found cognitive strategies to reduce anxiety in persons with MS (Akbari et al., 2021; Mohr et al., 2002; Pouyanfard et al., 2020); however, there is limited evidence on the treatment of anxiety with pharmacological and psychological interventions in persons with MS (Brenner & Piehl, 2016). As such, it is recommended that MS patients follow the treatment guidelines for the general population, using a combination of medication (notably antidepressants) and psychotherapy as first line treatments for anxiety (Brenner & Piehl, 2016).

2.6 Unmet Mental Health Needs in Persons with Multiple Sclerosis

Despite being highly prevalent among persons with MS, previous studies have found many MS patients with clinically meaningful depressive and/or anxiety symptoms to be undiagnosed (Korostil & Feinstein, 2007; Marrie et al., 2009; Marrie, Patten, et al., 2018; Ploughman et al., 2020), or to report persistent depressive symptoms despite receiving on-ongoing treatment (Koch et al., 2015; Marrie, Patten, et al., 2018; Ploughman et al., 2020; Raissi et al., 2015). The underdiagnosis and undertreatment of mental health comorbidities indicate that many MS patients experience unmet mental health needs (Minden et al., 2013).

2.6.1 Underdiagnosis of Mental Health Comorbidities in Persons with Multiple Sclerosis

Depression and, to a greater extent, anxiety, have been consistently underdiagnosed in MS patients (Korostil & Feinstein, 2007; Marrie et al., 2009, 2018; McGuigan & Hutchinson, 2006). Previous studies have found approximately one-third of MS patients to be undiagnosed for depression (Marrie et al., 2009; Marrie, Patten, et al., 2018; McGuigan & Hutchinson, 2006) and nearly two-thirds of MS patients to be underdiagnosed for anxiety (Korostil & Feinstein, 2007; Marrie, Patten, et al., 2018).

Investigations of bipolar disorder in MS patients are much more limited relative to depression and anxiety. The results of an Italian investigation suggest that bipolar disorder may be misdiagnosed as depression in MS patients (Carta, Moro, Lorefice, Trincas, et al., 2014); however, the extent of this finding remains unknown.

2.6.2 Undertreatment of Mental Health Comorbidities in Persons with Multiple Sclerosis

Mental health comorbidities are frequently undertreated in persons with MS. Previously, studies found a large proportion of MS patients with comorbid depression to be untreated (Beiske et al., 2008; Marrie et al., 2009; Mohr et al., 2006). For example, Mohr et al. (2006) found that two-thirds of MS patients with MDD had not received antidepressants. More recent studies suggest that the treatment of depression is becoming more common in MS patients, with upwards of 85% of MS patients reportedly receiving some form of treatment for depression (Marrie, Patten, et al., 2018; Orr et al., 2018; Ploughman et al., 2020; Raissi et al., 2015). That being said, many MS patients continue to report clinically meaningful depressive symptomology despite receiving treatment for depression (Marrie, Patten, et al., 2018; Ploughman et al., 2020; Raissi et al., 2015). Together, these findings indicate that depression has not been adequately treated in many MS patients (Marrie, Patten, et al., 2018; Ploughman et al., 2020; Raissi et al., 2015).

Anxiety has remained undertreated to a greater extent than depression in persons with MS (Hermann et al., 1996; Korostil & Feinstein, 2007; Marrie, Patten, et al., 2018). For instance, in 2007, a Canadian study found that over 50% of MS patients with an anxiety disorder were not receiving any form of treatment (Korostil & Feinstein, 2007). A decade later, a 2018 investigation reported a substantial gap between the number of Canadian MS patients with clinically meaningful anxiety symptoms (67.5%) and the number of participants receiving treatment for anxiety (26%).

Very few investigations have explored the undertreatment of bipolar disorder in persons with MS. An American study investigated the prevalence of bipolar disorder in MS using structured clinical interviews. Of the 10 MS patients identified, all were receiving some form of medication; however, half of the participants were treated exclusively with antidepressants (Jun-O’connell et al., 2017).

2.6.3 Consequences of Unmet Mental Health Needs in Persons with Multiple Sclerosis

Unmet mental health needs can adversely impact HRQOL and health behaviours of MS patients (Ploughman et al., 2020; Ponzio et al., 2020; Ytterberg et al., 2013). Undiagnosed depression and anxiety can affect HRQOL to the same degree as active, diagnosed comorbidities (Marrie, Patten, et al., 2018). Undertreated depression can adversely impact health behaviours (diet, exercise), participation in life roles, and HRQOL of MS patients (Ploughman et al., 2020).

In addition to health consequences, mental health comorbidities are associated with significantly greater utilization of health services (Marrie, Walld, et al., 2021; Ytterberg et al., 2013) and healthcare expenditures (Bhattacharjee et al., 2021). As such, improving mental health outcomes for MS patients may reduce the adverse health and economic consequences associated with mental health comorbidities. The following sections discuss the correlates, as well as the barriers, associated with mental health service use among MS patients using the framework provided by Andersen's Behavioural Model of Health Service Utilization.

2.7 The Utilization of Mental Health Services Among Persons with Multiple Sclerosis

Andersen's Model was initially developed in 1968 to examine the use of health services by families (Andersen, 1968). Since its conception, the model has undergone multiple revisions to be adapted to different contexts [e.g., Andersen & Newman (1973), Andersen (1995), Gelberg et al. (2000), Bradley et al. (2002) and Andersen & Davidson (2007)]. In its fourth iteration, Andersen's Behavioural Model of Health Service Utilization provides a framework to examine health service use at the level of the individual (Andersen, 1995).

In his model, Andersen stipulated that an individual's willingness and ability to access health services is determined by: (i) their predisposition to access health services (predisposing factors), (ii) individual- and community-level resources that can facilitate or hinder their access to health services care (e.g., income, health insurance coverage, availability and accessibility of health services) (enabling resources, hereafter referred to as enabling factors), and (iii) their perceived and evaluated needs for health services (need factors) (Andersen, 1995). The following sections summarize the literature on mental health service use in MS under the lens of predisposing, enabling and need factors.

2.7.1 Predisposing Factors Associated with the Use of Mental Health Services

According to Andersen (1995), predisposing factors include an individual's sociodemographic characteristics, social structure (e.g., education, occupation), and beliefs about health services.

The association between sociodemographic factors and mental health service use among MS patients has varied across studies. A 2009 investigation found that older adults with MS were more likely to receive mental health care from a mental health professional relative to younger persons with MS (Buchanan et al., 2009); however, other studies did not find age to be associated with mental health service use (Garcia & Finlayson, 2009; Minden et al., 2013;

Pimentel Maldonado et al., 2022). Sex has generally not been associated with differential usage of mental health services (Garcia & Finlayson, 2009; Minden et al., 2013; Pimentel Maldonado et al., 2022), though prior studies have found males to have a higher risk of untreated depression (Marrie et al., 2009; Ploughman et al., 2020). Reports of racial disparities in mental health service use among MS patients have varied across studies. An investigation of MS participants in the NARCOMS registry found that Latinos were more commonly untreated for mental health concerns compared to both Black and White respondents (Buchanan et al., 2010). A study investigating the treatment of depression in MS found that Black Americans with MS were less likely to be diagnosed and treated with psychotropic medication relative to White MS patients (Stepleman et al., 2014). Conversely, other studies did not find racial differences in the proportion of MS patients treated for depression (Marrie et al., 2009) or in the proportion of MS patients who had received mental health treatment in the past year (Minden et al., 2013; Pimentel Maldonado et al., 2022).

On the other hand, previous studies have generally found lower education to be associated with lower use of mental health services in persons with MS (Garcia & Finlayson, 2009; Minden et al., 2013). In MS patients diagnosed with depression reporting elevated depressive symptoms, Marrie et al. (2009) found low education to be the only predictor of non-treatment. In addition to lower education, Minden et al. (2013) found MS patients who were employed and married to have a lower likelihood of receiving mental health treatment.

Patient attitudes can also influence the use of health services. In qualitative analyses, MS patients have shared negative interactions with healthcare professionals when seeking mental health treatment (Methley, Chew-Graham, et al., 2017; Minden et al., 2013; Rintell et al., 2012). MS patients expressed frustrations with the lack of communication between medical and mental health services, mental health providers with limited knowledge and experience working with MS, and poor continuity of mental health services (Methley, Chew-Graham, et al., 2017; Minden et al., 2013; Rintell et al., 2012). The limited accessibility and availability of mental health services also contributed to negative patient perceptions of mental health care (Methley, Chew-Graham, et al., 2017; Minden et al., 2013; Rintell et al., 2012). Given that MS patients frequently use their previous experiences with healthcare services to inform future help-seeking behaviours (Pétrin et al., 2020, 2021), negative attitudes towards healthcare providers and mental health services may deter MS patients from accessing mental health treatment.

2.7.2 Enabling Factors Associated with the Use of Mental Health Services

According to Andersen (1995), the enabling factors that influence health service utilization operate on an individual- and community-level. The individual-level factors that can facilitate or hinder access to services include measures of SES (income, health insurance coverage), sources of care, travel to health services, and the waiting times for health services, while the community-level factors include the location and availability of health services (Andersen, 1995).

Previous investigations in persons with MS have found measures of SES, particularly health insurance coverage and income, to be important determinants of general and specialized service use (Beatty et al., 2003; Buchanan et al., 2006; Iezzoni et al., 2002; Minden et al., 2007; Rintell et al., 2012; Vickrey et al., 1999). For instance, in a sample of Americans with MS, Minden et al. (2007) found that participants without health insurance were significantly less likely to receive care when needed (Minden et al., 2007). Of those with current health insurance and a regular source of medical care, 2.4% (51/2143) of participants still reported difficulties accessing mental health care. The most prevalent barriers to mental health treatment were costs (59.3%), difficulties getting an appointment (14.2%) and accessibility concerns (12.2%) (Minden et al., 2007). Among other individual-level barriers, MS patients have reported that a lack of reliable transportation to MS centres, the presence of accessibility barriers (e.g., stairs and an absence of parking) and substantial wait times for appointments prevented them from accessing mental health care (Methley, Campbell, et al., 2017; Rintell et al., 2012).

Among community-level factors, persons with MS from rural areas have identified a lack of available mental health providers (Buchanan et al., 2006; Methley, Campbell, et al., 2017; Rintell et al., 2012). In an investigation of patient satisfaction with depression treatment in Americans with MS, Buchanan et al. (2006) found that participants from rural areas were significantly less likely to receive the recommended combination of psychotherapy and medication. Participants from rural areas were also less satisfied with their access to mental health care and more commonly perceived their mental health care to be of lower quality than those from urban areas (Buchanan et al., 2006).

2.7.3 Need Factors Associated with the Use of Mental Health Services

In Canada, MS patients reportedly have a higher perceived need for mental health treatment (31.8%) relative to the general population (~10%) (Orr et al., 2018; Sunderland &

Findlay, 2013). In a sample of Canadians with MS, Orr et al. (2018) found elevated symptoms of depression and anxiety to predict the perceived need for mental health treatment. Similarly, another investigation found MS patients with more severe mental health concerns to be significantly more likely to receive treatment (Minden et al., 2013). In general, MS patients in worse health (e.g., more severe disability, cognitive impairment, fatigue, pain, self-related health) tend to have greater utilization of health services (Hansen et al., 2002; McKay, Marrie, et al., 2018; Pétrin et al., 2020). That being said, MS patients with greater levels of physical impairment and those with lower mental HRQOL have reported significantly greater difficulty accessing mental health services (Wu et al., 2007). Race and ethnicity can further influence the perceived need for mental health treatment (Pimentel Maldonado et al., 2022). In a sample of Americans with MS, Black/African and Latino/Hispanic MS patients were significantly more likely to report negative attitudes toward mental health services relative to White MS patients (Pimentel Maldonado et al., 2022).

The evaluated need for health services reflects a healthcare provider's assessment of an individual's health status and need for health services (Andersen, 1995). Findings from qualitative studies suggest a need for more frequent mental health screening in persons with MS (Marck et al., 2022; Methley, Campbell, et al., 2017; Rintell et al., 2012). In an American qualitative study, MS patients expressed frustrations with the lack of mental health support shortly receiving a diagnosis of MS, with several participants suggesting that healthcare providers failed to identify their depression due to a lack of screening (Rintell et al., 2012). In a sample of Australian MS providers, many healthcare providers did not screen their patients for depression due to a lack of time and skill to manage depression once identified (Marck et al., 2022). In addition, healthcare providers from the United Kingdom have expressed difficulties identifying candidates for mental health care due to the heterogeneity in MS symptoms (Methley, Campbell, et al., 2017). MS providers were also unclear about their roles in managing the mental health concerns of their patients, often assuming this responsibility to fall on general practitioners (Methley, Campbell, et al., 2017).

Cumulatively, mental health comorbidities are often poorly diagnosed and treated in persons with MS. Previous studies have found several predisposing factors (education, health beliefs) and enabling factors (health insurance, income, transportation, accessibility) to influence the use of mental health services in persons with MS. The findings for sociodemographic characteristics (age, race, and ethnicity) and need factors (the severity of mental health symptoms and level of physical impairment) have been less consistent across studies. Further investigation is needed to identify disparities in mental health service use for the treatment of depression and anxiety in persons with MS.

3.0 Study Rationale and Research Questions

3.1 Study Rationale

Mental health comorbidities, such as depression, bipolar disorder, and anxiety, are highly prevalent in MS (Boeschoten et al., 2017; Joseph et al., 2021; Marrie et al., 2013; Marrie, Fisk, et al., 2015; Marrie, Reingold, et al., 2015). Mental health comorbidities contribute to substantial reductions in HRQOL, and their co-occurrence in MS increases the risk of suicide and mortality (Berrigan et al., 2016; Marrie et al., 2012; Marrie, Walld, et al., 2018). Unfortunately, mental health comorbidities are frequently underdiagnosed and undertreated in MS (Jun-O'connell et al., 2017; Korostil & Feinstein, 2007; Marrie et al., 2009; Marrie, Patten, et al., 2018; Raissi et al., 2015). Unmet mental health needs are associated with even greater health and economic consequences (Marrie, Walld, et al., 2021; Ploughman et al., 2020; Ponzio et al., 2020). As such, it is important to identify the barriers preventing persons with MS from accessing mental health services.

To date, there are limited investigations of the factors and barriers associated with untreated mental health comorbidities in persons with MS. Previous quantitative studies have generally found socioeconomic factors (such as inadequate or no health insurance and lower levels of education and income) to be associated with untreated mental health comorbidities in MS patients (Beatty et al., 2003; Buchanan et al., 2006; Garcia & Finlayson, 2009; Marrie et al., 2009; Minden et al., 2007); however, the findings for sociodemographic factors (i.e., age, race, and ethnicity) and clinical factors (i.e., severity of mental health symptoms and level of physical impairment) have been less consistent between studies. Further, relatively few quantitative studies have explored both the correlates and barriers associated with untreated mental health comorbidities in MS patients. Of these, two studies identified socioeconomic and accessibility barriers to mental health treatment (e.g., insurance, cost, transportation) (Buchanan et al., 2006; Minden et al., 2007), one study identified facilitators of positive experiences with mental health services (Minden et al., 2013), and a more recent study explored differences in mental health attitudes and health-seeking behaviours across racial and ethnic groups (Pimentel Maldonado et al., 2022). Qualitative studies also explored the facilitators and barriers to mental health service use in MS patients (A. Hunter et al., 2021; Marck et al., 2022; Methley, Campbell, et al., 2017; Methley, Chew-Graham, et al., 2017; Rintell et al., 2012); however, additional quantitative investigations are needed to identify the prevalence of these barriers in larger samples. As such, further research is needed to identify disparities in the use of mental health services for the treatment of depression, anxiety, and bipolar disorder in MS patients.

To address gaps in literature, we utilized 2011 to 2012 survey data collected by the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry to investigate: (i) the prevalence and correlates of untreated mental health comorbidities (correlates for depression and anxiety only) in MS patients diagnosed with depression, anxiety or bipolar disorder (Objectives 1A and 1B), (ii) the prevalence and correlates of barriers in those not receiving treatment for depression or anxiety (Objectives 1C and 1D) (iii) the prevalence and correlates of treatment modalities in those receiving treatment for depression or anxiety (Objective 1E), and (iv) the temporal association between untreated mental health comorbidities (at baseline) and depressive symptomology and HRQOL (in both mental and physical domains) at one-year follow-up (Objectives 2A and 2B).

The results of this study will identify disparities in the treatment of mental health comorbidities in MS patients and highlight significant sociodemographic and clinical correlates of untreated mental health comorbidities in MS patients to be considered in future research. The barriers identified in this study may inform future clinical and public health initiatives to improve access to care for disadvantaged MS patients.

3.2 Research Questions

Cross-sectional component [NARCOMS 2011 Spring Survey]

Objective 1 – To examine the prevalence and sociodemographic correlates of mental health treatment status among MS patients with a diagnosed mental health comorbidity.

For this objective, the following questions were addressed:

A. What proportion of the MS patient survey sample with diagnosed depression, bipolar disorder and/or anxiety disorder is currently receiving treatment?
B. What are the crude and adjusted associations between patients' sociodemographic and other key characteristics and unmet mental health needs (i.e., not receiving treatment)?
C. Among those not currently receiving treatment for their diagnosed mental health comorbidity, what are the common mental health treatment barriers, and how do these barriers vary by key sociodemographic and other characteristics of MS patient respondents?

D. Among those not receiving treatment for their diagnosed mental health comorbidity, how are mental health treatment barriers associated with the severity of depressive symptoms?
E. Among those receiving treatment for their diagnosed mental health comorbidity, what form of treatment is being administered and how does the type of treatment vary by key sociodemographic and other characteristics of MS patient respondents?

Longitudinal component [NARCOMS 2011 Survey for exposure and baseline characteristics; NARCOMS Spring 2012 Survey for outcomes at one-year follow-up]
Objective 2 – To examine the temporal association between unmet mental health needs and severity of depressive symptoms and mental/physical health-related quality of life among a longitudinal sample of MS survey respondents with a diagnosed mental health comorbidity. For this objective, the following question were addressed:

A. What are the crude and adjusted associations between respondents' baseline mental health treatment status and severity of depressive symptoms at one-year follow-up?
B. What are the crude and adjusted associations between respondents' baseline mental health treatment status and mental (and physical) health-related quality of life scores at one-year follow-up?

Depression, anxiety, and bipolar disorder were explored in Objective 1A; however, subsequent objectives were restricted to depression and anxiety only. Bipolar disorder was not investigated past Objective 1A due to sample sizes and feasibility concerns for statistical analyses.

3.3 Hypotheses

For Objective 1, it was hypothesized that low SES and racialized MS patients would be less likely to be treated for mental health comorbidities and would experience more barriers to treatment relative to White MS patients and those with higher SES. For Objective 2, it was hypothesized that unmet mental health needs at baseline would be positively associated with the presence of clinically meaningful depressive symptoms and a clinically meaningful decline in mental and physical HRQOL at one-year follow-up.

4.0 Methodology

4.1 Data Source: North American Research Committee on Multiple Sclerosis (NARCOMS) Registry

NARCOMS is a global longitudinal self-reported MS patient registry approved by the Institutional Review Board of Washington University in St. Louis (ClinicalTrials.gov, 2023; Maelstrom Research, 2023; Marrie, Cutter, et al., 2021). NARCOMS collects data on patient-reported health status, MS progression, contributing factors (demographic, lifestyle, and clinical factors) and DMT through initial enrolment and biannual follow-up surveys (ClinicalTrials.gov, 2023; Maelstrom Research, 2023). While follow-up surveys contain core items that are repeated across timepoints (e.g., validated measures of depressive symptoms, health status, health-related quality of life), additional items can be added to investigate specific topics. Self-reported MS diagnoses in NARCOMS have been validated using a random sample of American respondents (Marrie et al., 2007).

Individuals over the age of 18 years diagnosed with MS or clinically isolated syndrome (a single clinical attack on the central nervous system that progresses into MS in about 70% of patients) (Brownlee & Miller, 2014; D. Miller et al., 2005; Swanton et al., 2007) can voluntarily enroll in NARCOMS (ClinicalTrials.gov, 2023; Maelstrom Research, 2023; NARCOMS, 2023). Otherwise, NARCOMS has no exclusion criteria, and participants can withdraw at any time (ClinicalTrials.gov, 2023; Maelstrom Research, 2023; NARCOMS, 2023). Recruitment sources for NARCOMS include healthcare conferences, MS clinics (notably those a part of the Consortium of Multiple Sclerosis Centers), clinician offices, the National Multiple Sclerosis Society, NARCOMS magazines (*NARCOMS Now*), postings on the internet, and other sources of traditional media (Marrie, Cutter, et al., 2021). While NARCOMS accepts MS patients from across the globe, the majority of participants reside in the United States (Marrie, Cutter, et al., 2021).

NARCOMS surveys may be completed online or on paper. MS patients are not financially compensated for their participation in NARCOMS surveys, but they are notified of clinical trials and other studies in which they may be eligible to participate and can opt to receive a quarterly magazine to be updated on research findings (ClinicalTrials.gov, 2023; Maelstrom Research, 2023; NARCOMS, 2023). By participating in NARCOMS, respondents consent to their de-identified data being released for research purposes. Respondents are notified of the potential release of their responses upon enrolment and are reminded on each follow-up survey (ClinicalTrials.gov, 2023; Maelstrom Research, 2023; NARCOMS, 2023).

NARCOMS is not a population-based registry, meaning the findings are limited in generalizability and applicability to MS populations outside of NARCOMS (Marrie, Cutter, et al., 2021). Nevertheless, NARCOMS is still a valuable resource that can help to investigate salient questions in MS research and improve the general understanding of MS and associated health outcomes (Marrie, Cutter, et al., 2021).

The NARCOMS Spring 2011 Survey served as the foundation for this thesis, as this survey captured items on the prevalence of common mental health comorbidities (e.g., depression, anxiety, bipolar disorders), the treatment status of those affected (receiving treatment vs. not receiving treatment), and the reasons for mental health non-treatment among those not receiving treatment (mental health treatment barriers). To date, no investigation has used these data to examine the factors and barriers associated with mental health non-treatment in persons with MS. As a result, these data provided a unique opportunity to examine the correlates and consequences of mental health non-treatment among participants of a well-established MS patient registry.

4.2 Analytic Samples

4.2.1 Objective 1: Baseline Cohorts

For participants of the NARCOMS Spring 2011 Survey to be included in the analytic sample, they needed to report (i) a diagnosis of depression, anxiety and/or bipolar disorder and (ii) their current treatment status for each diagnosed mental health comorbidity (receiving treatment vs. not receiving treatment). Respondents who reported the presence of a mental health comorbidity without a discernable mental health treatment status (i.e., did not provide treatment status and did not report any mental health treatment barriers to suggest non-treatment) were excluded from Objective 1 analyses. A flowchart showing the creation of baseline cohorts and treatment variables is presented in Figure 1.

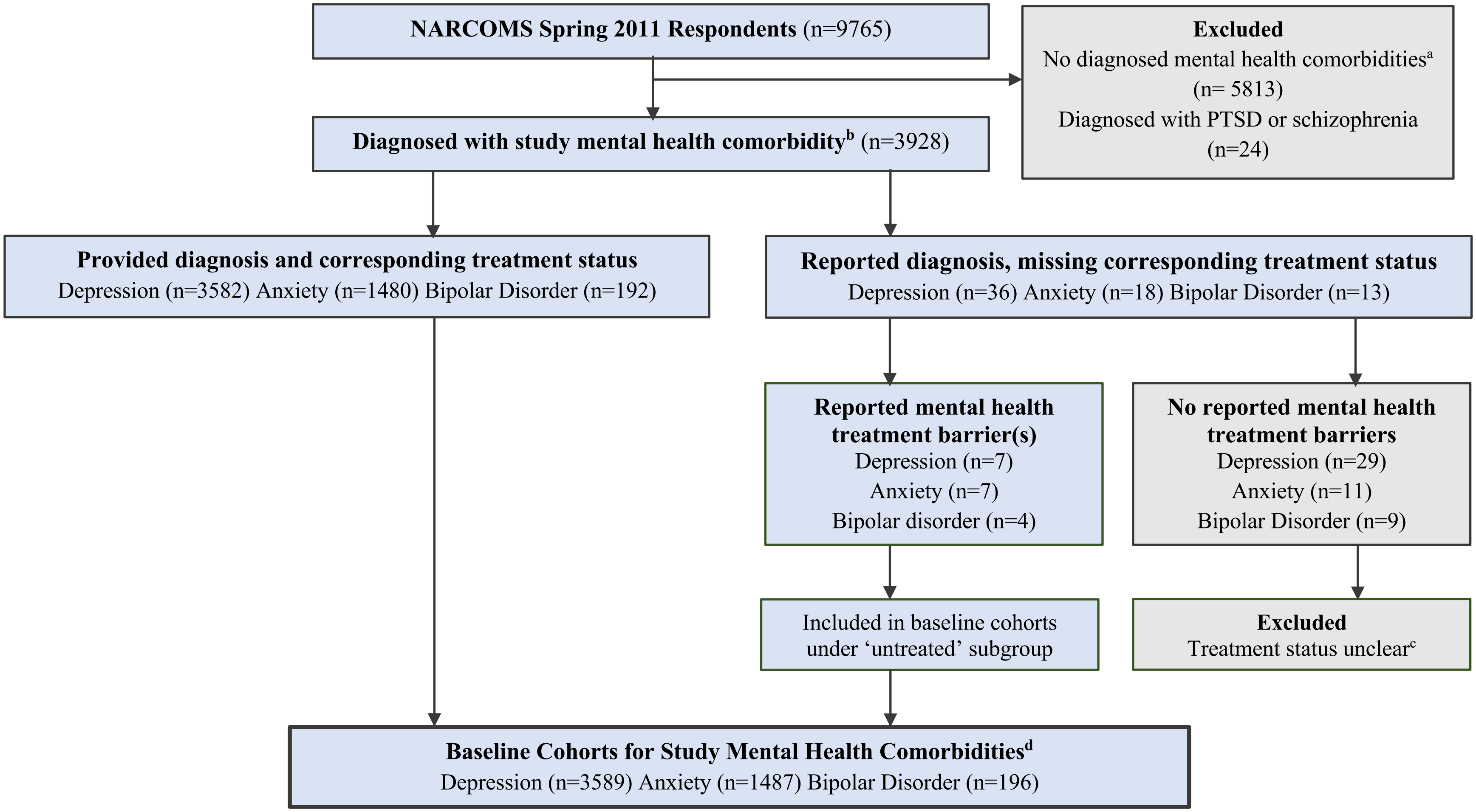
The NARCOMS Spring 2011 Survey had a total of 9765 respondents, 3928 of whom were diagnosed with one or more of depression, anxiety, or bipolar disorder. Post-traumatic stress disorder and schizophrenia were also captured on the NARCOMS Spring 2011 survey; however, these conditions are outside the scope of this project and were therefore excluded from analyses. To explore the prevalence of non-treatment among each mental health comorbidity and to facilitate clarity in analyses and interpretation, we chose to investigate depression, anxiety, and bipolar disorder separately. Respondents could report more than one mental health comorbidity and corresponding treatment status. Those who met the inclusion criteria for more than one mental health comorbidity were included in all relevant condition groups. As a result, we examined three non-mutually exclusive baseline samples: depression cohort (n=3589), anxiety cohort (n=1487), and bipolar disorder cohort (n=196). The depression and anxiety cohorts were assessed in all research questions identified for Objective 1 (Questions A through E). However, given the small sample sizes observed for MS survey respondents with bipolar disorder (both in terms of the overall sample [n=196] and for those not currently receiving treatment [n=46]) and associated feasibility and power concerns, it was decided to restrict analyses of those with bipolar disorder to Objective 1, Research Question A only.

4.2.2 Objective 2: Follow-Up Cohorts

For the longitudinal component of this investigation, we examined the association between baseline mental health treatment status and the severity of depressive symptoms (measured using the NARCOMS Depression Scale) and mental and physical HRQOL aggregate scores (measured using the RAND-12) at one-year follow-up. Descriptions of the NARCOMS Depression Scale and RAND-12 as validated assessment instruments are provided in Methods Section 4.3.2. We opted to create separate analytic cohorts for the NARCOMS Depression Scale and RAND-12 outcomes due to different missing values for each outcome (respondents could skip the items relating to these outcomes on baseline and follow-up surveys). A flowchart showing the creation of follow-up cohorts is presented in Figure 2.

Respondents needed to respond to the outcome measure at baseline (Spring 2011) and at follow-up (Spring 2012) to be included in our follow-up cohorts. As a result, our Objective 2 follow-up cohorts included baseline respondents who provided the NARCOMS Depression Scale at both timepoints (depression cohort [n=2891]; anxiety cohort [n=1181]) and baseline respondents who provided the RAND-12 at both timepoints (depression cohort [n=2784]; anxiety cohort (n=1140]). Follow-up cohorts were not mutually exclusive between outcomes. Approximately 20% of respondents from our baseline depression and anxiety cohorts were missing the NARCOMS Depression Scale and the RAND-12 at either timepoint (i.e., skipped the question at baseline or were missing at follow-up). A comparison of baseline characteristics among those missing vs. not missing for each outcome is provided in Objective 2 results.

Figure 1 Flowchart showing the creation of baseline depression, anxiety, and bipolar disorder cohorts from the NARCOMS Spring 2011 enrolment sample



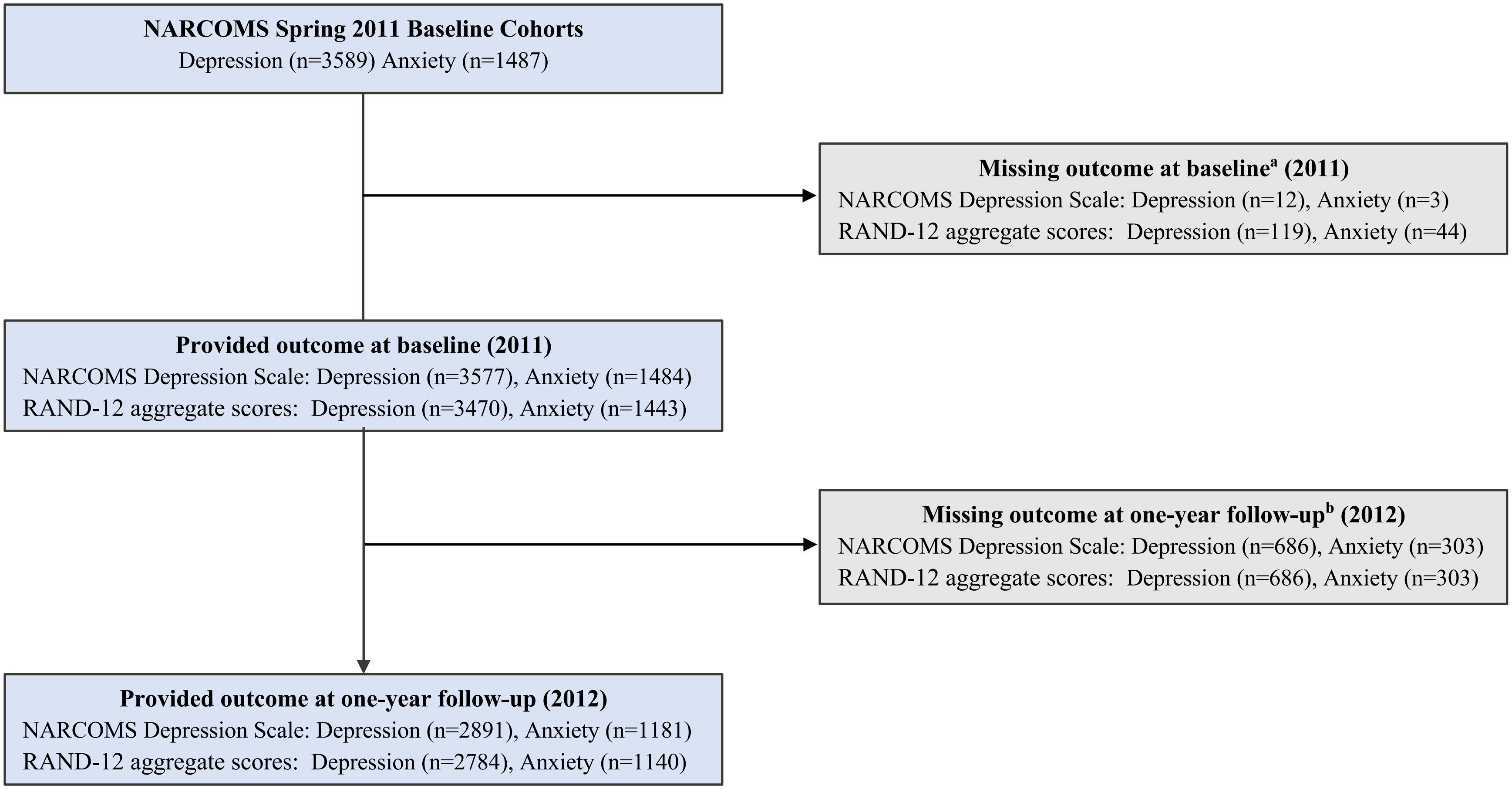
[a] Not diagnosed with any mental health comorbidity captured by NARCOMS Spring 2011 survey.

[b] Diagnosed with one or more of depression, anxiety, and/or bipolar disorder.

[c] Respondents did not clearly provide outcome of interest for this Objective 1 (i.e., not receiving treatment for diagnosed mental health comorbidity) and were therefore excluded from analyses.

[d] Study mental health comorbidities were not mutually exclusive; respondents appear in the overall count for each of their reported comorbidities.

Figure 2 Flowchart showing the sample sizes for the NARCOMS Depression Scale and the RAND-12 outcomes at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety



[an] Includes those who skipped the item(s) relating to the NARCOMS Depression Scale and/or the RAND-12 on the NARCOMS Spring 2011 Survey.

[b] Includes those who skipped relevant survey item(s) and those lost-to-follow-up.

4.3 Measures

The following sections provide a description of the key mental health and clinical outcome variables, as well as the sociodemographic, clinical, and MS-related covariates examined in the analyses of Objectives 1 and 2. Additional descriptions of mental health treatment barriers are provided in Table A1, and descriptions of coding decisions, categorizations, reference group selection for all baseline covariates are provided in Table A2.

4.3.1 Mental Health Exposure & Outcome Variables

Baseline Mental Health Treatment Status

Baseline mental health treatment status (receiving treatment vs. not receiving treatment) was a central variable included in the analyses of Objectives 1 and 2. Baseline mental health treatment status was queried on the NARCOMS Spring 2011 Survey using the format: "Has a doctor diagnosed you with any of the following conditions? […] If yes, please mark […] the condition you have been diagnosed with and indicate if you receive some type of treatment or medication for the condition." Due to the wording of this item, mental health treatment status could only be assessed for those reporting a diagnosed mental health comorbidity. Among respondents with more than one diagnosed mental health comorbidity, treatment status could vary between conditions (e.g., a respondent diagnosed with depression and anxiety could be receiving treatment for the former but not the latter, which is among the reasons why the depression and anxiety cohorts were analyzed separately [see Section 4.2.1]). Baseline mental health treatment status for the depression (treated: yes/no) and anxiety (treated: yes/no) cohorts were assessed as outcome variables in Objective 1B regression analyses.

Mental Health Treatment Barriers

Mental health treatment barriers were investigated among respondents diagnosed with a mental health comorbidity who were not receiving treatment. Barriers were queried on the NARCOMS Spring 2011 Survey using the format: "If you are not being treated for one of the conditions listed above, please indicate why by choosing all that apply." Respondents could select one or more of 11 possible mental health treatment barriers. These barriers were then classified using the framework provided by Anderson's Behavioural Model of Health Service Use (see Section 2.7). Andersen's Behavioural Model provides a relevant framework for this investigation as it has been previously applied in studies examining mental health service use (Alhalaseh et al., 2022; Graham et al., 2017; Van der Draai et al., 2021; Wang et al., 2022) and in populations with MS and other chronic conditions (Asano et al., 2019; Buhse et al., 2014, 2015; K. Y. Kim et al., 2020).

The 11 treatment barriers captured by the NARCOMS Spring 2011 were assigned as predisposing, enabling, or need factors according to Andersen's Behavioural Model (Andersen, 1995) (barrier groupings: predisposing factors [n=2], enabling factors [n=8] and need factors [n=1]) (see Table A1). Barrier groupings were coded as binary variables for untreated respondents who did vs. did not report any barriers from within each grouping. Barrier groupings were not mutually exclusive as untreated respondents could select more than one option on the survey. Predisposing, enabling and need factors were investigated separately in all descriptive analyses. Mental health treatment barriers were examined as the dependent and independent variables in Objective 1C and 1D bivariate analyses, respectively.

Mental Health Treatment Modality

Mental health treatment modality was investigated among respondents diagnosed with a mental health comorbidity who were receiving treatment. Treatment modality was captured on the NARCOMS Spring 2011 Survey using the format: "If you are currently being treated for one of the conditions listed above, does your treatment include […] psychotherapy, medication, or psychotherapy and medication?". This measure was coded as a three-level, mutually exclusive variable for respondents receiving treatment for depression and/or anxiety. Respondents who were reportedly receiving treatment, but did not disclose their treatment modality, were coded as "missing". Mental health treatment modality was examined as the dependent variable in Objective 1E bivariate analyses.

4.3.2 Clinical Outcomes Variables & Assessment Instruments

Severity of Depressive Symptoms

The severity of depressive symptoms was primarily assessed using the NARCOMS Depression Scale. The NARCOMS Depression Scale is a 6-level, ordinal scale that has been validated as a self-reported measure of depressive symptoms in MS (Marrie, Cutter, et al., 2008). Possible scores range from 0 (normal) to 5 (total depression), where a score greater than or equal to 2 suggests the presence of clinically meaningful depressive symptoms (Marrie, Cutter, et al., 2008). NARCOMS Depression score at baseline (2011) was assessed as a dependent variable in Objective 1D analyses. NARCOMS Depression score at one-year follow-up (with vs. without clinically meaningful depressive symptoms in 2012) was examined as the outcome variable in Objective 2A regression analyses.

The 20-item Center for Epidemiologic Studies–Depression Scale (CES-D20) was assessed as a secondary measure of depressive symptoms in 2011; this measure was not collected on the NARCOMS Spring 2012 survey. The CES-D20 is a validated, self-reported measure of depressive symptoms in MS (Pandya et al., 2005; Patten et al., 2005; Weissman et al., 1977). Scores on the CES-D20 can range from 0 to 60, where higher scores indicate more severe symptomology. A score greater or equal to 16 indicates clinically significant depression, while a score greater or equal to 21 has been used to indicate the presence of probable major depression in MS populations (Pandya et al., 2005; Patten et al., 2005; Weissman et al., 1977). Total scores were only calculated for respondents who completed all 20 questions. A lower cut-point (≥16) was selected to indicate the presence of elevated depressive symptoms (Pandya et al., 2005; Weissman et al., 1977). CES-D20 scores were compared with NARCOMS Depression scores in Objective 1D.

Health Related Quality of Life (HRQOL)

Mental and physical HRQOL were assessed using the 12-item RAND-Health Survey (RAND-12). The RAND-12 is an abbreviated version of the RAND-36, which is a validated measure of HRQOL in MS (Nortvedt et al., 2000). The RAND-12 and RAND-36 scales capture the same items as the commonly used 12- and 36-item Short-Form Health Surveys (SF-12 and SF-36), respectively, but the RAND surveys utilize different scoring algorithms (Hays et al., 1993). The scoring method used in the RAND-12 better assesses mental health in MS than the SF-12 (Nortvedt et al., 2000). The RAND-12 assesses eight health domains (physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, general mental health, social functioning, energy and fatigue, and general health perceptions) which can be used to generate physical (PCS-12) and mental health (MCS-12) aggregate scores (Hays et al., 1993; Hays & Morales, 2001; Ware et al., 1996). MCS-12 and PCS-12 aggregate scores are standardized to reflect a mean of 50 and a standard deviation of 10 in the general population (Ware et al., 1996). Standardized aggregate scores can range from 0 to 100, with higher scoring indicating better HRQOL (Ware et al., 1996).

For Objective 2 regression analyses, we used change scores to assess clinically meaningful changes in mental and physical HRQOL between NARCOMS Spring 2011 and 2012 surveys. Baseline MCS-12 and PCS-12 scores were subtracted from follow-up MCS-12 and PCS-12 scores, and a difference of greater than 3-points was used to indicate a clinically meaningful change in HRQOL (Hays & Morales, 2001; Janzen et al., 2013; Samsa et al., 1999). Specifically, for each of MCS-12 and PCS-12, the binary variable was defined as: declined (scores decreased by ≥3 points at follow-up) vs. those who improved or stayed the status (scores increased by ≥3 points or changed by <3 points in any direction at follow-up). Clinically meaningful declines in mental and physical HRQOL were examined as outcome variables for regression analyses in Objective 2B. Baseline (NARCOMS Spring 2011) MCS-12 and PCS-12 scores (continuous measures) were examined as independent variables in relevant bivariate analyses.

4.3.3 Exposures of Interest in Multivariable Regression Analyses

Sociodemographic characteristics (age, race, education, health insurance) were examined as exposures of interest for multivariable regression analyses in Objective 1B. Exposures of interest were selected based on previous literature to explore potential (age, race) and established correlates (education, health insurance) of untreated mental health comorbidities among persons with MS (Buchanan et al., 2006, 2009, 2010; Garcia & Finlayson, 2009; Marrie et al., 2009; Minden et al., 2007). Key sociodemographic characteristics were also explored as potential confounders in Objective 2A and 2B multivariable regression analyses. Descriptions of these variables are provided in Section 4.3.4.

Baseline mental health treatment status (assessed separately for depression and anxiety cohorts) was examined as the exposure of interest in multivariable regression analyses in Objective 2A and 2B multivariable regression analyses.

4.3.4 Covariates

Sociodemographic Characteristics (see Table A2)

Sociodemographic characteristics were obtained from respondents' enrolment and baseline (Spring 2011) surveys. Coding decisions for sociodemographic variables were informed by the distribution of the data, initial bivariate analyses with outcome variables (depression and anxiety treatment status), and variable groupings used in previous NARCOMS investigations.

Enrolment country (USA [reference] vs. Other), sex (female [reference] vs. male), marital status (married/cohabitating [reference] vs. single/living alone), residence (private residence [reference] vs. living with assistance) and employment status (employed [reference] vs. unemployed/missing) were examined as binary measures. Age (in 2011) was grouped into three levels, <45 years, 45–64 years (reference), and ≥65 years, based on the distribution of the data and according to standardized age groupings for adults vs. older adults (Statistics Canada, 2021). Age (in 2011) was also assessed as a continuous measure for initial descriptive analyses in Objective 1A. Year of birth was categorized into quintiles based on the distribution of the data and to correspond with <45 and ≥65-year age-groupings: ≤1946, 1947–1953, 1954–1959 (reference), 1960–1966, ≥1967. Year of birth was retained as a 5-level variable to examine any unique associations among respondents aged 45–64 years. Race was examined as a binary variable (White [reference] vs. non-White, hereafter referred to as People of Colour/Other) due to very small numbers of non-White respondents (i.e., Black/African American, and Latino respondents made up 1.7% [68/3928] and 1.0% [39/3928] of the total baseline sample, respectively). Education and income were categorized according to increasing levels of educational attainment (Secondary School/General Educational Development (GED), Associate/Technical Degree, Bachelor's Degree, Post-Bachelor's Degree [reference]), and annual family income (<$30,000, $30,000–$50,000, $50,001–$100,000, >$100,000 [reference], I do not wish to answer/missing). Health insurance was examined as a mutually exclusive nominal variable for private coverage, private and public coverage (reference), public coverage, and uninsured status.

Clinical Characteristics (see Table A2)

Baseline clinical measures were all obtained from the NARCOMS Spring 2011 survey. Coding decisions for clinical variables were informed by the distribution of the data, initial bivariate analyses with outcome variables (depression and anxiety treatment status), established clinical cut-points and/or relevant variable groupings used in previous NARCOMS investigations.

The severity of depressive symptoms was assessed as a binary measure using the NARCOMS Depression Scale (<2 [reference] vs. ≥2) as well as the CES-D20 (<16 [reference] vs. ≥16) (Marrie, Cutter, et al., 2008; Pandya et al., 2005) Baseline MCS-12 and PCS-12 scores, derived from the RAND-12, were kept as continuous measures in regression analyses as covariates (see Section 4.3.2).

Self-rated health was assessed using the general health perceptions item on the RAND-12. This item was presented as a 5-level ordinal measure where respondents could select the level that most accurately represented their current overall health, with scores ranging from excellent (1) to poor (5). Self-rated health was dichotomized among those reporting excellent/very good/good vs. fair/poor levels of current health (Zajacova & Dowd, 2011). We also examined whether respondents had been admitted to an overnight healthcare facility in the last six months for any reason (yes vs. no [reference]).

Cognitive impairment and fatigue were measured using the Performance Scales©. The Performance Scales© is a valid measure of disability in MS that assesses patient-reported impairment in eight health-related domains (mobility, hand function, vision, cognition, fatigue, bladder and bowel, sensory and spasticity symptoms) (Schwartz et al., 1999). The eight subscales are ordinal and are scored from 0 (normal) to 5 (total disability), apart from mobility, which is scored from 0 to 6 (Schwartz et al., 1999). The subscales can be summed to calculate a total score, with values ranging from 0 to 41, where higher scores indicate more severe impairment (Schwartz et al., 1999). Individually, the cognitive and fatigue subscales have each shown good construct validity (Marrie & Goldman, 2007) and test-rest reliability in MS (Schwartz et al., 1999). Cognitive impairment and fatigue were grouped into ordinal variables representing increasing levels of impairment: minimal (levels 0–1) (reference), moderate (levels 2–3), and severe (levels 4–5) (Salter et al., 2019).

Pain was assessed using a single-item, 6-level ordinal scale that assesses the severity of pain and the impact of pain on daily activities, where scores range from 0 (no pain) to 5 (total disabling pain) (Marrie, Cutter, Tyry, Hadjimichael, & Vollmer, 2005). The NARCOMS pain assessment has been validated as a self-reported measure of pain in MS (Marrie, Cutter, Tyry, Hadjimichael, & Vollmer, 2005). Pain was assessed as a three-level ordinal variable using the same groupings as the cognitive impairment and fatigue variables.

Disability was assessed using the Patient Determined Disease Steps (PDDS), which is a validated measure of functional disability in MS (Learmonth et al., 2013; Marrie, McFadyen, et al., 2023). The PDDS is a 9-level ordinal scale, with possible scores ranging from 0 (normal) to 8 (bed-ridden) (Hohol et al., 1995). Disability (PDDS) was assessed as a three-level ordinal variable for mild (levels 0–2) (reference), moderate (levels 3–4), and severe (levels 5–8) levels of impairment (Reider et al., 2017).

MS-related Characteristics (see Table A2)

MS characteristics were obtained from respondents' enrolment surveys. MS characteristics were assessed as categorical variables to address issues of potential collinearity among strongly correlated continuous variables. Coding decisions were informed by the distribution of the data and relevant findings from previous investigations.

Age of MS symptom onset was examined as a three-level variable (<25 years, 25–39 years [reference], ≥40 years) based on the findings from Esbjerg et al. (1999). Year of MS onset was examined as a five-level variable based on quintiles (≤1980 [reference], 1981–1985, 1986–1990, 1991–1995, ≥1996). Age of MS diagnosis was grouped into four levels based on ten-year increments (<30, 30–39, 40–49, ≥50 [reference]) Year of MS diagnosis was categorized using quartiles (≤1990 [reference], 1991–1995, 1996–2000, ≥2001). Disease duration was grouped into three levels according to ten-year increments (≤10, 11–20, ≥21 [reference]). Year of enrolment in NARCOMS was grouped into three levels based on terciles (≤2000 [reference], 2001–2004, ≥2005). Clinical course (at onset) was not yet available for investigation in 2011.

4.4 Statistical Analyses

All analyses were conducted using SAS Studio Enterprise Edition 9.4 (SAS Institute Inc., Cary, North Carolina). All tests used an alpha of 0.10 for statistical significance due to concerns of small cell sizes among key variables in analyses.

4.4.1 Descriptive Analyses

Descriptive analyses were conducted to summarize responses from study participants at baseline (Spring 2011) and one-year follow-up (Spring 2012). Univariate analyses were conducted for all relevant covariates, exposures of interest, and outcome variables to obtain frequency and percent distributions for categorical variables, as well as measures of central tendency and spread for continuous variables. The normality of continuous data was tested using the Kolmogorov-Smirnov test and by assessing the skewness and kurtosis of the distribution (H.-Y. Kim, 2013). Nonparametric tests were not needed as continuous data followed a normal distribution.

Initial bivariate analyses compared the distribution of baseline characteristics between participants included vs. excluded from our analytic samples at baseline and at one-year follow-up (Objective 1: NARCOMS participants with vs. without a diagnosed mental health commodity [separate analyses for depression and anxiety cohorts]; Objective 2: baseline participants with vs.

without response to key outcomes at one-year follow-up [separate analyses for NARCOMS Depression Scale and RAND-12]). Cross-tabulations with Pearson's chi-square test were used to assess significant differences in the distribution of categorical variables between samples, while t-tests were used to compare the means of continuous variables between the two samples.

Within our analytic cohorts, cross-tabulations with chi-square test were used to identify statistically significant associations between categorical exposure and outcome variables. If more than 20% of cells had expected frequencies <5, Fisher's Exact test was used to assess statistical significance between categorical variables (H.-Y. Kim, 2017). Two-sided t-tests were used to compare the means between binary exposures and continuous outcomes, and one-way ANOVAs were used to compare the means between categorical exposures (with three or more levels) and continuous outcomes.

Upon completing the descriptive analyses outlined in our research objectives, we repeated the bivariate analyses outlined in Objective 1E, stratifying participants according to their NARCOMS Depression score (absence vs. presence of clinically meaningful depressive symptoms) (analyses shown in Appendix B).

4.4.2 Multivariable Regression Analyses

Unadjusted and adjusted (multivariable) logistic regression analyses were used to examine specific research questions for binary outcome variables under Objectives 1 and 2 (Obj1B: receiving treatment vs. not receiving treatment; Obj2A: presence vs. absence of clinically meaningful depressive symptoms; Obj2B: presence vs. absence of a clinically meaningful decline in mental/physical HRQOL). Multivariable regression was pursued with consideration of model assumptions (Stoltzfus, 2011). Odds ratios (OR) and 95% confidence intervals (CI) were used to assess the strength and direction of associations between relevant exposure(s) of interest and binary outcome variables.

Multivariable regression analyses incorporated relevant sociodemographic and clinical covariates to adjust for potential confounding factors. Covariates for each outcome were selected based on findings from previous literature (see below for key citations), clinical relevance, and initial bivariate analyses. In Objectives 2A and 2B, multivariable regression analyses adjusted for baseline NARCOMS Depression Score and RAND-12 scores, respectively (D. M. Miller et al., 2003; Patten & Metz, 2001).

Starting with key exposure(s) of interest, followed by relevant covariates, a stepwise approach of adding variables one at a time was conducted to allow for an investigation of changes in model estimates (magnitude and/or direction of associations) as variables were added. Non-significant variables were retained in adjusted analyses if (i) they acted as key exposures or covariates of interest for applicable analyses, (ii) they were suggested to be important by previous literature, (iii) they helped to maintain consistency in the interpretation of findings between depression and anxiety cohorts, and (iv) there were no serious collinearity concerns with other model predictors.

The modelling approach considered potential collinearity concerns by examining correlations among study variables related to similar domains of interest (e.g., measures of SES; measures of MS clinical status) and by assessing multicollinearity diagnostics. The presence of serious multicollinearity was informed by (i) estimates showing Variance Inflation Factors (VIF) that were >10, (ii) condition indices that were >30, (iii) two or more variance decomposition proportions exceeding 80-90% (for condition indices >10), and (iv) eigenvalues close to zero (J. H. Kim, 2019; Midi et al., 2010). Upon identifying a collinearity issue between two highly correlated categorical predictors, the least informative covariate (assessed using relevant literature and the covariates' contribution to model fitness) was dropped from the applicable model(s).

Given these considerations, in Objective 1B, the associations between key sociodemographic characteristics (age [in 2011], race, education, health insurance) and baseline mental health treatment status were adjusted for marital status, NARCOMS Depression score, and disability (PDDS) (Minden et al., 2007, 2013; Wu et al., 2007). In Objective 2A, the association between baseline mental health treatment status and clinically meaningful depressive symptoms at one-year follow-up (in 2012) was adjusted for age, sex, race, marital status, education, income, employment status, depressive symptoms, disability, and disease duration (all assessed at baseline) (Beal et al., 2007; Beiske et al., 2008; Chwastiak et al., 2002; Ensari et al., 2013; Marrie et al., 2009; Patten et al., 2005; Patten & Metz, 2001). In Objective 2B, the association between baseline treatment status and clinically meaningful decline in RAND-12 scores (2011 to 2012) was adjusted for age, sex, race, marital status, education, income, employment, depressive symptoms (for PCS-12 only), disability (for MCS-12 only), relevant RAND-12 score, and disease duration (all assessed at baseline) (Buhse et al., 2014; Gil-González et al., 2021; Hopman et al., 2007; Janzen et al., 2013; Marrie, Bernstein, et al., 2023; D. M. Miller et al., 2003; O'Mahony et al., 2022; Wu et al., 2007).

Following initial descriptive analyses in our follow-up cohorts, we observed that our primary outcomes for Objective 2A and 2B regression analyses were common (>30%). As such, the odds ratios derived from our multivariable logistic regression analyses may have overestimated the relative risk (RR) (Zhang & Yu, 1998; Zou, 2004). Upon completing the logistic regression analyses described above, we repeated the multivariable analyses for Objectives 2A and 2B using a modified Poisson regression to generate the RR and 95% CI for the associations between exposures of interest and binary outcome variables. A comparison of adjusted estimates derived from logistic and modified Poisson regression analyses (adjusted ORs vs. RRs) for Objectives 2A and 2B models are presented in Appendices C and D, respectively.

4.4.3 Sensitivity Analyses

Following preliminary investigations of mental health treatment barriers, it was observed that the only need factor captured on the NARCOMS survey was "not having symptoms now." Given the nature of this barrier, we repeated the multivariable regression analyses described for Objectives 1B, 2A and 2B while excluding untreated participants whose only reported treatment barrier in 2011 was need factors (Objective 1B: depression cohort: [229/545], anxiety cohort: [191/388]; Objective 2A: depression cohort: [200/451], anxiety cohort: [157/313]; Objective 2B: depression cohort: [190/423], anxiety cohort: [153/300]). Adjusted odds ratios derived from sensitivity analyses were compared with those of our original models. These sensitivity analyses allowed us to identify changes in the magnitude and/or direction of associations between exposure(s) of interest and model covariates with binary outcome variables.

In addition, multivariable regression analyses in Objectives 2A and 2B were repeated without adjusting for baseline scores (i.e., Spring 2011 NARCOMS Depression score was excluded from Objective 2A models; Spring 2011 MCS-12 score was excluded from Objective 2B mental HRQOL models; Spring 2011 PCS-12 score was excluded from Objective 2B physical HRQOL models). Though adjusting for baseline is the preferred methodological approach, these sensitivity analyses allowed us to examine the results of multivariable regression analyses without the influence of baseline scores.

Sensitivity analyses for Objective 1B models are presented in Results, Section 5.1.5. Sensitivity analyses for Objective 2A and 2B models are presented in Appendices C and D, respectively.

4.5 Ethics, Data Access & Funding

This project was approved by the Clinical Research Ethics Board at the University of Waterloo on January 18, 2023 (ORE #44857) (renewed on December 18, 2023). A research proposal and request for de-identified NARCOMS Spring 2011 and 2012 data was submitted to the registry in November 2022; approval was granted by NARCOMS in December 2022. The NARCOMS Data Center provided this research team (Lucie Lundenberg and Dr. Colleen Maxwell) with an initial dataset for the requested baseline and follow-up measures in January 2023. Upon noticing initial issues, the NARCOMS Data Center provided a revised dataset in February 2023.

To maintain the confidentiality of registry participants, the NARCOMS Data Centre assigned each respondent a unique, randomized screening ID. No direct identifiers (no specific dates of birth or zip codes) were provided to this research team. All NARCOMS data were stored in a secure data encryption drive, issued to Dr. Colleen Maxwell by the University of Waterloo, and on computers with password-protected access. Upon completing this project, all data will be destroyed or returned to the NARCOMS Data Center.

This project was funded by the University Research Chair held by Dr. Colleen Maxwell (10/2017 – 10/2024).

5.0 Results

5.1 Objective 1 – Prevalence and sociodemographic correlates of mental health treatment status among MS patients with a diagnosed mental health comorbidity.

5.1.1 Objective 1A: What proportion of the MS patient survey sample with diagnosed depression, bipolar disorder and/or anxiety disorder is currently receiving treatment?

The distribution of baseline characteristics among NARCOMS Spring 2011 respondents is presented in Table 1. Only select sociodemographic, clinical and MS characteristics were provided for analysis among all NARCOMS Spring 2011 respondents; a comprehensive distribution of baseline characteristics among participants diagnosed with a mental health comorbidity is provided in Objective 1B. The prevalence of mental health comorbidities and treatment status of respondents are presented in Table 2 and Figure 3. A comparison of baseline characteristics among NARCOMS Spring 2011 respondents with a diagnosis of depression or anxiety and those without a diagnosed mental health comorbidity are presented in Tables 3.1 and 3.2, respectively.

Total NARCOMS Spring 2011 Sample (Table 1) – Among all NARCOMS Spring 2011 respondents, the mean age was 56.1 (SD 10.5) years, and the majority resided in the United States (99.3%), were female (77.9%) and identified as White (89.3%). Respondents most commonly reported excellent/very good/good self-rated health (69.6%), minimal cognitive impairment (54.8%), minimal pain (50.6%), moderate fatigue (47.4%), and severe disability (37.8%). Respondents tended to have a moderate disease duration (42.4% with a duration of 11–20 years), and 43.9% had been enrolled in NARCOMS for at least a decade (2000 or earlier).

Mental Health Comorbidities (Table 2) – Among all NARCOMS Spring 2011 survey respondents, 40.2% reported having been diagnosed with a mental health comorbidity by a health professional. Depression was the most prevalent mental health comorbidity overall (36.8%, 3589/9765) and among those diagnosed with one or more mental health comorbidities (91.4%, 3589/3928). Anxiety and bipolar disorder were less prevalent overall (15.2% and 2.0%, respectively) and among those diagnosed with one or more mental health comorbidities (37.9% [1487/3928] and 5.0% [196/3928], respectively).

Among respondents with a diagnosed mental health comorbidity, respondents diagnosed with anxiety or bipolar disorder had a higher proportion who reported not receiving treatment at the time of the Spring 2011 survey (26.1% and 23.5%, respectively) (Table 2 and Figure 3).

Respondents diagnosed with depression reported the lowest proportion of mental health non-treatment (15.2%). As noted in Methods Section 4.2, no additional analyses were conducted among the bipolar disorder cohort because of the small sample sizes overall and among those not receiving treatment.

Depression Cohort (Table 3.1) – Relative to those without any diagnosed mental health comorbidities, respondents diagnosed with depression were more likely to be younger (mean age of 54.4 vs. 57.3 years) and female (83.4% vs. 74.3%). Respondents diagnosed with depression reported a significantly higher proportion with fair/poor self-rated health (36.9% vs. 26.3%), moderate or severe cognitive impairment (60.7% vs. 35.1%), severe fatigue (38.4% vs. 22.2%), moderate or severe pain (58.9% vs. 43%) and moderate disability (31.9% vs. 22.9%), but a significantly lower proportion with severe disability (32.8% vs. 41.5%), relative to those without any diagnosed mental health comorbidities. Respondents with depression were less likely to have an earlier year of MS onset (≤1980), more likely to have a shorter duration of MS (≤10 years) and to have a more recent year of enrollment in NARCOMS (≥2005) compared to those without any diagnosed mental health comorbidities.

Anxiety Cohort (Table 3.2) – Relative to those without any diagnosed mental health comorbidities, respondents diagnosed with anxiety were more likely to be younger (mean age of 52.2 vs. 57.3 years), female (86.9% vs. 74.3%), and People of Colour/Other (13.0% vs. 10.5%). Respondents diagnosed with anxiety reported a significantly higher proportion with fair/poor self-rated health (39.5% vs. 26.3%), moderate or severe cognitive impairment (64.1% vs. 35.1%), severe fatigue (39.0% vs. 22.2%), moderate or severe pain (62.9% vs. 43%), and moderate disability (33.6% vs. 22.9%), but a significantly lower proportion with severe disability (24.8% vs. 41.5%). Respondents diagnosed with anxiety were also more likely to have a more recent year of MS onset (≥1996), a shorter duration of MS (≤10 years) and a more recent year of enrollment in NARCOMS (≥2005) compared to those without a diagnosed mental health comorbidity.

Table 1 Distribution of baseline characteristics among NARCOMS Spring 2011 respondents (n, column%, unless otherwise noted)

Baseline Characteristics	**Total NARCOMS Spring 2011 Sample** (n= 9765)		
	n	**%**	**missing (n)**
Country of enrolment			
- USA	9620	(99.3)	79
- Other	66	(0.7)	
Year of birth			
- ≤1946	1939	(19.9)	20
- 1947–1953	2584	(26.5)	
- 1954–1959	2192	(22.5)	
- 1960–1966	1708	(17.5)	
- ≥1967	1322	(13.6)	
Age in 2011 (years)			
Mean (SD)	56.1	(10.5)	20
Sex			
- Female	7593	(77.9)	17
- Male	2155	(22.1)	
Race			
- White	8695	(89.3)	23
- People of Colour/Other	1047	(10.8)	
Self-rated health			
- Excellent/very good/good	6748	(69.6)	73
- Fair/poor	2944	(30.4)	
Cognitive impairment			
- Minimal	5243	(54.8)	198
- Moderate	3679	(38.5)	
- Severe	645	(6.7)	
Fatigue			
- Minimal	2305	(24.1)	195
- Moderate	4540	(47.4)	
- Severe	2725	(28.5)	
Pain			
- Minimal	4856	(50.6)	162
- Moderate	3459	(36.0)	
- Severe	1288	(13.4)	
Disability (PDDS)			
- Mild	3427	(35.8)	194
- Moderate	2523	(26.4)	
- Severe	3621	(37.8)	
Year of MS onset			
- ≤ 1980	2935	(30.7)	202
- 1981–1985	1296	(13.6)	
- 1986–1990	1552	(16.2)	
- 1991–1995	1527	(16.0)	
- ≥1996	2253	(23.6)	
Disease duration in 2011 (years)			
- ≤10	2493	(25.9)	134
- 11–20	4087	(42.4)	
- ≥21	3051	(31.7)	
Year of enrolment in NARCOMS			
- ≤2000	4278	(43.9)	17
- 2001–2004	2875	(29.5)	
- ≥2005	2595	(26.6)	

Abbreviations: MS – multiple sclerosis; PDDS – Patient Determined Disease Steps; SD – standard deviation; USA – United States of America.

Table 2 Prevalence of diagnosed mental health comorbidities, and corresponding treatment status, among NARCOMS Spring 2011 respondents (n, column%, unless otherwise noted)

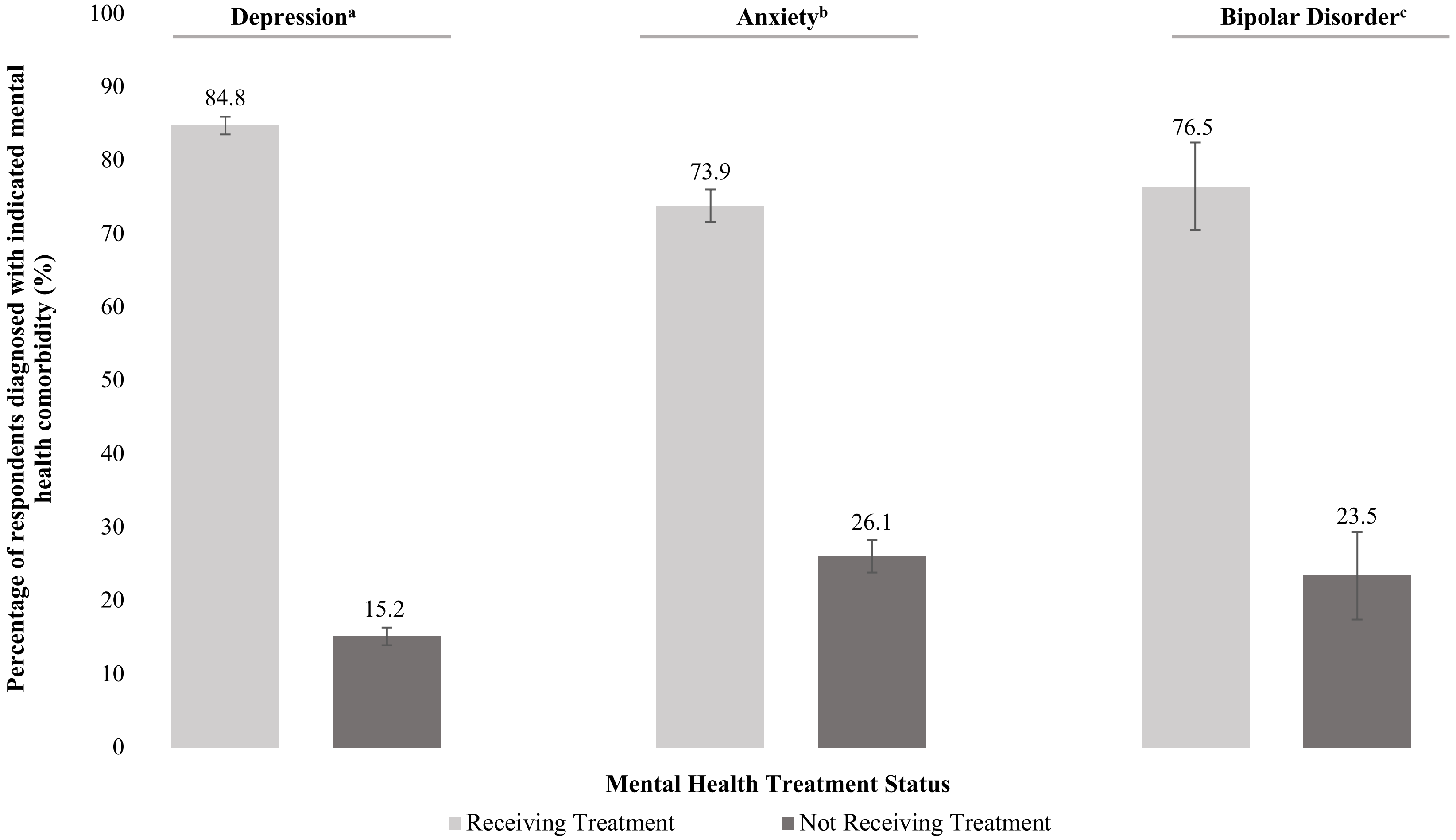
Diagnosed Mental Health Comorbidities	**NARCOMS Spring 2011 Survey Respondents**					
	Among Total Sample (n=9765)			**Among Subgroups**		
	n	%	95% CI	n	%	95% CI
No reported mental health comorbidities[a]	5813	59.5	(58.6, 60.5)			
Diagnosed with ≥1 study mental health comorbidities[b,c]	3928	40.2	(39.3, 41.2)			
- **Depression**	3589	36.8	(35.8, 37.7)			
o Receiving Treatment				3044	84.8	(83.6, 86.0)
o Not Receiving Treatment				545	15.2	(14.0, 16.4)
- **Anxiety**	1487	15.2	(14.2, 16.0)			
o Receiving Treatment				1099	73.9	(71.7, 76.1)
o Not Receiving Treatment				388	26.1	(23.9, 28.3)
- **Bipolar Disorder**	196	2.0	(1.7, 2.3)			
o Receiving Treatment				150	76.5	(70.6, 82.5)
o Not Receiving Treatment				46	23.5	(17.5, 29.4)

[a] No reported mental comorbidities includes those who did not report any mental health comorbidity, including study mental health comorbidities (depression, anxiety, bipolar disorder) and excluded mental health comorbidities (PTSD, schizophrenia). “No reported mental health comorbidities” and study mental health comorbidities are mutually exclusive.

[b] PTSD and schizophrenia were also captured on NARCOMS Spring 2011 Survey. Respondents diagnosed with at least one of these conditions without a comorbid diagnosis of depression, anxiety and/or bipolar disorder were excluded from analyses (n=24).

[c] Diagnosed mental health comorbidities (i.e., depression, anxiety, bipolar disorder) are not mutually exclusive as respondents could disclose more than one diagnosed mental health comorbidity. Respondents with more than one diagnosed mental health comorbidity are present in once in the count for each diagnosed mental health comorbidity.

Figure 3 Prevalence of mental health treatment and non-treatment among NARCOMS Spring 2011 respondents with a diagnosis of depression, anxiety and/or bipolar disorder



[a] Diagnosed with depression (n=3589).
[b] Diagnosed with anxiety (n=1487).
[c] Diagnosed with bipolar disorder (n=196).
Error bars show 95% confidence interval for estimates.

Table 3.1 Distribution of respondents' baseline characteristics, overall and by depression diagnosis, among NARCOMS Spring 2011 respondents (n, column%, unless otherwise noted)

Baseline Characteristics	**Depression Cohort**						
	Full Spring 2011 Sample (n= 9765)		**Diagnosed with Depression** (n=3589)		**No Mental Health Comorbidities**[a] (n=5813)		***p*-value**[b]
Enrolment country							
- USA	9620	(99.3)	3548	(99.1)	5728	(99.3)	0.40
- Other	66	(0.7)	31	(0.9)	41	(0.7)	
- Missing	79		10		44		
Year of birth							
- ≤1946	1939	(19.9)	478	(13.3)	1411	(24.3)	**<0.0001**
- 1947–1953	2584	(26.5)	937	(26.1)	1558	(26.8)	
- 1954–1959	2192	(22.5)	877	(24.5)	1235	(21.3)	
- 1960–1966	1708	(17.5)	744	(20.8)	888	(15.3)	
- ≥1967	1322	(13.6)	548	(15.3)	714	(12.3)	
- Missing	20		5		7		
Age in 2011 (years)							
Mean (SD)	56.1	(10.5)	54.4	(9.7)	57.3	(10.7)	**<0.0001**
- <45	1322	(13.6)	548	(15.3)	714	(12.3)	**<0.0001**
- 45–64	6484	(66.5)	2558	(71.4)	3681	(63.4)	
- ≥65	1939	(19.9)	478	(13.3)	1411	(24.3)	
- Missing	20		5		7		
Sex							
- Female	7593	(77.9)	2988	(83.4)	4317	(74.3)	**<0.0001**
- Male	2155	(22.1)	597	(16.7)	1491	(25.7)	
- Missing	17		4		5		
Race							
- White	8695	(89.3)	3181	(88.8)	5195	(89.5)	0.28
- People of Colour/Other	1047	(10.8)	402	(11.2)	610	(10.5)	
- Missing	23		6		8		
Self-rated health							
- Excellent/very good/good	6748	(69.6)	2253	(63.1)	4248	(73.7)	**<0.0001**
- Fair/poor	2944	(30.4)	1316	(36.9)	1513	(26.3)	
- Missing	73		20		52		
Cognitive impairment							
- Minimal	5243	(54.8)	1399	(39.2)	3659	(64.9)	**<0.0001**
- Moderate	3679	(38.5)	1776	(49.8)	1750	(31.0)	
- Severe	645	(6.7)	390	(10.9)	231	(4.1)	
- Missing	198		24		173		

Baseline Characteristics	**Depression Cohort**						
	Full Spring 2011 Sample (n= 9765)		**Diagnosed with Depression** (n=3589)		**No Mental Health Comorbidities**[a] (n=5813)		***p*-value**[b]
Fatigue							
- Minimal	2305	(24.1)	515	(14.4)	1703	(30.2)	**<0.0001**
- Moderate	4540	(47.4)	1683	(47.2)	2689	(47.7)	
- Severe	2725	(28.5)	1368	(38.4)	1251	(22.2)	
- Missing	195		23		170		
Pain							
- Minimal	4856	(50.6)	1472	(41.1)	3227	(57.0)	**<0.0001**
- Moderate	3459	(36.0)	1453	(40.6)	1861	(32.9)	
- Severe	1288	(13.4)	656	(18.3)	573	(10.1)	
- Missing	162		8		152		
Disability (PDDS)							
- Mild	3427	(35.8)	1259	(35.3)	2011	(35.6)	**<0.0001**
- Moderate	2523	(26.4)	1136	(31.9)	1293	(22.9)	
- Severe	3621	(37.8)	1168	(32.8)	2348	(41.5)	
- Missing	194		26		161		
Year of MS onset							
- ≤ 1980	2935	(30.7)	993	(28.2)	1846	(32.4)	**0.0004**
- 1981–1985	1296	(13.6)	519	(14.8)	739	(13.0)	
- 1986–1990	1552	(16.2)	578	(16.4)	909	(16.0)	
- 1991–1995	1527	(16.0)	594	(16.9)	882	(15.6)	
- ≥1996	2253	(23.6)	833	(23.7)	1318	(23.2)	
- Missing	202		72		119		
Disease duration in 2011 (years)							
- ≤10	2493	(25.9)	1032	(29.2)	1351	(23.5)	**<0.0001**
- 11–20	4087	(42.4)	1541	(43.5)	2403	(41.9)	
- ≥21	3051	(31.7)	966	(27.3)	1987	(34.6)	
- Missing	134		50		72		
Year of enrolment in NARCOMS							
- ≤2000	4278	(43.9)	1429	(39.9)	2705	(46.6)	**<0.0001**
- 2001–2004	2875	(29.5)	1115	(31.1)	1652	(28.4)	
- ≥2005	2595	(26.6)	1041	(29.0)	1451	(25.0)	
- Missing	17		4		5		

[a] Includes respondents who did not report a diagnosis of study mental health comorbidities (depression, anxiety, bipolar disorder) or any excluded mental health comorbidities also captured by NARCOMS Spring 2011 survey (PTSD, schizophrenia). "No mental health comorbidities" and study conditions are mutually exclusive groups.

[b] *p*-values provided for the bivariate associations between respondents with depression vs. without any reported mental health comorbidities.

Bolded estimates indicate p<0.10.

Abbreviations: MS – multiple sclerosis; PDDS – Patient Determined Disease Steps; SD – standard deviation; USA – United States of America.

Table 3.2 Distribution of respondents' baseline characteristics, overall and by anxiety diagnosis, among NARCOMS Spring 2011 respondents (n, column%, unless otherwise noted)

Baseline Characteristics	**Anxiety Cohort**						
	Full Spring 2011 Sample (n= 9765)		**Diagnosed with Anxiety** (n=1487)		**No Mental Health Comorbidities**[a] (n=5813)		***p*-value**[b]
Country of Enrolment							
- USA	9620	(99.3)	1470	(99.2)	5728	(99.3)	0.69
- Other	66	(0.7)	12	(0.8)	41	(0.7)	
- Missing	79		5		44		
Year of birth							
- ≤1946	1939	(19.9)	150	(10.1)	1411	(24.3)	**<0.0001**
- 1947–1953	2584	(26.5)	311	(21.0)	1558	(26.8)	
- 1954–1959	2192	(22.5)	358	(24.2)	1235	(21.3)	
- 1960–1966	1708	(17.5)	336	(22.7)	888	(15.3)	
- ≥1967	1322	(13.6)	327	(22.1)	714	(12.3)	
- Missing	20		5		7		
Age in 2011 (years)							
Mean (SD)	56.1	(10.5)	52.2	(10.2)	57.3	(10.7)	**<0.0001**
- <45	1322	(13.6)	327	(22.1)	714	(12.3)	**<0.0001**
- 45–64	6484	(66.5)	1005	(67.8)	3681	(63.4)	
- ≥65	1939	(19.9)	150	(10.1)	1411	(24.3)	
- Missing	20		5		7		
Sex							
- Female	7593	(77.9)	1288	(86.9)	4317	(74.3)	**<0.0001**
- Male	2155	(22.1)	195	(13.2)	1491	(25.7)	
- Missing	17		4		5		
Race							
- White	8695	(89.3)	1290	(87.0)	5195	(89.5)	**0.0072**
- People of Colour/Other	1047	(10.8)	192	(13.0)	610	(10.5)	
- Missing	23		5		8		
Self-rated health							
- Excellent/very good/good	6748	(69.6)	898	(60.6)	4248	(73.7)	**<0.0001**
- Fair/poor	2944	(30.4)	583	(39.5)	1513	(26.3)	
- Missing	73		6		52		
Cognitive impairment							
- Minimal	5243	(54.8)	530	(35.8)	3659	(64.9)	**<0.0001**
- Moderate	3679	(38.5)	765	(51.7)	1750	(31.0)	
- Severe	645	(6.7)	184	(12.4)	231	(4.1)	
- Missing	198		8		173		

Baseline Characteristics	**Anxiety Cohort**						
	Full Spring 2011 Sample (n= 9765)		**Diagnosed with Anxiety** (n=1487)		**No Mental Health Comorbidities**[a] (n=5813)		***p*-value**[b]
Fatigue							
- Minimal	2305	(24.1)	212	(14.3)	1703	(30.2)	**<0.0001**
- Moderate	4540	(47.4)	690	(46.7)	2689	(47.7)	
- Severe	2725	(28.5)	577	(39.0)	1251	(22.2)	
- Missing	195		8		170		
Pain							
- Minimal	4856	(50.6)	549	(37.1)	3227	(57.0)	**<0.0001**
- Moderate	3459	(36.0)	619	(41.8)	1861	(32.9)	
- Severe	1288	(13.4)	313	(21.1)	573	(10.1)	
- Missing	162		6		152		
Disability (PDDS)							
- Mild	3427	(35.8)	614	(41.6)	2011	(35.6)	**<0.0001**
- Moderate	2523	(26.4)	496	(33.6)	1293	(22.9)	
- Severe	3621	(37.8)	365	(24.8)	2348	(41.5)	
- Missing	194		12		161		
Year of MS onset							
- ≤ 1980	2935	(30.7)	340	(23.3)	1846	(32.4)	**<0.0001**
- 1981–1985	1296	(13.6)	197	(13.5)	739	(13.0)	
- 1986–1990	1552	(16.2)	247	(16.9)	909	(16.0)	
- 1991–1995	1527	(16.0)	251	(17.2)	882	(15.6)	
- ≥1996	2253	(23.6)	424	(29.1)	1318	(23.2)	
- Missing	202		28		119		
Disease duration in 2011 (years)							
- ≤10	2493	(25.9)	548	(37.6)	1351	(23.5)	**<0.0001**
- 11–20	4087	(42.4)	593	(40.7)	2403	(41.9)	
- ≥21	3051	(31.7)	316	(21.7)	1987	(34.6)	
- Missing	134		30		72		
Year of enrolment in NARCOMS							
- ≤2000	4278	(43.9)	508	(34.3)	2705	(46.6)	**<0.0001**
- 2001–2004	2875	(29.5)	435	(29.3)	1652	(28.4)	
- ≥2005	2595	(26.6)	540	(36.4)	1451	(25.0)	
- Missing	17		4		5		

[a] Includes respondents who did not report a diagnosis of study mental health comorbidities (depression, anxiety, bipolar disorder) or any excluded mental health comorbidities also captured by NARCOMS Spring 2011 survey (PTSD, schizophrenia). "No mental health comorbidities" and study conditions are mutually exclusive groups.

[b] *p*-values provided for the bivariate associations between respondents with anxiety vs. without any reported mental health comorbidities.

Bolded estimates indicate p<0.10.

Abbreviations: MS – multiple sclerosis; PDDS – Patient Determined Disease Steps; SD – standard deviation; USA – United States of America.

5.1.2 Objective 1B: What are the crude and adjusted associations between patients' sociodemographic and other key characteristics and unmet mental health needs (i.e., not receiving treatment)?

The bivariate associations between respondents' baseline characteristics (sociodemographic, clinical, MS) and mental health treatment status are presented in Tables 4.1A–C for the depression cohort and in Tables 4.2A–C for the anxiety cohort. Relevant unadjusted and adjusted odds ratios derived from logistic regression models illustrating the crude and independent associations between key baseline characteristics and mental health treatment status are presented in Tables 5.1 and 5.2 for the depression and anxiety cohorts, respectively. The associations between key sociodemographic characteristics (age [in 2011], race, education, health insurance) and baseline mental health treatment status were adjusted for marital status, NARCOMS Depression score, and disability (PDDS). Supplemental tables provide the unadjusted odds ratios for depression and anxiety non-treatment treatment for all baseline characteristics (Tables B1.A–C).

<u>Depression Cohort (Tables 4.1.A–C)</u> – Among bivariate associations, age was significantly associated with depression treatment status, with both younger (19.3% for <45 years) and older respondents (16.1% for ≥65 years) being more likely to report not receiving treatment for depression compared to those aged between 45 and 64 years (14.1%) (Table 4.1.A). People of Colour/Other (18.4% vs. 14.7% for White), those who were employed (18.6% vs 13.6% for unemployed or missing employment) and those who were uninsured (20.6% vs 12.1% with private and public health insurance) were significantly more likely to report depression non-treatment. Respondents without clinically meaningful depressive symptoms were significantly more likely to be untreated for depression relative to those with clinically meaningful depressive symptoms when assessed with either the NARCOMS Depression Scale (20.0% with vs. 12.1% without) or the CES-D20 (16.5% with vs. 13.8% without) (Table 4.1.B). Respondents who had not been admitted to an overnight healthcare facility reported a significantly higher proportion of depression non-treatment (15.8%) compared to those who had been admitted for any reason (9.3%). Respondents with better self-rated health (16.1% for excellent/very good/good vs. 13.6% for fair/poor), minimal or moderate cognitive impairment (~16% vs. 11.0% for severe), minimal fatigue (22.9% vs. 13.1% for severe), and mild disability (19.8% vs. 12.2% for severe) were significantly more likely to not receive treatment for depression. Respondents not receiving

treatment for depression showed significantly higher mean PCS-12 scores (i.e., better physical health-related quality of life) compared to those receiving treatment for depression (PCS-12: mean 39.0 vs 36.7). Respondents who developed MS symptoms at an age <25 years were significantly more likely to not receive treatment for depression (17.2%) relative to those who developed MS symptoms after 40 years of age (14.1%) (Table 4.1.C).

Anxiety Cohort (Tables 4.2.A–C) – Among those diagnosed with anxiety, those who were living in a private residence (26.8% vs. 13.1% for living with assistance), employed (31.9% vs. 23.2% for unemployed/missing) and who were uninsured (35.5% vs. 22.9% for private and public health insurance) were significantly more likely to not be receiving treatment for anxiety (Table 4.2.A). Respondents without clinically meaningful depressive symptoms were significantly more likely to be untreated for anxiety relative to those with clinically meaningful depressive symptoms when assessed with either the NARCOMS Depression Scale (33.0% with vs. 21.8% without) or the CES-D20 (29.8% with vs 23.5% without) (Table 4.2.B). Respondents who had not been admitted to an overnight healthcare facility reported a significantly higher proportion of anxiety non-treatment (27.1%) compared to those who had been admitted for any reason (17.6%). Those with better self-rated health (28.6% for excellent/very good/good vs. 22.5% for fair/poor), minimal (28.1%) or moderate cognitive impairment (26.7%) (vs. 18.5% for severe), minimal (33.0%) or moderate fatigue (28.3%) (vs. 21.1% for severe), minimal (28.8%) or moderate pain (26.2%) (vs. 20.8% for severe), and mild (29.8%) or moderate disability (26.0%) (vs. 20.3% for severe) were significantly more likely to not receive treatment for anxiety. Respondents not receiving treatment for anxiety showed significantly higher mean MCS-12 and PCS-12 scores (i.e., better mental and physical health-related quality of life) compared to those receiving treatment for anxiety (MCS-12: mean 42.0 vs. 39.0; PCS-12: mean 38.8 vs. 37.3). No MS characteristics were significantly associated with anxiety treatment status (Table 4.2.C).

Logistic Models for Depression Cohort (Table 5.1) – Among NARCOMS Spring 2011 respondents diagnosed with depression, 15.2% were not receiving treatment at the time of survey response. Adjusted analyses showed that respondents aged <45 years (adjOR=1.26, 95% CI=0.98, 1.62) and ≥65 years (adjOR=1.40, 95% CI=1.04,1.87) had significantly higher odds of depression non-treatment relative to respondents aged 45 to 64 years. People of Colour/Other had significantly higher odds of not receiving treatment for depression compared to White respondents (adjOR=1.29, 95%CI=0.97,1.72). Relative to respondents with both private and public health insurance coverage, those with only private coverage (adjOR=1.27, 95%CI=0.99,1.64), only public coverage (adjOR=1.27, 95%CI=0.96,1.68), or no health insurance coverage (uninsured) (adjOR=2.09, 95% CI=1.22, 3.57) had significantly higher odds of depression non-treatment. Respondents with clinically meaningful depression symptoms had significantly lower odds of depression non-treatment relative to those without clinically meaningful depressive symptoms (adjOR=0.55, 95% CI=0.46, 0.67). Those with moderate (adjOR=0.69, 95% CI=0.54, 0.87) or severe levels of disability (adjOR=0.62, 95% CI=0.48, 0.80) had significantly lower odds of depression non-treatment compared to those with mild disability. Education and marital status were not associated with depression treatment status in crude or adjusted analyses.

As discussed in Methods Section 4.4.2, adjusted models were informed by findings from previous literature indicating potential correlates of mental health service use among persons with MS (Buchanan et al., 2006, 2009, 2010; Marrie et al., 2009; Minden et al., 2007, 2013; Orr et al., 2018; Wu et al., 2007), as well as observations from bivariate analyses and unadjusted odds ratios. Adjusted models were built with considerations of potential collinearity among covariates.

Prior studies found lower education to be a significant correlate of untreated depression and lower mental health service use (Garcia & Finlayson, 2009; Marrie et al., 2009; Minden et al., 2013), so this variable was selected as a key exposure of interest a priori. As such, we retained education in adjusted analyses despite not showing a significant association with the untreated outcome. Though marital status was not significantly associated with depression non-treatment in either crude or adjusted analyses, we retained this variable to adjust for confounding (Minden et al., 2013). Employment was also investigated as a potential confounder for depression treatment based on findings from previous literature (Minden et al., 2013) as well as initial bivariate analyses. However, employment was not significantly associated with the outcome after adjusting for key covariates and did not provide adjustments for confounding (i.e., the estimates of other covariates were unchanged upon the addition and subsequent removal of this variable). Bivariate analyses also revealed that employment and health insurance were strongly correlated, and the addition of employment presented concerns of potential collinearity.

While sex was also considered as a potential confounder, the addition of this variable did not provide adjustment for confounding.

Logistic Models for Anxiety Cohort (Table 5.2) – Among NARCOMS Spring 2011 respondents diagnosed with anxiety, 26.1% were not receiving treatment at the time of survey response. Adjusted analyses showed that respondents aged ≥65 years had significantly higher odds of anxiety non-treatment relative to those aged 45 to 64 years (adjOR=1.59, 95%CI=1.05, 2.40). People of Colour/Other showed increased odds of anxiety non-treatment compared to White respondents in both unadjusted (OR=1.27; 95% CI=0.91,1.77) and adjusted models (adjOR=1.27, 95% CI=0.89,1.80), although neither of these estimates reached statistical significance. Respondents who had obtained an associate or technical degree (adjOR=1.56, 95% CI=1.06, 2.30) or who had a bachelor's degree (adjOR=1.36, 95% CI=0.95, 1.94) had significantly higher odds of anxiety non-treatment compared to those with a post-bachelor's degree. Respondents with only private health insurance coverage (adjOR=1.31, 95% CI=0.95, 1.80) or no health insurance (uninsured) (adjOR=1.72, 95%CI=0.89, 3.33) showed increased, but not statistically significant, odds of anxiety non-treatment relative to those with both private and public health insurance coverage. Respondents with clinically meaningful depression symptoms (vs. without, adjOR=0.61, 95% CI=0.48, 0.79) and those with severe disability (vs. mild, adjOR=0.63 95% CI=0.44, 0.89) had significantly lower odds of anxiety non-treatment.

Similar to the depression cohort, marital status was retained in the final multivariable model to adjust for confounding. Employment was tested in the adjusted models among those diagnosed with anxiety but was not retained in the final model for the same reasons discussed above (i.e., not significant and did not adjust for confounding). While bivariate associations suggested that residence was significantly associated with anxiety treatment status, this variable was not retained in the final model due to concerns about small cell sizes (particularly among those living with assistance) and the presence of a high standard error surrounding the crude estimate (0.33). Findings from bivariate analyses also revealed that residence was strongly associated with other model covariates (age, marital status, health insurance, NARCOMS Depression score, disability), so the addition of residence to adjusted analyses presented concerns of potential collinearity.

Table 4.1.A Bivariate associations between respondents’ baseline sociodemographic characteristics and depression treatment status among NARCOMS Spring 2011 respondents diagnosed with depression (n, row%, unless otherwise noted)

Baseline Sociodemographic Characteristics	**Depression Cohort**						
	Full Cohort[a] (n=3589)		**Receiving Treatment** (n=3044)		**Not Receiving Treatment** (n=545)		***p*-value**[b]
Year of birth[c]							
- ≤1946	478	(13.3)	401	(83.9)	77	(16.1)	**0.023**
- 1947–1953	937	(26.1)	813	(86.8)	124	(13.2)	
- 1954–1959	877	(24.5)	745	(85.0)	132	(15.1)	
- 1960–1966	744	(20.8)	640	(86.0)	104	(14.0)	
- ≥1967	548	(15.3)	442	(80.7)	106	(19.3)	
Age in 2011[c] (years)							
- <45	548	(15.3)	442	(80.7)	106	(19.3)	**0.0063**
- 45–64	2558	(71.4)	2198	(85.9)	360	(14.1)	
- ≥65	478	(13.3)	401	(83.9)	77	(16.1)	
Sex[d]							
- Female	2988	(83.4)	2541	(85.0)	447	(15.0)	0.49
- Male	597	(16.7)	501	(93.9)	96	(16.1)	
Race[e]							
- White	3181	(88.8)	2712	(85.3)	469	(14.7)	**0.054**
- People of Colour/Other	402	(11.2)	328	(81.6)	74	(18.4)	
Marital status[f]							
- Married/cohabitating	2358	(66.5)	2002	(84.9)	356	(15.1)	0.76
- Single/living alone	1188	(33.5)	1004	(84.5)	184	(15.5)	
Residence[g]							
- Private residence	3319	(93.6)	2809	(84.6)	510	(15.4)	0.47
- Living with assistance	228	(6.4)	197	(86.4)	31	(13.6)	
Education[h]							
- Secondary School/GED	1101	(31.3)	939	(85.3)	162	(14.7)	0.89
- Associate/Technical Degree	641	(18.2)	547	(85.3)	94	(14.7)	
- Bachelor’s	1009	(28.7)	852	(84.4)	157	(15.6)	
- Post Bachelor’s	767	(21.8)	646	(84.2)	121	(15.8)	
Income							
- <$30,000	935	(26.1)	791	(84.6)	144	(15.4)	0.44
- $30,000–$50,000	638	(17.8)	551	(86.4)	87	(13.6)	
- $50,001–$100,000	893	(24.9)	766	(85.8)	127	(14.2)	
- > $100,000	440	(12.3)	367	(83.4)	73	(16.7)	
- Unanswered/missing	683	(19.0)	569	(83.3)	114	(16.7)	
Employment							
- Employed	1146	(31.9)	933	(81.4)	213	(18.6)	**0.0001**

Baseline Sociodemographic Characteristics	**Depression Cohort**						
	Full Cohort[a] (n=3589)		**Receiving Treatment** (n=3044)		**Not Receiving Treatment** (n=545)		***p*-value**[b]
- Unemployed/missing	2443	(68.1)	2111	(86.5)	332	(13.6)	
Health insurance[i]							
- Private	1511	(42.1)	1251	(82.8)	260	(17.2)	**0.0011**
- Private and public	1139	(31.7)	1001	(87.9)	138	(12.1)	
- Public	813	(22.7)	692	(85.1)	121	(14.9)	
- Uninsured	126	(3.5)	100	(79.4)	26	(20.6)	

[a] Full depression cohort; column %.
[b] *p*-values provided for the bivariate associations between treatment subgroups.
[c] Year of birth and Age in 2011 (missing n=5).
[d] Sex (missing n=4).
[e] Race (missing n=6).
[f] Marital status (missing n=43).
[g] Residence (missing n=42).
[h] Education (missing n=71).
[i] Health insurance (n=0).
Bolded estimates indicate p<0.10.
Abbreviations: GED – General Educational Development.

Table 4.1.B Bivariate associations between respondents' clinical characteristics and depression treatment status among NARCOMS Spring 2011 respondents with diagnosed with depression (n, row%, unless otherwise noted)

Baseline Clinical Characteristics	**Depression Cohort**						
	Full Cohort[a] (n=3589)		**Receiving Treatment** (n=3044)		**Not Receiving Treatment** (n=545)		*p*-value[b]
NARCOMS Depression score[c]							
- <2	1384	(38.7)	1107	(80.0)	277	(20.0)	**<0.0001**
- ≥2	2193	(61.3)	1927	(87.9)	266	(12.1)	
CES-D20 score[d]							
- <16	1567	(46.3)	1308	(83.5)	259	(16.5)	**0.026**
- ≥16	1815	(53.7)	1565	(86.2)	250	(13.8)	
Admission to overnight healthcare facility[e]							
- Yes	346	(9.6)	314	(90.8)	32	(9.3)	**0.0012**
- No	3243	(90.4)	2730	(84.2)	513	(15.8)	
Self-rated health[f]							
- Excellent/very good/good	2255	(63.2)	1890	(83.9)	363	(16.1)	**0.044**
- Fair/poor	1316	(36.9)	1137	(86.4)	179	(13.6)	
Cognitive impairment[g]							
- Minimal	1399	(39.2)	1175	(84.0)	224	(16.0)	**0.047**
- Moderate	1776	(49.8)	1500	(84.5)	276	(15.6)	
- Severe	390	(10.9)	347	(89.0)	43	(11.0)	
Fatigue[h]							
- Minimal	515	(14.4)	397	(77.1)	118	(22.9)	**<0.0001**
- Moderate	1683	(47.2)	1436	(85.3)	247	(14.7)	
- Severe	1368	(38.4)	1189	(86.9)	179	(13.1)	
Pain[i]							
- Minimal	1472	(41.1)	1228	(83.4)	244	(16.6)	0.14
- Moderate	1453	(40.6)	1243	(85.6)	210	(14.5)	
- Severe	656	(18.3)	566	(86.3)	90	(13.7)	
Disability[j] (PDDS)							
- Mild	1259	(35.3)	1010	(80.2)	249	(19.8)	**<0.0001**
- Moderate	1136	(31.9)	986	(86.8)	150	(13.2)	
- Severe	1168	(32.8)	1026	(87.8)	142	(12.2)	
MCS-12[k] (mean, SD)	41.2	(11.5)	41.1	(11.5)	41.7	(11.4)	**0.25**
PCS-12[k] (mean, SD)	37.1	(11.1)	36.7	(11.0)	39.0	(11.6)	**<0.0001**

[a] Full depression cohort; column %.

[b] p-values provided for the bivariate associations between treatment subgroups.

[c] NARCOMS Depression score (missing n=12). [d] CES-D20 score – only includes those with all 20 responses (missing n=207). [e] Admission to overnight healthcare facility (missing n=0). [f] Self-rated health (missing n=20). [g] Cognitive impairment (missing n=24). [h] Fatigue (missing n=23). [i] Pain (missing n=8). [j] Disability (PDDS) (missing n=26). [k]MCS-12 and PCS-12 (missing n=119). Bolded estimates indicate p<0.10. Abbreviations: CES-D20 – Centre for Epidemiological Studies Depression Scale; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; PCS – Physical Component Score; PDDS – Patient Determined Disease Step; SD – standard deviation.

Table 4.1.C Bivariate associations between respondents’ baseline MS characteristics and depression treatment status among NARCOMS Spring 2011 respondents diagnosed with depression (n, row%, unless otherwise noted)

Baseline MS Characteristics	**Depression Cohort**						
	Full Cohort[a] (n=3589)		**Receiving Treatment** (n=3044)		**Not Receiving Treatment** (n=545)		***p*-value**[b]
Age of MS symptom onset[c] (years)							
- < 25	1077	(30.6)	892	(82.8)	185	(17.2)	**0.083**
- 25–39	1809	(51.4)	1550	(85.7)	259	(14.3)	
- ≥ 40	632	(18.0)	543	(85.9)	89	(14.1)	
Year of MS onset[d]							
- ≤ 1980	993	(28.2)	838	(84.4)	155	(15.6)	0.58
- 1981–1985	519	(14.8)	453	(87.3)	66	(12.7)	
- 1986–1990	578	(16.4)	486	(84.1)	92	(16.1)	
- 1991–1995	594	(16.9)	502	(84.5)	92	(15.5)	
- ≥1996	833	(23.7)	706	(84.8)	127	(15.3)	
Age at MS diagnosis[e] (years)							
- <30	671	(19.0)	557	(83.0)	114	(17.0)	0.49
- 30–39	1241	(35.1)	1061	(85.5)	180	(14.5)	
- 40–49	1190	(33.6)	1016	(85.4)	174	(14.6)	
- ≥50	437	(12.4)	372	(85.1)	65	(14.9)	
Year of MS diagnosis[f]							
- ≤1990	966	(27.3)	831	(86.0)	135	(14.0)	0.55
- 1991–1995	652	(18.4)	554	(85.0)	98	(15.0)	
- 1996–2000	890	(25.1)	758	(85.2)	132	(14.8)	
- ≥2001	1032	(29.2)	864	(83.7)	168	(16.3)	
Disease duration[g] (years)							
- ≤10	1032	(29.1)	864	(83.7)	168	(16.3)	0.35
- 11–20	1543	(43.6)	1311	(85.1)	230	(14.9)	
- ≥21	966	(27.3)	831	(86.0)	135	(14.0)	

[a] Full depression cohort; column %.
[b] p-values provided for the bivariate associations between treatment subgroups.
[c] Age of MS symptom onset (missing n=71).
[d] Year of MS onset (missing n=72).
[e] Age of MS diagnosis (missing n=50).
[f] Year of MS diagnosis (missing n=49).
[g] Disease duration (missing n=50).
Bolded estimates indicate $p<0.10$.
Abbreviations: MS – multiple sclerosis.

Table 4.2.A Bivariate associations between respondents' baseline sociodemographic characteristics and anxiety treatment status among NARCOMS Spring 2011 respondents diagnosed with anxiety (n, row%, unless otherwise noted)

Baseline Sociodemographic Characteristics	**Anxiety Cohort**						
	Full Cohort[a] (n=1487)		**Receiving Treatment** (n=1099)		**Not Receiving Treatment** (n=388)		***p*-value**[b]
Year of birth[c]							
- ≤1946	150	(10.1)	103	(68.7)	47	(31.3)	0.42
- 1947–1953	311	(21.0)	238	(76.5)	73	(23.5)	
- 1954–1959	358	(24.2)	268	(74.9)	90	(25.1)	
- 1960–1966	336	(22.7)	243	(72.3)	93	(27.7)	
- ≥1967	327	(22.1)	243	(74.3)	84	(25.7)	
Age in 2011[c] (years)							
- <45	327	(22.1)	243	(74.3)	84	(25.7)	0.31
- 45–64	1005	(67.8)	749	(74.5)	256	(25.5)	
- ≥65	150	(10.1)	103	(68.7)	47	(31.3)	
Sex[d]							
- Female	1288	(86.9)	946	(73.5)	342	(26.6)	0.30
- Male	195	(13.2)	150	(76.9)	45	(23.1)	
Race[e]							
- White	1290	(87.0)	962	(74.6)	328	(25.4)	0.16
- People of Colour/Other	192	(13.0)	134	(69.8)	58	(30.2)	
Marital status[f]							
- Married/cohabitating	961	(65.5)	705	(73.4)	256	(26.6)	0.32
- Single/living alone	507	(34.5)	384	(75.7)	123	(24.3)	
Residence[g]							
- Private residence	1380	(94.3)	1010	(73.2)	370	(26.8)	**0.0054**
- Living with assistance	84	(5.7)	73	(86.9)	11	(13.1)	
Education[h]							
- Secondary School/GED	473	(32.5)	354	(74.8)	119	(25.2)	0.25
- Associate/Technical Degree	280	(19.2)	198	(70.7)	82	(29.3)	
- Bachelor's	406	(27.9)	294	(72.4)	112	(27.6)	
- Post Bachelor's	297	(20.4)	230	(77.4)	67	(22.6)	
Income							
- <$30,000	405	(27.2)	304	(75.1)	101	(24.9)	0.46
- $30,000–$50,000	265	(17.8)	201	(75.9)	64	(24.2)	
- $50,001–$100,000	345	(23.2)	260	(75.4)	85	(24.6)	
- > $100,000	188	(12.6)	133	(70.7)	55	(29.3)	
- Unanswered/missing	284	(19.1)	201	(70.8)	83	(29.2)	
Employment							
- Employed	499	(33.6)	340	(68.1)	159	(31.9)	**0.0003**

Baseline Sociodemographic Characteristics	**Anxiety Cohort**						
	Full Cohort[a] (n=1487)		**Receiving Treatment** (n=1099)		**Not Receiving Treatment** (n=388)		***p*-value**[b]
- Unemployed/missing	988	(66.4)	759	(76.8)	229	(23.2)	
Health insurance[i]							
- Private	633	(42.6)	449	(70.9)	184	(29.1)	**0.021**
- Private and public	446	(30.0)	344	(77.1)	102	(22.9)	
- Public	346	(23.3)	266	(76.9)	80	(23.1)	
- Uninsured	62	(4.2)	40	(64.5)	22	(35.5)	

[a] Full anxiety cohort; column %.
[b] p-values provided for the bivariate associations between treatment subgroups.
[c] Year of birth and Age in 2011 (missing n=5)
[d] Sex (missing n=4).
[e] Race (missing n=5).
[f] Marital status (missing n=19).
[g] Residence (missing n=23).
[h] Education (missing n=31)
[i] Health insurance (n=0).
Bolded estimates indicate p<0.10.
Abbreviations: GED – General Educational Development.

Table 4.2.B Bivariate associations between respondents' baseline clinical characteristics and anxiety treatment status among NARCOMS Spring 2011 respondents diagnosed with anxiety (n, row%, unless otherwise noted)

Baseline Clinical Characteristics	**Anxiety Cohort**						
	Full Cohort[a] (n=1487)		**Receiving Treatment** (n=1099)		**Not Receiving Treatment** (n=388)		***p*-value**[b]
NARCOMS Depression score[c]							
- <2	570	(38.4)	382	(67.0)	188	(33.0)	**<0.0001**
- ≥2	914	(61.6)	715	(78.2)	199	(21.8)	
CES-D20 score[d]							
- <16	611	(43.7)	492	(70.2)	182	(29.8)	**0.0081**
- ≥16	787	(56.3)	602	(76.5)	185	(23.5)	
Admission to overnight healthcare facility[e]							
- Yes	159	(10.7)	131	(82.4)	28	(17.6)	**0.010**
- No	1328	(89.3)	968	(72.9)	360	(27.1)	
Self-rated health[f]							
- Excellent/very good/good	898	(60.6)	641	(71.4)	257	(28.6)	**0.0086**
- Fair/poor	583	(39.4)	452	(77.5)	131	(22.5)	
Cognitive impairment[g]							
- Minimal	530	(35.8)	381	(71.9)	149	(28.1)	**0.034**
- Moderate	765	(51.7)	561	(73.3)	204	(26.7)	
- Severe	184	(12.4)	150	(81.5)	34	(18.5)	
Fatigue[h]							
- Minimal	212	(14.3)	142	(67.0)	70	(33.0)	**0.0008**
- Moderate	690	(46.7)	495	(71.7)	195	(28.3)	
- Severe	577	(39.0)	455	(78.9)	122	(21.1)	
Pain[i]							
- Minimal	549	(37.1)	391	(71.2)	158	(28.8)	**0.0036**
- Moderate	619	(41.8)	457	(73.8)	162	(26.2)	
- Severe	313	(21.1)	248	(79.2)	65	(20.8)	
Disability[j] (PDDS)							
- Mild	614	(41.6)	431	(70.2)	183	(29.8)	**0.0046**
- Moderate	496	(33.6)	367	(74.0)	129	(26.0)	
- Severe	365	(24.8)	291	(79.7)	74	(20.3)	
MCS-12[k] (mean, SD)	39.8	(11.4)	39.0	(11.4)	42.0	(11.0)	**<0.0001**
PCS-12[k] (mean, SD)	37.7	(11.6)	37.3	(11.5)	38.8	(11.7)	**0.028**

[a] Full anxiety cohort; column %.

[b] p-values provided for the bivariate associations between treatment subgroups.

[c] NARCOMS Depression score (missing n=3). [d] CES-D20 score – only includes those with all 20 responses (missing n=89). [e] Admission to overnight healthcare facility (missing n=0). [f] Self-rated health (missing n=6). [g] Cognitive impairment (missing n=8). [h] Fatigue (missing n=8). [i] Pain (missing n=6) [j] Disability (PDDS) (missing n=12). [k] MCS-12 and PCS-12 (missing n=44). Bolded estimates indicate p<0.10. Abbreviations: CES-D20 – Centre for Epidemiological Studies Depression Scale; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; PCS – Physical Component Score; PDDS – Patient Determined Disease Step; SD – standard deviation.

Table 4.2.C Bivariate associations between respondents' baseline MS characteristics and anxiety treatment status among NARCOMS Spring 2011 respondents diagnosed with anxiety (n, row%, unless otherwise noted)

Baseline MS Characteristics	**Anxiety Cohort**						
	Full Cohort[a] (n=1487)		**Receiving Treatment** (n=1099)		**Not Receiving Treatment** (n=388)		*p*-**value**[b]
Age of MS symptom onset[c] (years)							
- < 25	472	(32.4)	337	(71.4)	135	(28.6)	0.15
- 25–39	741	(50.8)	549	(74.1)	192	(25.9)	
- ≥ 40	246	(16.9)	192	(78.1)	54	(22.0)	
Year of MS onset[d]							
- ≤ 1980	340	(23.3)	244	(71.8)	96	(28.2)	0.34
- 1981–1985	197	(13.5)	150	(76.1)	47	(23.9)	
- 1986–1990	247	(16.9)	173	(70.0)	74	(30.0)	
- 1991–1995	251	(17.2)	192	(79.5)	59	(23.5)	
- ≥1996	424	(29.1)	319	(75.2)	105	(24.8)	
Age at MS diagnosis[e] (years)							
- <30	315	(21.6)	229	(72.7)	86	(27.3)	0.89
- 30–39	501	(34.4)	371	(74.1)	130	(26.0)	
- 40–49	477	(32.7)	357	(74.8)	120	(25.2)	
- ≥50	164	(11.3)	119	(72.6)	45	(27.4)	
Year of MS diagnosis[f]							
- ≤1990	316	(21.7)	232	(73.4)	84	(26.6)	0.78
- 1991–1995	229	(15.7)	167	(72.9)	62	(27.1)	
- 1996–2000	365	(25.0)	265	(72.6)	100	(27.4)	
- ≥2001	548	(37.6)	413	(75.4)	135	(24.6)	
Disease duration[g] (years)							
- ≤10	548	(37.6)	413	(75.4)	135	(24.6)	0.58
- 11–20	593	(40.7)	431	(72.7)	162	(27.3)	
- ≥21	316	(21.7)	232	(73.4)	84	(26.6)	

[a] Full anxiety cohort; column %.
[b] p-values provided for the bivariate associations between treatment subgroups.
[c] Age of MS symptom onset (missing n=28).
[d] Year of MS onset (missing n=28).
[e] Age of MS diagnosis (missing n=30).
[f] Year of MS diagnosis (missing n=29)
[g] Disease duration (missing n=30).
Bolded estimates indicate p<0.10.
Abbreviations: MS – multiple sclerosis.

Table 5.1 Unadjusted and adjusted associations between respondents' baseline characteristics and not receiving treatment for depression among NARCOMS Spring 2011 respondents diagnosed with depression

Baseline Characteristics	**Depression Cohort** (n=3589) Not Receiving Treatment for Depression						
	Not Treated	**Unadjusted**			**Adjusted**[a]		
	%	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Age in 2011 (years)							
- <45	19.3	1.47	(1.15, 1.86)	**0.0018**	1.26	(0.98, 1.62)	**0.069**
- 45–64	14.1	1.0			1.0		
- ≥65	16.1	1.17	(0.90, 1.53)	0.25	1.40	(1.04, 1.87)	**0.027**
Race							
- White	14.7	1.0			1.0		
- People of Colour/Other	18.4	1.31	(1.00, 1.71)	**0.054**	1.29	(0.97, 1.72)	**0.075**
Marital status							
- Married/cohabitating	15.1	1.0			1.0		
- Single/living alone	15.5	1.03	(0.85, 1.25)	0.76	1.06	(0.86, 1.30)	0.58
Education							
- Secondary School/GED	14.7	0.92	(0.71, 1.19)	0.53	1.02	(0.78, 1.34)	0.87
- Associate/Technical Degree	14.7	0.92	(0.69, 1.23)	0.56	1.01	(0.75, 1.37)	0.93
- Bachelor's Degree	15.6	0.98	(0.76, 1.27)	0.90	1.02	(0.78, 1.32)	0.91
- Post Bachelor's Degree	15.8	1.0			1.0		
Health insurance							
- Private	17.2	1.51	(1.21, 1.88)	**0.0003**	1.27	(0.99, 1.64)	**0.064**
- Private and public	12.1	1.0			1.0		
- Public	14.9	1.27	(0.98, 1.65)	**0.076**	1.27	(0.96, 1.68)	**0.096**
- Uninsured	20.6	1.89	(1.83, 3.01)	**0.0077**	2.09	(1.22, 3.57)	**0.0070**
NARCOMS Depression score							
- <2	20.0	1.0			1.0		
- ≥2	12.1	0.55	(0.46, 0.66)	**<0.0001**	0.55	(0.46, 0.67)	**<0.0001**
Disability (PDDS)							
- Mild	19.8	1.0			1.0		
- Moderate	13.2	0.62	(0.50, 0.77)	**<0.0001**	0.69	(0.54, 0.87)	**0.0015**
- Severe	12.2	0.56	(0.45, 0.70)	**<0.0001**	0.62	(0.48, 0.80)	**0.0002**

[a] Adjusted for all variables listed in above table; missing n=149.
Bolded estimates indicate p<0.10.
Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table 5.2 Unadjusted and adjusted associations between respondents' baseline characteristics and not receiving treatment for anxiety among NARCOMS Spring 2011 respondents diagnosed with anxiety

Baseline Characteristics	**Anxiety Cohort** (n=1487) Not Receiving Treatment for Anxiety						
	Not Treated	**Unadjusted**			**Adjusted**^{a}		
	%	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Age in 2011 (years)							
- <45	25.7	1.01	(0.76, 1.34)	0.94	0.88	(0.65, 1.20)	0.42
- 45–64	25.5	1.0			1.0		
- ≥65	31.3	1.34	(0.92, 1.94)	0.13	1.59	(1.05, 2.40)	**0.029**
Race							
- White	25.4	1.0			1.0		
- People of Colour/Other	30.2	1.27	(0.91, 1.77)	0.16	1.27	(0.89, 1.80)	0.19
Marital status							
- Married/cohabitating	26.6	1.0			1.0		
- Single/living alone	24.3	0.88	(0.69, 1.13)	0.32	0.95	(0.73, 1.23)	0.69
Education							
- Secondary School/GED	25.2	1.15	(0.82, 1.63)	0.41	1.25	(0.87, 1.79)	0.23
- Associate/Technical Degree	29.3	1.42	(0.98, 2.07)	**0.066**	1.56	(1.06, 2.30)	**0.025**
- Bachelor's Degree	27.6	1.31	(0.92, 1.85)	0.13	1.36	(0.95, 1.94)	**0.094**
- Post Bachelor's Degree	22.7	1.0			1.01		
Health insurance							
- Private	29.1	1.38	(1.05, 1.83)	**0.023**	1.31	(0.95, 1.80)	0.10
- Private and public	22.9	1.0			1.0		
- Public	23.1	1.01	(0.73, 1.42)	**0.93**	1.13	(0.79, 1.62)	0.50
- Uninsured	35.5	1.86	(1.05, 3.27)	**0.032**	1.72	(0.89, 3.33)	0.11
NARCOMS Depression score							
- <2	33.0	1.0			1.0		
- ≥2	21.8	0.57	(0.45, 0.72)	**<0.0001**	0.61	(0.48, 0.79)	**0.0001**
Disability (PDDS)							
- Mild	29.8	1.0			1.0		
- Moderate	26.0	0.83	(0.64, 1.08)	0.16	0.89	(0.66, 1.19)	0.42
- Severe	20.3	0.60	(0.44, 0.82)	**0.0011**	0.63	(0.44, 0.89)	**0.0093**

[a] Adjusted for all variables listed in above table; missing n=65.
Bolded estimates indicate p<0.10.
Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

5.1.3 Objective 1C: Among those not currently receiving treatment for their diagnosed mental health comorbidity, what are the common barriers to treatment and how do these barriers vary by key sociodemographic and other characteristics of MS patient respondents?

The distribution of mental health treatment barriers reported by respondents with untreated depression or anxiety is presented in Table 6 and Figure 4. The bivariate associations between key baseline characteristics and mental health treatment barriers are provided in Tables 7A–C for predisposing, enabling, and need factors, respectively.

<u>Mental Health Treatment Barriers (Table 6)</u> – Among respondents with untreated depression, 43.1% (95% CI=39.0, 47.3) reported one or more predisposing factors, 19.5% (95% CI=16.1, 22.8) reported one or more enabling factors, and 57.4% (95% CI=53.3, 61.6) reported need factors as barriers to depression treatment. Among respondents reporting any predisposing factors, 89.7% reported that they “chose not to [receive treatment] or made a personal decision,” while 10.3% “did not know where to go to get care.” The most commonly reported enabling factors among respondents with untreated depression were: “could not afford care” (37.7%), “insurance would not approve or pay for care” (20.4%), and “problems getting to the doctor’s office” (16.0%). The only need factor captured by the survey was one of perceived need, where 57.4% of those untreated for depression cited that they were “not having symptoms now.” Of those not receiving treatment for depression, 5.7% did not report any barriers to mental health treatment.

Among respondents with untreated anxiety, 32.5% (95% CI=27.7, 37.1) reported one or more predisposing factors, 22.2% (95% CI=18.0, 26.3) reported one or more enabling factors, and 65.2% (95% CI=60.5, 70.0) reported need factors as barriers to anxiety treatment. Among respondents reporting predisposing factors, 82.1% reported that they “chose not to [receive treatment] or made a personal decision,” while 17.9% “did not know where to go to get care.” The most commonly reported enabling factors among respondents with untreated anxiety were: “could not afford care” (33.8%), “problems getting to the doctor’s office” (21.8%), and “insurance would not approve or pay for care” (19.5%). Need factors (i.e., “not having symptoms now”) were reported by 65.2% of respondents with untreated anxiety. Of those not receiving treatment for anxiety, 5.7% did not report any barriers to mental health treatment.

Predisposing Factors (Table 7A) – Among respondents with untreated depression, those who were younger (54.7% for <45 years vs. 31.2% for ≥65 years) and had lower levels of education (e.g., 48.9% for associate/technical degree vs. 33.9% for post bachelor's degree) were significantly more likely to report one or more predisposing factors. Respondents with clinically meaningful depressive symptoms (58.3% vs. 28.9% without) or severe fatigue (49.7% vs. 36.4% for minimal) were also significantly more likely to report one or more predisposing factors.

Among respondents with untreated anxiety, those with clinically meaningful depressive symptoms (38.7% vs. 26.1% without) and those with severe fatigue (41.8% vs. 25.7% for minimal) were significantly more likely to report one or more predisposing factors. While no other associations reached statistical significance among the anxiety cohort, age (in 2011) and education showed similar direction of associations as the depression cohort.

Enabling Factors (Table 7B) – Among respondents with untreated depression, respondents who were single or living alone (25.5% vs. 16.3% for married or cohabitating) and had lower levels of annual family income (e.g., 36.1% for <\$30,000 vs. 12.3% for >\$100,000) were significantly more likely to report one or more enabling factors. Respondents with a bachelor's degree were significantly less likely to report enabling factors than those with any other level of education (e.g., 12.1 % for bachelor's vs. 22.8% for secondary school/GED education). Respondents with only public health insurance (28.9%) and those who were uninsured (46.2%) were significantly more likely to report one or more enabling factors relative to those with both private and public health insurance coverages (11.6%). Respondents with clinically meaningful depressive symptoms (29.7% vs. 9.4% without), moderate (22.5%) or severe cognitive impairment (34.9%) (vs 12.5% for minimal), and severe fatigue (29.1% vs 12.7% for minimal) were also significantly more likely to report one or more enabling factors.

Among respondents with untreated anxiety, People of Colour/Other (32.8% vs. 20.4% for White) and those who were single or living alone (30.9% vs. 17.2% for married or cohabitating) were significantly more likely to report one or more enabling factors. Respondents with lower levels of education (e.g., 29.3% for associate/technical degree vs. 14.3% for bachelor's degree), those with lower levels of annual family income (e.g., 39.6% for <\$30,000 vs. 1.8% for >\$100,000), and those who were unemployed or missing employment (25.8% vs. 17.0% for employed) were significantly more likely to report one or more enabling factors. Respondents with only public health insurance (33.8%) and those who were uninsured (45.5%) were significantly more likely to report one or more enabling factors relative to those with private health insurance coverage (16.3%). Respondents with clinically meaningful depressive symptoms (32.7% vs. 11.2% without), moderate (27.9%) or severe cognitive impairment (32.4%) (vs. 12.1% for minimal), and moderate (19.0%) or severe fatigue (36.9%) (vs. 5.7% for minimal) were also significantly more likely to report one or more enabling factors.

Need Factors (Table 7C) – Among respondents with untreated depression, those with higher levels of annual family income (e.g., 64.4% for >$100,000 vs. 47.2% for <$30,000) and those who were employed (63.9% vs. 53.3% for unemployed/missing) were significantly more likely to report need factors. Those with only private health insurance (63.1%) and those with both private and public health insurance coverage (56.5%) were significantly more likely to report need factors relative to those with only public health insurance coverage (40.4%) and those who were uninsured (38.5%). Respondents without clinically meaningful depressive symptoms (80.9% vs. 33.5 with), minimal cognitive impairment (64.3% vs. 51.2% for severe), and minimal (66.1%) or moderate fatigue (64.0%) (vs. 43.0% for severe) were also significantly more likely to report need factors.

Among respondents with untreated anxiety, those who were born in earlier birth cohorts (e.g., 70.2% for ≤1946 vs. 56.0% for ≥1967), as well as those with higher levels of education (e.g., 73.1% for post bachelor’s vs. 52.1% for secondary school/GED) and annual family income (e.g., 78.2% for >$100,000 vs. 53.5% for <$30,000) were significantly more likely to report need factors. Those with only private health insurance (69.6%) and those with both private and public health insurance coverage (70.5%) were significantly more likely to report need factors relative to those with only public health insurance coverage (53.8%) and those who were uninsured (45.5%). Respondents without clinically meaningful depressive symptoms (79.8% vs. 51.3% with), with minimal cognitive impairment (73.2% vs. 58.8% for severe), and minimal (78.6%) or moderate fatigue (67.2%) (vs. 54.9% for severe) were also significantly more likely to report need factors.

Table 6 Distribution of mental health treatment barriers, by individual responses and by barrier groupings, reported by NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment (n, column%, unless otherwise noted)

Mental Health Treatment Barriers[a]	**Not Receiving Treatment for Diagnosed Mental Health Comorbidity**					
	Untreated for Depression (n=545)			**Untreated for Anxiety** (n=388)		
	Number of responses	% of summed responses for barrier grouping[b]	% of total untreated sample[c]	Number of responses	% of summed responses for barrier grouping[b]	% of total untreated sample[d]
Predisposing Factors						
- Did not know where to go to get care	25	10.3		24	17.9	
- Chose not to or personal decision	218	89.7		110	82.1	
Number of respondents reporting 1+ predisposing factors	235		43.1	126		32.5
Enabling Factors[e]						
- Could not afford care	61	37.7		45	33.8	
- Insurance would not approve or pay for care	33	20.4		26	19.5	
- Doctor refused to accept insurance plan	8	4.9		5	3.8	
- Problems getting to doctor's office	26	16.0		29	21.8	
- Could not get time off of work	6	3.7		5	3.8	
- Did not have time or took too long	17	10.5		12	9.0	
- Could not get child care	3	1.9		6	4.5	
- Was refused services	8	4.9		5	3.8	
Number of respondents reporting 1+ enabling factors	106		19.5	86		22.2
Need Factors						
- Not having symptoms now	313	100.0		253	100.0	
Number of respondents reporting 1+ need factors	313		57.4	253		65.2
No Treatment Barriers Reported	31		5.7	22		5.7

[a] Barriers to mental health treatment were not mutually exclusive as respondents were permitted to select more than one response. Respondents who selected multiple barriers across different groupings (i.e., one or more of predisposing, enabling and need factors) appeared once in the overall count for each selected barrier subgroup.

[b] Calculated by dividing the number of responses by the sum of total responses for each grouping (e.g., for predisposing factors in depression cohort: 25/(25+218)).

[c] 95% CI for estimates among untreated depression sample: predisposing factors (39.0, 47.3); enabling factors (16.1, 22.8), need factors (53.3, 61.6).

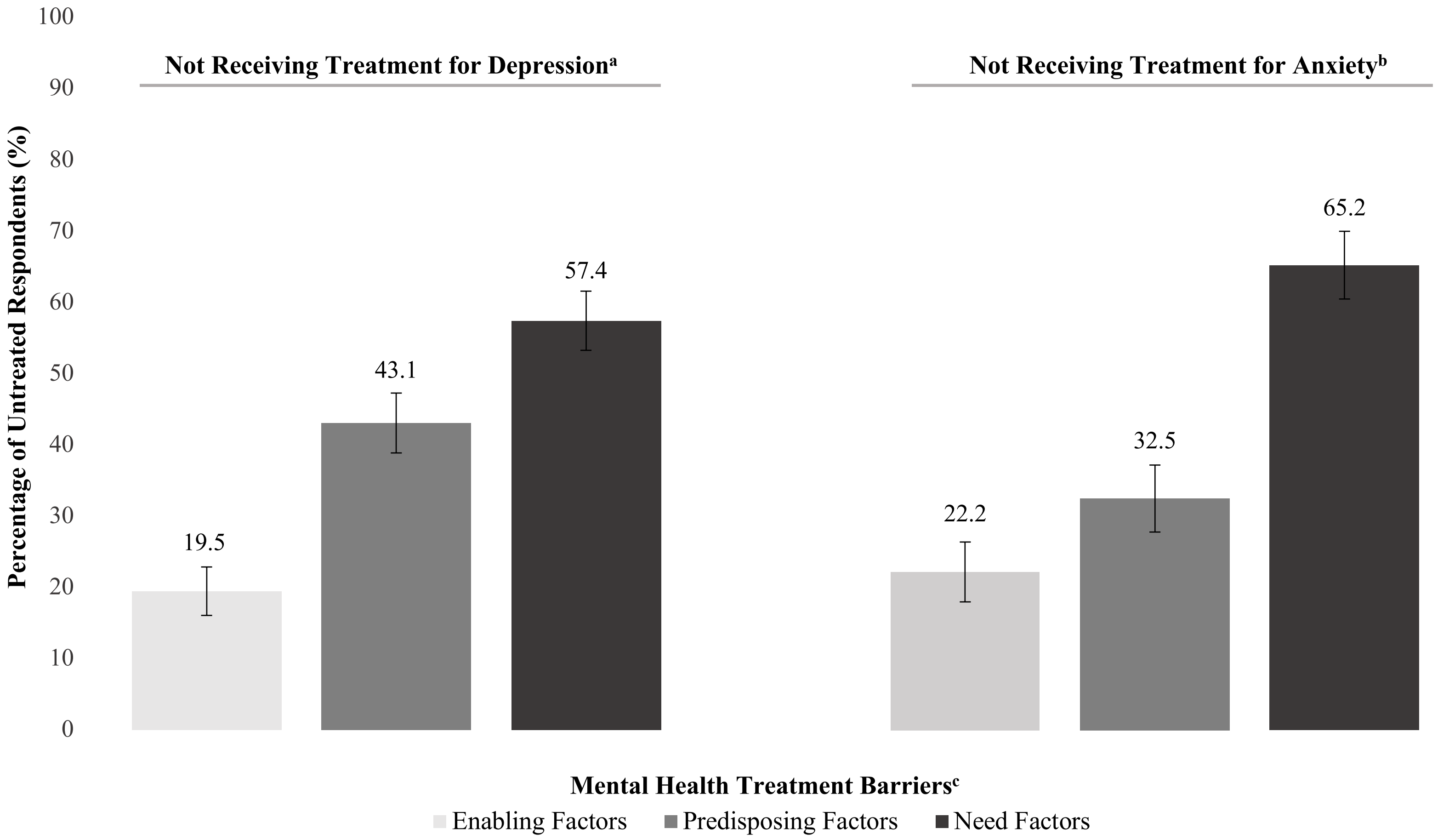
[d] 95% CI for estimates among untreated anxiety sample: predisposing factors (27.7, 37.1) enabling factors (18.0, 26.3); need factors (60.5, 70.0).

[e] Number of enabling factors reported among untreated participants: Depression cohort: 1 factor, 68.9% (73/106); 2 factors,19.8% (21/106); 3 or more factors, 11.3% (12/106); Anxiety cohort: 1 factor, 64.0%% (55/86,); 2 factors, 27.9 % (24/86,); 3 or more factors, 8.1% (7/86).

Bolded estimates indicate $p<0.10$.

Abbreviations: CI – confidence interval.

Figure 4 Distribution of mental health treatment barriers reported by NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment



[a] Among respondents diagnosed with depression, 15.2% (545/3589) were not receiving treatment.
[b] Among respondents diagnosed with anxiety, 26.1% (388/1487) were not receiving treatment.
[c] Mental health treatment barriers are not mutually exclusive as respondents were permitted to select more than one response. Respondents who selected multiple barriers across different groupings (i.e., one or more of enabling, predisposing and need factors) appeared once in the overall count for each selected barrier subgroup.
Error bars show 95% confidence interval.

Table 7.A Bivariate associations between respondents' baseline characteristics and predisposing factors among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment (n, row%, unless otherwise noted)

Baseline Characteristics[a]	**Predisposing Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=235)		None Reported[b] (n=310)		*p*-value	≥1 Reported (n=126)		None Reported[b] (n=262)		*p*-value
Year of birth										
- ≤1946	24	(31.2)	53	(68.8)	**0.010**	15	(31.9)	32	(68.1)	0.38
- 1947–1953	46	(37.1)	78	(62.9)		17	(23.3)	56	(76.7)	
- 1954–1959	56	(42.4)	76	(57.6)		30	(33.3)	60	(66.7)	
- 1960–1966	50	(48.1)	54	(51.9)		32	(34.4)	61	(65.6)	
- ≥1967	58	(54.7)	48	(45.3)		32	(38.1)	52	(61.9)	
Age in 2011 (years)										
- <45	58	(54.7)	48	(45.3)	**0.0055**	32	(38.1)	52	(61.9)	0.47
- 45–64	152	(42.2)	208	(57.8)		79	(30.9)	177	(69.1)	
- ≥65	24	(31.2)	53	(68.8)		15	(31.9)	32	(68.1)	
Sex										
- Female	190	(42.5)	257	(57.5)	0.55	109	(31.9)	233	(68.1)	0.43
- Male	44	(45.8)	52	(54.2)		17	(37.8)	28	(62.2)	
Race										
- White	206	(43.9)	263	(56.1)	0.33	106	(32.3)	222	(67.7)	0.75
- People of Colour/Other	28	(37.8)	46	(62.2)		20	(34.5)	38	(65.5)	
Marital status										
- Married/cohabitating	158	(44.4)	198	(55.6)	0.42	87	(34.0)	169	(66.0)	0.45
- Single/living alone	75	(40.8)	109	(59.2)		37	(30.1)	86	(69.9)	
Residence										
- Private residence	224	(43.9)	286	(56.1)	0.10	123	(33.3)	247	(66.8)	0.52
- Living with assistance	9	(29.0)	22	(71.0)		2	(18.2)	9	(81.8)	
Education										
- Secondary School/GED	71	(43.8)	91	(56.2)	**0.088**	45	(37.8)	74	(62.2)	0.34
- Associate/Technical Degree	46	(48.9)	48	(51.1)		27	(32.9)	55	(67.1)	
- Bachelor's Degree	74	(47.1)	83	(52.9)		34	(30.4)	78	(69.6)	
- Post Bachelor's Degree	41	(33.9)	80	(66.1)		17	(25.4)	50	(74.6)	
Income										
- <$30,000	56	(38.9)	88	(61.1)	0.76	35	(34.7)	66	(65.4)	0.94
- $30,000–$50,000	39	(44.8)	48	(55.2)		22	(34.4)	42	(65.6)	
- $50,001–$100,000	55	(43.3)	72	(56.7)		25	(29.4)	60	(70.6)	
- > $100,000	35	(48.0)	38	(52.1)		18	(32.7)	37	(67.3)	
- Unanswered/missing	50	(43.9)	64	(56.1)		26	(31.3)	57	(68.7)	

Baseline Characteristics[a]	**Predisposing Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=235)		None Reported[b] (n=310)		*p*-value	≥1 Reported (n=126)		None Reported[b] (n=262)		*p*-value
Employment										
- Employed	95	(44.6)	118	(55.4)	0.58	50	(31.5)	109	(68.6)	0.72
- Unemployed/missing	140	(42.2)	192	(57.8)		76	(33.2)	153	(66.8)	
Health insurance										
- Private	112	(43.1)	148	(56.9)	0.62	58	(31.5)	126	(68.5)	0.49
- Private and public	61	(44.2)	77	(55.8)		29	(28.4)	73	(71.6)	
- Public	54	(44.6)	67	(55.4)		31	(38.8)	49	(61.3)	
- Uninsured	8	(30.8)	18	(69.2)		8	(36.4)	14	(63.6)	
NARCOMS Depression score										
- <2	80	(28.9)	197	(71.1)	**<0.0001**	49	(26.1)	139	(73.9)	**0.0080**
- ≥2	155	(58.3)	111	(41.7)		77	(38.7)	122	(61.3)	
Cognitive impairment										
- Minimal	93	(41.5)	131	(58.5)	0.83	40	(26.9)	109	(73.2)	0.18
- Moderate	122	(44.2)	154	(55.8)		72	(35.3)	131	(64.7)	
- Severe	18	(41.9)	25	(58.1)		13	(38.2)	21	(61.8)	
Fatigue										
- Minimal	43	(36.4)	75	(63.6)	**0.059**	18	(25.7)	52	(74.3)	**0.023**
- Moderate	102	(41.3)	145	(58.7)		56	(28.7)	139	(71.3)	
- Severe	89	(49.7)	90	(50.3)		51	(41.8)	71	(58.2)	
Disability (PDDS)										
- Mild	108	(43.4)	141	(56.6)	0.95	62	(33.9)	121	(66.1)	0.38
- Moderate	66	(44.0)	84	(56.0)		36	(27.9)	93	(72.1)	
- Severe	60	(42.3)	82	(57.8)		27	(36.5)	47	(63.5)	
Age of MS symptom onset (years)										
- < 25	75	(40.5)	110	(59.5)	0.54	48	(35.6)	87	(64.4)	0.44
- 25–39	118	(45.6)	141	(54.4)		63	(32.8)	129	(67.2)	
- ≥ 40	37	(41.6)	52	(58.4)		14	(25.9)	40	(74.1)	

[a] Relevant baseline characteristics include all sociodemographic variables, and select clinical and MS variables based on the bivariate analyses and findings from the literature on potential confounders for mental health treatment among people with MS.

[b] Respondents who did not report predisposing factors includes those who selected reported enabling and/or need factors, and those who did not report any barriers.

Among both cohorts, all listed variables were missing no more than 3%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; PDDS – Patient Determined Disease Steps.

Table 7.B Bivariate associations between respondents' baseline characteristics and enabling factors among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment (n, row%, unless otherwise noted)

Baseline Characteristics[a]	**Enabling Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=106)		None Reported[b] (n=439)		*p*-value	≥1 Reported (n=86)		None Reported[b] (n=302)		*p*-value
Year of birth										
- ≤1946	10	(13.0)	67	(87.0)	0.17	9	(19.2)	38	(80.9)	0.20
- 1947–1953	18	(14.5)	106	(85.5)		14	(19.2)	59	(80.8)	
- 1954–1959	30	(22.7)	102	(77.3)		14	(15.6)	76	(84.4)	
- 1960–1966	25	(24.0)	79	(76.0)		26	(28.0)	67	(72.0)	
- ≥1967	22	(20.8)	84	(79.3)		23	(27.4)	61	(72.6)	
Age in 2011 (years)										
- <45	22	(20.8)	84	(79.3)	0.31	23	(27.4)	61	(72.6)	0.41
- 45–64	73	(20.3)	287	(79.7)		54	(21.1)	202	(78.9)	
- ≥65	10	(13.0)	67	(87.0)		9	(19.2)	38	(80.9)	
Sex										
- Female	87	(19.5)	360	(80.5)	0.87	79	(32.1)	263	(76.9)	0.25
- Male	18	(18.8)	78	(81.3)		7	(15.6)	38	(84.4)	
Race										
- White	88	(18.8)	381	(81.2)	0.39	67	(20.4)	261	(79.6)	**0.038**
- People of Colour/Other	17	(23.0)	57	(77.0)		19	(32.8)	39	(67.2)	
Marital status										
- Married/cohabitating	58	(16.3)	298	(83.7)	**0.010**	44	(17.2)	212	(82.8)	**0.0024**
- Single/living alone	47	(25.5)	137	(74.5)		38	(30.9)	85	(69.1)	
Residence										
- Private residence	101	(18.9)	409	(80.2)	0.62	81	(21.9)	289	(78.1)	1.0
- Living with assistance	5	(16.1)	26	(83.9)		2	(18.2)	9	(81.8)	
Education										
- Secondary School/GED	37	(22.8)	125	(77.2)	**0.062**	33	(27.7)	86	(72.3)	**0.020**
- Associate/Technical Degree	19	(20.2)	75	(79.8)		24	(29.3)	58	(70.7)	
- Bachelor's Degree	19	(12.1)	138	(87.9)		16	(14.3)	96	(85.7)	
- Post Bachelor's Degree	27	(22.3)	94	(77.7)		11	(16.4)	56	(83.6)	
Income										
- <$30,000	52	(36.1)	92	(63.9)	**<0.0001**	40	(39.6)	61	(60.4)	**<0.0001**
- $30,000–$50,000	13	(14.9)	74	(85.1)		8	(12.5)	56	(87.5)	
- $50,001–$100,000	18	(14.2)	109	(85.8)		16	(18.8)	69	(81.2)	
- > $100,000	9	(12.3)	64	(87.7)		1	(1.8)	54	(98.2)	
- Unanswered/missing	14	(12.3)	100	(87.7)		21	(25.3)	62	(74.7)	

Baseline Characteristics[a]	**Enabling Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=106)		None Reported[b] (n=439)		*p*-value	≥1 Reported (n=86)		None Reported[b] (n=302)		*p*-value
Employment										
- Employed	36	(16.9)	177	(83.1)	0.23	27	(17.0)	132	(83.0)	**0.041**
- Unemployed/missing	70	(21.1)	262	(78.9)		59	(25.8)	170	(74.2)	
Health insurance										
- Private	43	(16.5)	217	(83.5)	**<0.0001**	30	(16.3)	154	(83.7)	**0.0005**
- Private and public	16	(11.6)	122	(88.4)		19	(18.6)	83	(81.4)	
- Public	35	(28.9)	86	(71.1)		27	(33.8)	53	(66.3)	
- Uninsured	12	(46.2)	14	(53.9)		10	(45.5)	12	(54.6)	
NARCOMS Depression score										
- <2	26	(9.4)	251	(90.6)	**<0.0001**	21	(11.2)	167	(89.8)	**<0.0001**
- ≥2	79	(29.7)	187	(70.3)		65	(32.7)	134	(67.3)	
Cognitive impairment										
- Minimal	28	(12.5)	196	(87.5)	**0.0005**	18	(12.1)	131	(87.9)	**0.0006**
- Moderate	62	(22.5)	214	(77.5)		57	(27.9)	147	(72.1)	
- Severe	15	(34.9)	28	(65.1)		11	(32.4)	23	(67.7)	
Fatigue										
- Minimal	15	(12.7)	103	(87.3)	**0.0003**	4	(5.7)	66	(94.3)	**<0.0001**
- Moderate	39	(15.8)	208	(84.2)		37	(19.0)	158	(81.0)	
- Severe	52	(29.1)	127	(71.0)		45	(36.9)	77	(63.1)	
Disability (PDDS)										
- Mild	50	(20.1)	199	(79.9)	0.96	36	(19.7)	147	(80.3)	0.46
- Moderate	29	(19.3)	121	(80.7)		33	(25.6)	96	(74.4)	
- Severe	27	(19.0)	115	(81.0)		17	(23.0)	57	(77.0)	
Age of MS symptom onset (years)										
- < 25	41	(22.2)	144	(77.8)	0.15	30	(22.2)	105	(77.8)	0.90
- 25–39	50	(19.3)	209	(80.7)		43	(22.4)	149	(77.6)	
- ≥ 40	11	(12.4)	78	(87.6)		11	(20.4)	44	(79.6)	

[a] Relevant baseline characteristics include all sociodemographic variables, and select clinical and MS variables based on the bivariate analyses and findings from the literature on potential confounders for mental health treatment among people with MS.

[b] Respondents who did not report enabling factors includes those who selected reported predisposing and/or need factors, and those who did not report any barriers.

Among both cohorts, all listed variables were missing no more than 3%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; PDDS – Patient Determined Disease Steps,

Table 7.C Bivariate associations between respondents' baseline characteristics and need factors among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment (n, row%, unless otherwise noted)

Baseline Characteristics[a]	**Need Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=313)		None Reported[b] (n=232)		*p*-value	≥1 Reported (n=253)		None Reported[b] (n=135)		*p*-value
Year of birth										
- ≤1946	40	(52.0)	37	(48.1)	0.28	33	(70.2)	14	(29.8)	**0.063**
- 1947–1953	77	(62.1)	47	(37.9)		50	(68.5)	23	(31.5)	
- 1954–1959	82	(62.1)	50	(37.9)		67	(74.4)	23	(26.0)	
- 1960–1966	59	(56.7)	45	(43.3)		55	(59.1)	38	(40.9)	
- ≥1967	54	(50.9)	52	(49.1)		47	(56.0)	37	(44.1)	
Age in 2011 (years)										
- <45	54	(50.9)	52	(49.1)	0.12	47	(56.0)	37	(44.1)	0.13
- 45–64	218	(60.6)	142	(39.4)		172	(67.2)	84	(32.8)	
- ≥65	40	(52.0)	37	(48.1)		33	(70.2)	14	(29.8)	
Sex										
- Female	263	(58.8)	184	(41.2)	0.16	224	(65.5)	118	(34.5)	0.66
- Male	49	(51.0)	47	(49.0)		28	(62.2)	17	(37.8)	
Race										
- White	266	(56.7)	203	(43.3)	0.38	217	(66.2)	111	(33.8)	0.27
- People of Colour/Other	46	(62.2)	28	(37.8)		34	(58.6)	24	(41.4)	
Marital status										
- Married/cohabitating	211	(59.3)	145	(40.7)	0.22	166	(64.8)	90	(35.2)	0.51
- Single/living alone	99	(53.8)	85	(46.2)		84	(68.3)	39	(31.7)	
Residence										
- Private residence	294	(57.7)	216	(42.4)	0.51	242	(65.4)	128	(34.6)	0.34
- Living with assistance	16	(51.6)	15	(48.4)		9	(81.8)	2	(18.2)	
Education										
- Secondary School/GED	85	(52.5)	77	(47.5)	0.28	62	(52.1)	57	(47.9)	**0.0021**
- Associate/Technical Degree	52	(55.3)	42	(44.7)		53	(64.6)	29	(35.4)	
- Bachelor's Degree	98	(62.4)	59	(37.6)		84	(74.1)	29	(25.9)	
- Post Bachelor's Degree	73	(60.3)	48	(39.7)		49	(73.1)	18	(26.9)	
Income										
- <$30,000	68	(47.2)	76	(52.8)	**0.020**	54	(53.5)	47	(46.5)	**0.010**
- $30,000–$50,000	59	(67.8)	28	(32.2)		48	(75.0)	16	(25.0)	
- $50,001–$100,000	75	(59.1)	52	(40.9)		56	(65.9)	29	(32.1)	
- > $100,000	47	(64.4)	26	(35.6)		43	(78.2)	12	(21.8)	
- Unanswered/missing	64	(56.1)	50	(43.9)		52	(62.7)	31	(37.4)	

Baseline Characteristics[a]	**Need Factors**									
	Not Receiving Treatment for Depression (n=545)					**Not Receiving Treatment for Anxiety** (n=388)				
	≥1 Reported (n=313)		None Reported[b] (n=232)		*p*-value	≥1 Reported (n=253)		None Reported[b] (n=135)		*p*-value
Employment										
- Employed	126	(63.9)	77	(36.2)	**0.015**	109	(68.6)	50	(31.5)	0.25
- Unemployed/missing	177	(53.3)	155	(46.7)		144	(62.9)	85	(37.1)	
Health insurance										
- Private	163	(63.1)	96	(36.9)	**0.021**	128	(69.6)	56	(30.4)	**0.010**
- Private and public	78	(56.5)	60	(43.5)		72	(70.5)	30	(29.4)	
- Public	61	(40.4)	60	(49.6)		43	(53.8)	37	(46.3)	
- Uninsured	10	(38.5)	16	(61.5)		10	(45.5)	12	(54.6)	
NARCOMS Depression score										
- <2	224	(80.9)	53	(19.1)	**<0.0001**	150	(79.8)	38	(20.2)	**<0.0001**
- ≥2	89	(33.5)	177	(66.5)		102	(51.3)	97	(48.7)	
Cognitive impairment										
- Minimal	144	(64.3)	80	(35.7)	**0.031**	109	(73.2)	40	(26.7)	**0.038**
- Moderate	147	(53.3)	129	(46.7)		124	(60.8)	80	(39.2)	
- Severe	22	(51.2)	21	(48.8)		20	(58.8)	14	(41.2)	
Fatigue										
- Minimal	78	(66.1)	40	(33.9)	**<0.0001**	55	(78.6)	15	(21.4)	**0.0031**
- Moderate	158	(64.0)	89	(36.0)		131	(67.2)	64	(32.8)	
- Severe	77	(43.0)	102	(57.0)		67	(54.9)	55	(45.1)	
Disability (PDDS)										
- Mild	139	(55.8)	110	(44.2)	0.70	119	(65.0)	64	(35.0)	0.98
- Moderate	90	(60.0)	60	(40.0)		85	(65.9)	44	(34.1)	
- Severe	84	(59.2)	58	(40.9)		48	(64.9)	26	(35.1)	
Age of MS symptom onset (years)										
- < 25	106	(57.3)	79	(42.7)	0.79	82	(60.7)	53	(39.3)	0.37
- 25–39	153	(59.1)	106	(40.9)		130	(67.7)	62	(32.3)	
- ≥ 40	49	(55.1)	40	(44.9)		37	(68.5)	17	(31.5)	

[a] Relevant baseline characteristics include all sociodemographic variables, and select clinical and MS variables based on the bivariate analyses and findings from the literature on potential confounders for mental health treatment among people with MS.

[b] Respondents who did not report need factors includes those who selected reported enabling and/or predisposing factors, and those who did not report any barriers.

Among both cohorts, all listed variables were missing no more than 3%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; PDDS – Patient Determined Disease Steps

5.1.4 Objective 1D: Among those not receiving treatment for their diagnosed mental health comorbidity, how are mental health treatment barriers associated with the severity of depressive symptoms?

Table 8 presents the bivariate associations between mental health treatment barriers and the severity of depressive symptoms, using both the NARCOMS Depression Scale and the CES-D20, among respondents not receiving treatment for depression or anxiety. Figure 5 illustrates the associations between mental treatment barriers and clinically meaningful depressive symptoms using the NARCOMS Depression Scale.

<u>Depression Cohort (Table 8)</u> – Among respondents diagnosed with depression who were not receiving treatment, approximately half (49.0% [using the NARCOMS Depression Scale] and 49.1% [using the CES-D20]) reported clinically meaningful depressive symptoms. Predisposing, enabling and need factors were significantly associated with depressive symptoms when assessed with either the NARCOMS Depression Scale or the CES-D20. Respondents reporting one or more predisposing factors (66.0% vs. 36.0% with none) or enabling factors (75.2% vs. 42.7% with none) as barriers to depression treatment were significantly more likely to report clinically meaningful depressive symptoms. In contrast, those who reported need factors (28.4% vs. 77.0% with none) were significantly less likely to report clinically meaningful depressive symptoms (when assessed using the NARCOMS Depression Scale).

<u>Anxiety Cohort (Table 8)</u> – Among respondents diagnosed with anxiety who were not receiving treatment, approximately half (51.4% [using the NARCOMS Depression Scale] and 50.4% [using the CES-D20]) reported clinically meaningful depressive symptoms. Predisposing, enabling and need factors were significantly associated with depressive symptoms when assessed with either the NARCOMS Depression Scale or the CES-D20. Respondents reporting one or more predisposing factors (61.1% vs. 46.7% with none) or enabling factors (75.6% vs. 44.5% with none) as barriers to anxiety treatment were significantly more likely to report clinically meaningful depressive symptoms. In contrast, those who reported need factors (40.5% vs. 71.9% with none) were significantly less likely to report clinically meaningful depressive symptoms (when assessed using the NARCOMS Depression Scale).

Table 8 Bivariate associations between mental health treatment barriers and the severity of depressive symptoms (NARCOMS Depression Scale and CES-D20 scores) among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety who were not receiving treatment (n, row%, unless otherwise noted)

Mental Health Treatment Barriers Reported by Untreated Respondents	**Severity of Depressive Symptoms**									
	NARCOMS Depression Scale					**CES-D20[a]**				
	< 2		≥ 2		*p*-value	< 16		≥ 16		*p*-value
Not Receiving Treatment for Depression[b] (n=545)	277	(51.0)	266	(49.0)		259	(50.9)	250	(49.1)	
o 1+ Predisposing Factors										
▪ Yes	80	(34.0)	155	(66.0)	**<0.0001**	81	(36.5)	141	(63.5)	**<0.0001**
▪ No	197	(64.0)	111	(36.0)		178	(62.0)	106	(38.0)	
o 1+ Enabling Factors										
▪ Yes	26	(24.8)	79	(75.2)	**<0.0001**	21	(20.8)	80	(79.2)	**<0.0001**
▪ No	251	(57.3)	187	(42.7)		238	(58.3)	170	(41.7)	
o 1+ Need Factors										
▪ Yes	224	(71.6)	89	(28.4)	**<0.0001**	208	(70.0)	89	(30.0)	**<0.0001**
▪ No	53	(23.0)	177	(77.0)		51	(24.1)	161	(75.9)	
Not Receiving Treatment for Anxiety[c] (n=388)	188	(48.6)	199	(51.4)		182	(49.6)	185	(50.4)	
o 1+ Predisposing Factors										
▪ Yes	49	(38.9)	77	(61.1)	**0.0080**	44	(37.0)	75	(63.0)	**0.0008**
▪ No	139	(53.3)	122	(46.7)		138	(55.7)	110	(44.4)	
o 1+ Enabling Factors										
▪ Yes	21	(24.4)	65	(75.6)	**<0.0001**	14	(16.9)	69	(83.1)	**<0.0001**
▪ No	167	(55.5)	134	(44.5)		168	(59.2)	116	(40.9)	
o 1+ Need Factors										
▪ Yes	150	(59.5)	102	(40.5)	**<0.0001**	150	(62.2)	91	(37.8)	**<0.0001**
▪ No	38	(28.2)	97	(71.9)		32	(25.4)	94	(74.6)	

[a] CES-D20 only includes respondents with answers to all 20 questions. Respondents with ≥1 missing value were excluded from analyses.

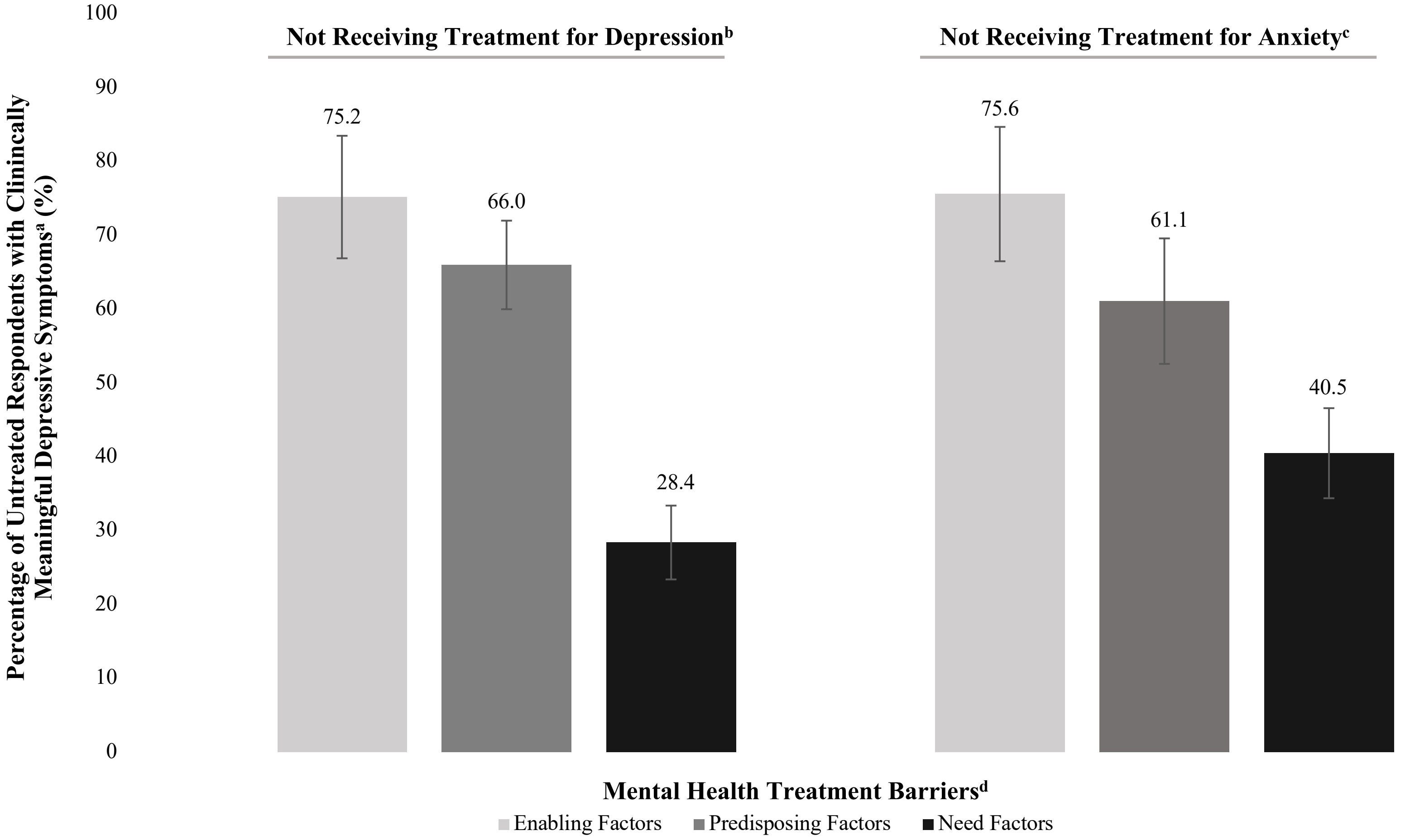
[b] Among untreated depression cohort, NARCOMS Depression Scale (missing n=2); CES-D20 (missing n=36).

[c] Among untreated anxiety cohort, NARCOMS Depression Scale (missing n=1); CES-D20 (missing n=21).

Bolded estimates indicate p<0.10.

Abbreviations: NARCOMS – North American Research Committee on Multiple Sclerosis; CES-D20 – Centre for Epidemiological Studies - Depression Scale (20-item).

Figure 5 Proportion of untreated NARCOMS Spring 2011 respondents with clinically meaningful depressive symptoms reporting barriers to mental health treatment (assessed using the NARCOMS Depression Scale)



[a] Assessed using NARCOMS Depression Scale.
[b] Among respondents with untreated depression, 266/545 scored ≥2 on NARCOMS Depression Scale (missing n=2).
[c] Among respondents with untreated anxiety, 199/388 scored ≥2 on NARCOMS Depression Scale (missning n=1).
[d] Mental health treatment barriers are not mutually exclusive as respondents were permitted to select more than one response. Respondents who selected multiple barriers across different groupings (i.e., one or more of enabling, predisposing and need factors) appeared once in the overall count for each selected barrier subgroup.
Error bars show 95% confidence interval.

5.1.5 Objective 1B Revisited: Sensitivity analyses illustrating adjusted associations between respondents' sociodemographic and other key characteristics and unmet mental health needs (i.e., not receiving treatment)

Tables 9.1 and 9.2 present a comparison of the original adjusted models of depression and anxiety treatment status, respectively (as shown previously in Tables 5.1 and 5.2), along with revised adjusted models excluding untreated respondents reporting need factors (i.e., "not having symptoms now") as their only barrier to mental health treatment.

Depression Cohort (Table 9.1) – Among NARCOMS Spring 2011 respondents reporting depression non-treatment, 42.0% (229/545) reported need factors (i.e., "not having symptoms now") as their only barrier to treatment. When excluding these respondents from the analyses, the adjusted association between NARCOMS Depression score and depression treatment status reversed direction from that observed in the original model. While this association did not reach statistical significance in the revised model, those with clinically meaningful depressive symptoms (vs. without) showed higher odds of depression non-treatment (adjOR=1.21; 95% CI=0.93, 1.56). The adjusted associations originally observed for age, public only health insurance, uninsured status and disability were comparable or even more pronounced than observed in the original model. Race and private health insurance were no longer statistically significant correlates of untreated depression.

Anxiety Cohort (Table 9.2) – Among NARCOMS Spring 2011 respondents reporting anxiety non-treatment, 49.2% (191/388) reported need factors (i.e., "not having symptoms now") as their only barrier to treatment. When excluding these respondents from the analyses, the presence of clinically meaningful depressive symptoms was no longer significantly associated with anxiety non-treatment. Other associations generally remained consistent or showed more pronounced estimates relative to the original model (e.g., lower education level and uninsured status).

Table 9.1 Adjusted associations between respondents' baseline characteristics and not receiving treatment for depression among NARCOMS Spring 2011 respondents diagnosed with depression, including vs. excluding untreated respondents reporting need factors as their only barrier to treatment.

Baseline Characteristics	**Depression Cohort** Not Receiving Treatment for Depression					
	Full Cohort (n=3589) Adjusted[b]			**Restricted Cohort**[a] (n=3360) Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Age in 2011 (years)						
- <45	1.26	(0.98, 1.62)	**0.069**	1.45	(1.06, 1.97)	**0.019**
- 45–64	1.0			1.0		
- ≥65	1.40	(1.04, 1.87)	**0.027**	1.43	(0.98, 2.08)	**0.061**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.29	(0.97, 1.72)	**0.075**	1.13	(0.78, 1.62)	0.52
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.06	(0.86, 1.30)	0.58	1.07	(0.83, 1.38)	0.61
Education						
- Secondary School/GED	1.02	(0.78, 1.34)	0.87	1.18	(0.83, 1.67)	0.35
- Associate/Technical Degree	1.01	(0.75, 1.37)	0.93	1.16	(0.79, 1.72)	0.45
- Bachelor's Degree	1.02	(0.78, 1.32)	0.91	1.12	(0.79, 1.60)	0.52
- Post Bachelor's Degree	1.0			1.0		
Health insurance						
- Private	1.27	(0.99, 1.64)	**0.064**	1.17	(0.84, 1.61)	0.35
- Private and public	1.0			1.0		
- Public	1.27	(0.96, 1.68)	**0.096**	1.34	(0.95, 1.89)	**0.099**
- Uninsured	2.09	(1.22, 3.57)	**0.0070**	2.38	(1.30, 4.37)	**0.005**
NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	0.55	(0.46, 0.67)	**<0.0001**	1.21	(0.93, 1.56)	0.16
Disability (PDDS)						
- Mild	1.0			1.0		
- Moderate	0.69	(0.54, 0.87)	**0.0015**	0.61	(0.45, 0.82)	**0.0012**
- Severe	0.62	(0.48, 0.80)	**0.0002**	0.57	(0.41, 0.78)	**0.0005**

[a] Restricted depression cohort excludes untreated respondents reporting absence of symptoms as only treatment barrier (n=229).

[b,c] Adjusted for all variables listed in above table ([b] missing n=149; [c] missing n=143).

Bolded estimates indicate p<0.10. Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps

Table 9.2 Adjusted associations between respondents' baseline characteristics and not receiving treatment for anxiety among NARCOMS Spring 2011 respondents diagnosed with anxiety, including vs. excluding untreated respondents reporting need factors as their only barrier to treatment.

Baseline Characteristics	**Anxiety Cohort** Not Receiving Treatment for Anxiety					
	Full Cohort (n=1487) Adjusted[b]			**Restricted Cohort**[a] (n=1296) Adjusted[c]		
	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Age in 2011 (years)						
- <45	0.88	(0.65, 1.20)	0.42	1.04	(0.70, 1.53)	0.86
- 45–64	1.0			1.0		
- ≥65	1.59	(1.05, 2.40)	**0.029**	1.62	(0.93, 2.82)	**0.086**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.27	(0.89, 1.80)	0.19	1.39	(0.89, 2.15)	0.14
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.73, 1.23)	0.69	0.94	(0.67, 1.32)	0.72
Education						
- Secondary School/GED	1.25	(0.87, 1.79)	0.23	2.19	(1.30, 3.67)	**0.0020**
- Associate/Technical Degree	1.56	(1.06, 2.30)	**0.025**	2.54	(1.46, 4.39)	**0.0009**
- Bachelor's Degree	1.36	(0.95, 1.94)	**0.094**	1.59	(0.93, 2.73)	**0.094**
- Post Bachelor's Degree	1.0			1.0		
Health insurance						
- Private	1.31	(0.95, 1.80)	0.10	1.33	(0.86, 2.05)	0.19
- Private and public	1.0			1.0		
- Public	1.13	(0.79, 1.62)	0.50	1.28	(0.81, 2.02)	0.30
- Uninsured	1.72	(0.89, 3.33)	0.11	2.93	(1.42, 6.04)	**0.0036**
NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	0.61	(0.48, 0.79)	**0.0001**	1.05	(0.75, 1.48)	0.78
Disability (PDDS)						
- Mild	1.0			1.0		
- Moderate	0.89	(0.66, 1.19)	0.42	0.85	(0.58, 1.24)	0.40
- Severe	0.63	(0.44, 0.89)	**0.0093**	0.57	(0.36, 0.90)	**0.016**

[a] Restricted anxiety cohort excludes untreated respondents reporting absence of symptoms as only treatment barrier (n=191).

[b,c] Adjusted for all variables listed in above table ([b] missing n=65; [c] missing n=55).

Bolded estimates indicate p<0.10. Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

5.1.6 Objective 1E: Among those receiving treatment for their mental health comorbidity, what form of treatment is being administered and how does the type of treatment vary by key sociodemographic and other characteristics of MS patient respondents?

The bivariate associations between respondents' baseline characteristics and mental health treatment modality among respondents receiving treatment for depression or anxiety are presented in Tables 10.1 and 10.2, respectively. Figure 6 illustrates the illustrates the distribution of mental health treatment modalities among respondents with clinically meaningful depressive symptoms. Supplemental tables show the bivariate associations presented in Tables 10.1 and 10.2 stratified by the presence or absence of clinically meaningful depressive symptoms (using the NARCOMS Depression Scale) for the depression and anxiety cohorts (Tables B2.A and B2.B, respectively).

<u>Depression Cohort (Table 10.1)</u> – Among respondents diagnosed with depression, 84.9% (3044/3589) were receiving treatment at the time of survey response, with 3.9% treated with psychotherapy, 74.1% treated with medication, and 20.1% treated with a combination of psychotherapy and medication (note: 1.9% [59/3044] did not provide current treatment modality). Respondents who were younger (23.9% for <45 years vs. 15.6% for ≥65 years), single or living alone (24.0% vs.18.7% for married or cohabitating), living with assistance (26.3% vs. 20.0% for private residence) and had higher levels of education (e.g., 23.9% for post-bachelor's vs. 17.2% for secondary school/GED) were significantly more likely to be treated for depression with both psychotherapy and medication. People of Colour/Other were significantly less likely to be treated exclusively with medication relative to White respondents (68.4% vs. 76.4% for White). Respondents with clinically meaningful depressive symptoms (24.3% vs. 13.9% without), severe cognitive impairment (27.4% vs. 17.0% for minimal), severe fatigue (23.5% vs. 16.9% for minimal), and mild disability (22.5% vs. 18.4% for severe) were also significantly more likely to be treated with both psychotherapy and medication.

<u>Anxiety Cohort (Table 10.2)</u> – Among respondents diagnosed with anxiety, 73.9% (1099/1487) were receiving treatment at the time of survey response, with 5.4% treated with psychotherapy, 64.6% treated with medication, and 27.7% treated with a combination of psychotherapy and medication (note: 2.4% [26/1099] did not provide current treatment modality). Respondents who were aged 45–64 years (29.0% vs. 26.8% for <45 years), single or living alone (34.4% vs. 25.3% for married or cohabitating), unemployed or missing employment

(29.9% vs. 24.9% for employed), and had higher levels of education (e.g., 31.3% for post-graduate vs. 24.6% for secondary school/GED) were significantly more likely to be treated for anxiety with both psychotherapy and medication. Respondents who reported clinically meaningful depressive symptoms (34.2% vs. 17.6% without), severe cognitive impairment (37.2% vs. 21.6% for mild) and severe fatigue (34.2% vs. 22.1 for mild) were also significantly more likely to be treated with both psychotherapy and medication.

Figure 6 – Among respondents with clinically meaningful depressive symptoms receiving treatment for depression (1927/3044) 4.5% were treated with psychotherapy, 69.7% were treated with medication, and 23.8% were treated with both psychotherapy and medication. Among respondents with clinically meaningful depressive symptoms receiving treatment for anxiety (715/1099), 5.9% were treated with psychotherapy, 58.0% were treated with medication, and 33.3% were treated with both psychotherapy and medication.

Table 10.1 Bivariate associations between respondents' baseline characteristics and mental health treatment modality among NARCOMS Spring 2011 respondents diagnosed with depression who were receiving treatment (n, row%, unless otherwise noted)

Baseline Characteristics	**Depression Cohort[a]** Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=3044)						
	Psychotherapy[c] (n=119, 3.9%)		**Medication[c]** (n=2255, 74.1%)		**Combination[c]** (n=611, 20.1%)		***p*-value**
Year of birth							
- ≤1946	6	(1.6)	313	(82.8)	59	(15.6)	**<0.0001**
- 1947–1953	35	(4.4)	625	(78.4)	137	(17.2)	
- 1954–1959	25	(3.4)	548	(74.7)	161	(21.9)	
- 1960–1966	24	(3.8)	460	(72.7)	149	(23.5)	
- ≥1967	28	(6.4)	307	(69.8)	105	(23.9)	
Age in 2011 (years)							
- <45	28	(6.4)	307	(69.8)	105	(23.9)	**0.0001**
- 45–64	84	(3.9)	1633	(75.5)	447	(20.7)	
- ≥65	6	(1.6)	313	(82.8)	59	(15.6)	
Sex							
- Female	101	(4.0)	1895	(74.9)	502	(20.1)	0.48
- Male	18	(3.7)	358	(73.8)	109	(22.5)	
Race							
- White	96	(3.6)	2032	(76.4)	533	(20.0)	**0.0008**
- People of Colour/Other	23	(7.2)	219	(68.4)	78	(24.4)	
Marital status							
- Married/cohabitating	64	(3.3)	1537	(78.1)	368	(18.7)	**<0.0001**
- Single/living alone	55	(5.6)	691	(70.4)	235	(24.0)	
Residence							
- Private residence	110	(4.0)	2101	(76.0)	554	(20.0)	**0.086**
- Living with assistance	9	(4.8)	128	(68.8)	49	(26.3)	
Education							
- Secondary School/GED	32	(3.5)	726	(79.3)	157	(17.2)	**0.0020**
- Associate/Technical Degree	17	(3.2)	422	(78.2)	101	(18.7)	
- Bachelor's Degree	38	(4.5)	605	(72.2)	195	(23.3)	
- Post Bachelor's Degree	31	(4.9)	451	(71.3)	151	(23.9)	
Income							
- <$30,000	26	(3.4)	588	(76.9)	151	(19.7)	0.75
- $30,000–$50,000	22	(4.0)	412	(75.2)	114	(20.8)	
- $50,001–$100,000	35	(4.6)	565	(74.6)	157	(20.7)	
- > $100,000	12	(3.3)	263	(73.3)	84	(23.4)	
- Unanswered/missing	24	(4.3)	427	(76.8)	105	(18.9)	

Baseline Characteristics	**Depression Cohort**[a] Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=3044)						
	Psychotherapy[c] (n=119, 3.9%)		**Medication**[c] (n=2255, 74.1%)		**Combination**[c] (n=611, 20.1%)		***p*-value**
Employment							
- Employed	46	(5.0)	703	(75.8)	178	(19.2)	0.12
- Unemployed/missing	73	(3.6)	1552	(75.4)	433	(21.0)	
Health insurance							
- Private	59	(4.8)	950	(76.5)	233	(18.8)	0.29
- Private and public	32	(3.3)	733	(74.9)	214	(21.9)	
- Public	26	(3.9)	500	(74.5)	145	(21.6)	
- Uninsured	2	(2.2)	72	(77.4)	19	(20.4)	
NARCOMS Depression score							
- <2	32	(3.0)	903	(83.2)	151	(13.9)	**<0.0001**
- ≥2	87	(4.6)	1343	(71.1)	459	(24.3)	
Cognitive impairment							
- Minimal	56	(4.8)	904	(78.2)	196	(17.0)	**<0.0001**
- Moderate	53	(3.6)	1097	(74.6)	320	(21.8)	
- Severe	8	(2.4)	238	(70.2)	93	(27.4)	
Fatigue							
- Minimal	20	(5.1)	304	(78.0)	66	(16.9)	**0.012**
- Moderate	57	(4.0)	1085	(77.0)	268	(19.0)	
- Severe	40	(3.4)	851	(73.1)	274	(23.5)	
Disability (PDDS)							
- Mild	49	(4.9)	723	(72.6)	224	(22.5)	**0.052**
- Moderate	34	(3.5)	738	(76.0)	199	(20.5)	
- Severe	35	(3.5)	780	(78.1)	184	(18.4)	
Age of MS symptom onset (years)							
- < 25	34	(3.9)	650	(74.0)	194	(22.1)	0.35
- 25–39	66	(4.3)	1148	(75.5)	306	(20.1)	
- ≥ 40	16	(3.0)	415	(78.2)	100	(18.8)	

[a] Among those receiving treatment for depression (n=3044), treatment modality was missing for n=59 respondents.

[b] Mental health treatment modalities were captured generally for respondents with one or more diagnosed mental health comorbidity who were receiving treatment for at least one condition at the time of survey response.

[c] Treatment modalities among depression cohort are mutually exclusive. Respondents receiving both psychotherapy and medication are listed under "combination".

All listed variables were missing no more than 4%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; PDDS – Patient Determined Disease Steps.

Table 10.2 Bivariate associations between respondents' baseline characteristics and mental health treatment modality among NARCOMS Spring 2011 respondents diagnosed with anxiety who were receiving treatment (n, row%, unless otherwise noted)

Baseline Characteristics	**Anxiety Cohort**[a] Receiving Treatment for Diagnosed Mental Health Comorbidity[b] (n=1099)						
	Psychotherapy[c] (n=59, 5.4%)		**Medication**[c] (n= 710, 64.6%)		**Combination**[c] (n=304, 27.7%)		*p*-value
Year of birth							
- ≤1946	3	(3.1)	67	(69.8)	26	(27.1)	**0.062**
- 1947–1953	12	(5.1)	166	(70.9)	56	(23.9)	
- 1954–1959	13	(5.0)	167	(64.5)	79	(30.5)	
- 1960–1966	7	(3.0)	153	(64.6)	77	(32.5)	
- ≥1967	22	(9.1)	156	(64.2)	65	(26.8)	
Age in 2011 (years)							
- <45	22	(9.1)	156	(64.2)	65	(26.8)	**0.057**
- 45–64	32	(4.4)	486	(66.6)	212	(29.0)	
- ≥65	3	(3.1)	67	(69.8)	26	(27.1)	
Sex							
- Female	53	(5.7)	615	(66.6)	256	(27.7)	0.38
- Male	5	(3.4)	94	(64.4)	47	(32.2)	
Race							
- White	50	(5.3)	624	(66.5)	265	(28.2)	0.91
- People of Colour/Other	8	(6.1)	85	(64.9)	38	(29.0)	
Marital status							
- Married/cohabitating	35	(5.1)	480	(69.7)	174	(25.3)	**0.026**
- Single/living alone	24	(6.4)	222	(59.2)	129	(34.4)	
Residence							
- Private residence	53	(5.3)	663	(66.8)	276	(27.8)	0.12
- Living with assistance	6	(8.7)	38	(55.1)	25	(36.2)	
Education							
- Secondary School/GED	12	(3.5)	249	(72.0)	85	(24.6)	**0.031**
- Associate/Technical Degree	8	(4.2)	130	(68.4)	52	(27.4)	
- Bachelor's Degree	20	(6.8)	181	(61.8)	92	(31.4)	
- Post Bachelor's Degree	18	(8.0)	136	(60.7)	70	(31.3)	
Income							
- <$30,000	17	(5.8)	184	(62.8)	92	(31.4)	0.21
- $30,000–$50,000	3	(1.5)	137	(69.2)	58	(29.3)	
- $50,001–$100,000	19	(7.4)	172	(66.9)	66	(25.7)	
- > $100,000	8	(6.2)	84	(64.6)	38	(29.2)	
- Unanswered/missing	12	(6.2)	133	(68.2)	50	(25.6)	

Baseline Characteristics	**Anxiety Cohort**[a] Receiving Treatment for Diagnosed Mental Health Comorbidity[b] (n=1099)						
	Psychotherapy[c] (n=59, 5.4%)		**Medication**[c] (n= 710, 64.6%)		**Combination**[c] (n=304, 27.7%)		*p*-value
Employment							
- Employed	24	(7.1)	230	(68.1)	84	(24.9)	**0.097**
- Unemployed/missing	35	(4.8)	480	(65.3)	220	(29.9)	
Health insurance							
- Private	30	(6.7)	302	(67.7)	114	(25.6)	0.49
- Private and public	14	(4.2)	218	(65.5)	101	(30.3)	
- Public	13	(5.1)	164	(63.8)	80	(31.1)	
- Uninsured	2	(5.4)	26	(70.3)	9	(24.3)	
NARCOMS Depression score							
- <2	17	(4.5)	293	(77.9)	66	(17.6)	**<0.0001**
- ≥2	42	(6.0)	415	(59.7)	238	(34.2)	
Cognitive impairment							
- Minimal	27	(7.2)	267	(71.2)	81	(21.6)	**0.0016**
- Moderate	26	(4.8)	353	(64.5)	168	(30.7)	
- Severe	5	(3.5)	86	(59.3)	54	(37.2)	
Fatigue							
- Minimal	10	(7.1)	99	(70.7)	31	(22.1)	**0.0074**
- Moderate	26	(5.4)	340	(70.0)	120	(24.7)	
- Severe	22	(5.0)	268	(60.8)	151	(34.2)	
Disability (PDDS)							
- Mild	26	(6.1)	279	(65.2)	123	(28.7)	0.94
- Moderate	18	(5.1)	236	(66.5)	101	(28.5)	
- Severe	14	(5.0)	190	(67.6)	77	(27.4)	
Age of MS symptom onset (years)							
- < 25	19	(5.7)	206	(62.2)	106	(32.0)	0.37
- 25–39	27	(5.1)	362	(67.9)	144	(27.0)	
- ≥ 40	10	(5.3)	132	(69.8)	47	(24.9)	

[a] Among those receiving treatment for anxiety (n=1099), treatment modality was missing for n=26 respondents.

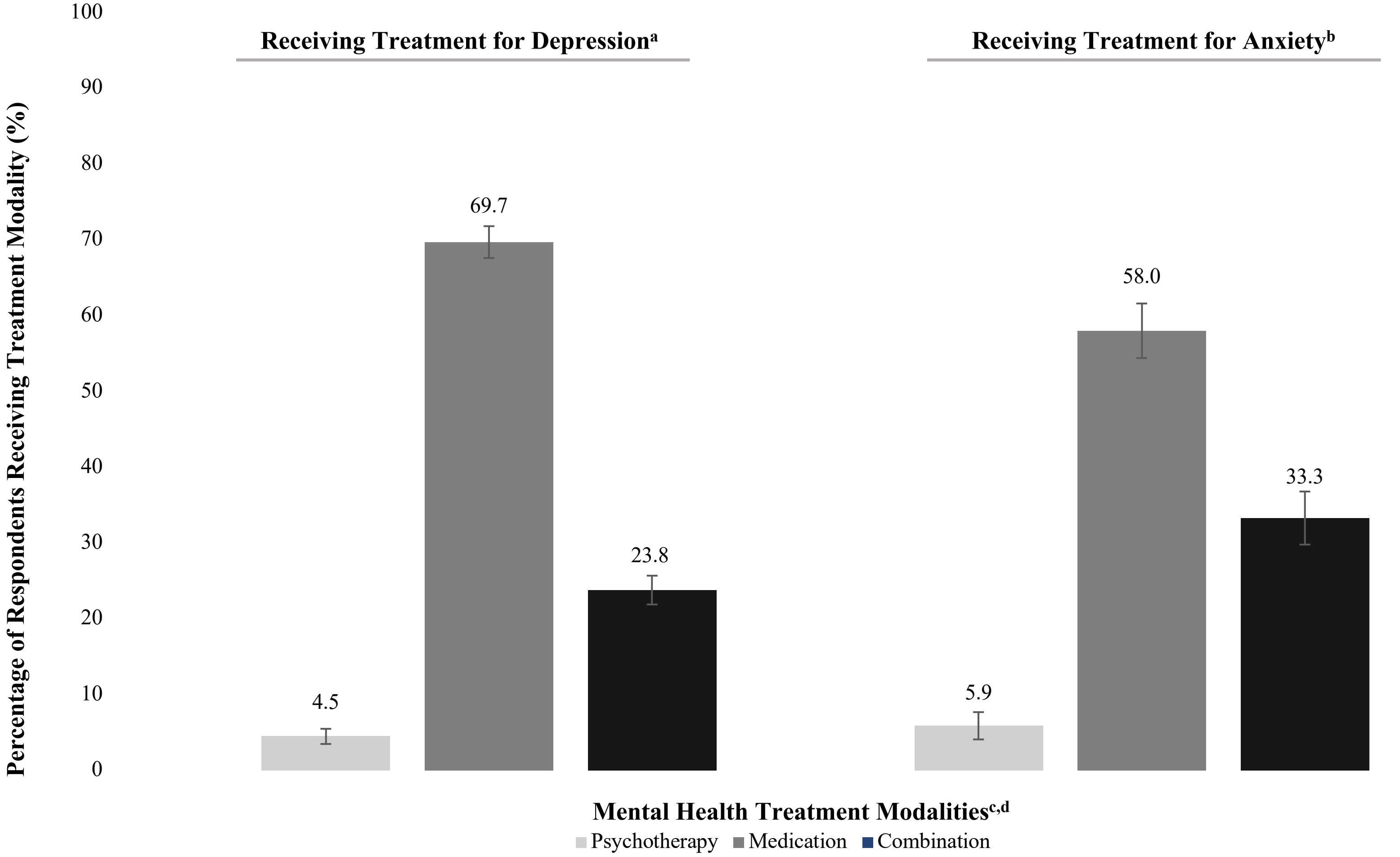
[b] Mental health treatment modalities were captured generally for respondents with one or more diagnosed mental health comorbidity who were receiving treatment for at least one condition at the time of survey response.

[c] Treatment modalities among anxiety cohort are mutually exclusive. Respondents receiving both psychotherapy and medication are listed under "combination".

All listed variables were missing no more than 4%, apart from education and Age of MS symptom onset where missing was <5%.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; PDDS – Patient Determined Disease Steps.

Figure 6 Distribution of mental health treatment modalities reported by NARCOMS Spring 2011 respondents with clinically meaningful depressive symptoms, by mental health comorbidity



[a] Among respondents diagnosed with depression, 84.8% (3044/3589) were receiving treatment, of which 63.3% (1927/3044) had clinically meaningful depressive symptoms (n=10 missing for the NARCOMS Depression Scale).

[b] Among respondents diagnosed with anxiety, 73.9% (1099/1487) were receiving treatment, of which 65.1% (715/1099) had clinically meaningful depressive symptoms (n=2 missing for the NARCOMS Depression Scale).

[c] Mental health treatment modalities were captured generally for respondents with one or more diagnosed mental health comorbidity who were receiving treatment for at least one condition at the time of survey response.

[d] Treatment modalities are mutually exclusive within depression and anxiety cohorts.

5.2 Objective 2 – Temporal association between unmet mental health needs and severity of depressive symptoms and mental/physical health-related quality of life among a longitudinal sample of MS survey respondents with a diagnosed mental health comorbidity.

5.2.1 Objective 2A: What are the crude and adjusted associations between respondents' baseline mental health treatment status and severity of depressive symptoms at one-year follow-up?

A comparison of baseline characteristics among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety, by the presence or absence of the NARCOMS Depression Scale variable at one-year follow-up, are presented in Tables 11.A–C for sociodemographic, clinical, and MS characteristics, respectively.

Relevant unadjusted and adjusted odds ratios derived from logistic regression models illustrating the crude and independent associations between baseline mental health treatment status and relevant confounders and clinically meaningful depressive symptoms at one-year follow-up (Spring 2012 Survey) are presented in Tables 12.1 and 12.2 for the depression and anxiety cohorts, respectively. The association between baseline mental health treatment status and clinically meaningful depressive symptoms at one-year follow-up (in 2012) was adjusted for age, sex, race, marital status, education, income, employment status, depressive symptoms, disability, and disease duration (all assessed at baseline).

Supplemental tables for this objective include (i) the unadjusted associations between all baseline characteristics and clinically meaningful depressive symptoms at one-year follow-up (Tables C1.A–C), (ii) adjusted models excluding untreated respondents reporting need factors as their only barrier to mental health treatment at baseline, (iii) adjusted models excluding baseline depressive symptoms, and (iv) adjusted models using a modified Poisson regression to derive RR (Tables C2.A–C and C3.A–C for the depression and anxiety cohorts, respectively).

<u>Sociodemographic Characteristics & Missing Depressive Symptoms Outcome (Table 11.A)</u> – Among respondents diagnosed with depression, 80.8% (2891/3577) responded to the NARCOMS Depression Scale on both Spring 2011 and 2012 surveys, and 19.2% (686/3577) responded at baseline only (including those missing in the follow-up survey and those who skipped the measure). Baseline mental health treatment status was not significantly different between those missing vs. not missing the NARCOMS Depression Scale at one-year follow-up. Compared to those who responded to the NARCOMS Depression Scale on both surveys,

respondents who were missing at follow-up were significantly more likely to be younger (born ≥1960), People of Colour/Other, single or live alone, living with assistance, unemployed (or missing employment), have the lowest levels of education (secondary school/GED) and annual family income (<$30,000) at baseline. Those missing (vs. not missing) at the NARCOMS Depression Scale at one-year follow-up were significantly less likely to have only private health insurance at baseline.

Among respondents diagnosed with anxiety, 79.6% (1181/1484) responded to the NARCOMS Depression Scale on both surveys, and 20.4% (303/1484) responded at baseline only. Baseline mental health treatment status was not significantly different between those missing vs. not missing the NARCOMS Depression Scale at one-year follow-up. Compared to those who responded to the NARCOMS Depression Scale on both surveys, those who were missing at follow-up were significantly more likely to be younger (aged <45 years; born ≥1960), People of Colour/Other, be unemployed (or missing employment), and have the lowest level of education (secondary school/GED) at baseline.

Clinical Characteristics & Missing Depressive Symptoms Outcome (Table 11.B) – Among respondents diagnosed with depression, those who were missing (vs. not missing) the NARCOMS Depression Scale at one-year follow-up were significantly more likely to have been admitted overnight to a healthcare facility, have clinically meaningful depressive symptoms, poorer self-rated health, moderate or severe cognitive impairment, severe fatigue, severe pain, and worse mental HRQOL (lower MCS-12 scores) at baseline.

Among respondents diagnosed with anxiety, those who were missing (vs. not missing) the NARCOMS Depression Scale at one-year follow-up were significantly more likely to have clinically meaningful depressive symptoms, severe pain and worse mental HRQOL (lower MCS-12 scores) at baseline.

MS Characteristics & Missing Depressive Symptoms Outcome (Table 11.C) – Among respondents diagnosed with depression, those who were missing (vs. not missing) NARCOMS Depression Scale at one-year follow-up were significantly more likely to have a more recent year of MS onset (≥1996) and MS diagnosis (≥2001), shorter disease duration (≤10 years), and a more recent enrollment in NARCOMS (≥2005) at baseline. Comparable findings were observed for respondents diagnosed with anxiety in relation to MS characteristics associated with missing responses at follow-up.

Logistic Regression Models for Depression Cohort (Table 12.1) – Among respondents diagnosed with depression, 56.6% (1636/2891) reported clinically meaningful depressive symptoms at one-year follow-up. Crude estimates showed that not receiving treatment for depression at baseline was associated with significantly lower odds of clinically meaningful depressive symptoms at one-year follow-up (OR=0.65; 95% CI=0.53, 0.80). This association was no longer statistically significant in the adjusted model (adjOR=0.90; 95% CI=0.70, 1.16). Among covariates, the strongest association with clinically meaningful depressive symptoms at follow-up was observed for the presence of clinically meaningful depressive symptoms at baseline (vs. absence; adjOR=10.26; 95% CI=8.55-12.32). Race, education, annual family income and disability also showed significant associations with the severity of depressive symptoms at follow-up in the adjusted model. Specifically, respondents representing People of Colour/Other (vs. White), those with lower education (associate/technical degree vs. post-bachelor's), lower levels of income (e.g., <$30,000 vs. >$100,000) and severe disability (vs. mild) at baseline had significantly higher odds of clinically meaningful depressive symptoms at follow-up. Though sex was not statistically significant in the final model, the adjusted association showed a similar direction of association as the crude estimate, suggesting higher odds of clinically meaningful depressive symptoms at follow-up among males compared to females.

Findings from the original model (Table 12.1) remained relatively consistent after excluding respondents who reported need factors (i.e., "not having symptoms now") as the only barrier to treatment at baseline (Table C2.A). When baseline depressive symptoms were excluded from the model, there was once again a significant association observed between not receiving depression treatment at baseline and depressive symptoms at follow-up (adjOR=0.69; 95% CI=0.56, 0.85) (Table C2.B) and most covariates showed significant associations with this one-year outcome.

Logistic Regression Models for Anxiety Cohort (Table 12.2) – Among respondents diagnosed with anxiety, 56.8% (671/1181) reported clinically meaningful depressive symptoms at one-year follow-up. Crude estimates showed that not receiving treatment for anxiety at baseline was associated with significantly lower odds of clinically meaningful depressive symptoms at one-year follow-up (OR=0.76; 95% CI=0.58, 0.98). This association was no longer statistically significant in the model adjusted for relevant covariates (adjOR=1.18; 95% CI=0.84, 1.66). Among covariates, the presence of clinically significant depressive symptoms at baseline had the strongest association with the presence of depressive symptoms at follow-up (vs. absence; adjOR=13.13, 95%CI=9.71,17.77). Other covariates associated with significantly higher odds of depressive symptoms at follow-up included the male sex (vs. female), lower income (<\$30,000 vs. >\$100,000) and severe disability (vs. mild). Participants with older ages at baseline (≥65 years vs. 45–64 years) had significantly lower odds of clinically meaningful depressive symptoms at one-year follow-up.

Findings from the original model (Table 12.2), including for the key exposure of interest (not receiving treatment for anxiety), remained largely consistent in models that excluded untreated respondents who reported need factors (i.e., “not having symptoms now”) as the only barrier to treatment (Table C3.A) or excluded respondents’ baseline NARCOMS Depression Scale score (Table C3.B). For the latter, significantly higher odds for depressive symptoms at follow-up were observed for respondents who were unemployed and those with moderate disability.

Table 11.A Distribution of respondents' baseline sociodemographic characteristics, by response to the NARCOMS Depression Scale at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (n, column%, unless otherwise noted)

Baseline Sociodemographic Characteristics (2011)	**Spring 2012 NARCOMS Depression Scale**									
	Depression Cohort[a] (n=3577)					**Anxiety Cohort**[b] (n=1484)				
	Provided[c] (n=2891)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1181)		Missing[d] (n=303)		*p*-value
Baseline treatment status										
- Receiving treatment	2440	(84.4)	594	(86.6)	0.16	868	(73.5)	229	(75.6)	0.46
- Not receiving treatment	451	(15.6)	92	(13.4)		313	(26.5)	74	(24.4)	
Country of Enrolment										
- USA	2867	(99.2)	669	(98.7)	0.15	1173	(99.4)	294	(98.3)	**0.055**
- Other	22	(0.8)	9	(1.3)		7	(0.6)	5	(1.7)	
Missing	2		8			1		4		
Year of birth										
- ≤1946	384	(13.3)	89	(13.1)	**0.0019**	127	(10.9)	21	(7.0)	**0.0089**
- 1947–1953	791	(27.4)	142	(20.9)		258	(21.8)	53	(17.7)	
- 1954–1959	712	(24.6)	164	(24.1)		293	(24.8)	64	(21.4)	
- 1960–1966	578	(20.0)	164	(24.1)		257	(21.8)	79	(26.4)	
- ≥1967	426	(14.7)	122	(17.9)		245	(20.8)	82	(27.4)	
Missing	0		5			1		4		
Age in 2011 (years)										
- <45	426	(14.7)	122	(17.9)	0.11	245	(20.8)	82	(27.4)	**0.014**
- 45–64	2081	(72.0)	470	(69.0)		807	(68.4)	196	(65.6)	
- ≥65	384	(13.3)	89	(13.1)		128	(10.9)	21	(7.0)	
Missing	0		5			1		4		
Sex										
- Female	2405	(83.2)	572	(83.9)	0.67	1031	(87.4)	254	(84.7)	0.22
- Male	486	(16.8)	110	(16.1)		149	(12.6)	46	(15.3)	
Missing	0		4			1		3		
Race										
- White	2622	(90.8)	550	(80.7)	**<0.0001**	1061	(89.9)	227	(75.9)	**<0.0001**
- People of Colour/Other	267	(9.2)	132	(19.4)		119	(10.1)	72	(24.1)	
Missing	2		4			1		4		
Marital status										
- Married/cohabitating	1935	(67.6)	416	(62.0)	**0.0058**	771	(66.0)	188	(63.5)	0.43
- Single/living alone	930	(32.4)	255	(38.0)		398	(34.1)	108	(36.5)	
Missing	28		15			12		7		
Residence										
- Private residence	2699	(94.3)	612	(91.1)	**0.0022**	1102	(94.4)	275	(93.5)	0.56

Baseline Sociodemographic Characteristics (2011)	**Spring 2012 NARCOMS Depression Scale**									
	Depression Cohort[a] (n=3577)					**Anxiety Cohort[b]** (n=1484)				
	Provided[c] (n=2891)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1181)		Missing[d] (n=303)		*p*-value
- Living with assistance	164	(5.7)	60	(8.9)		65	(5.6)	19	(6.5)	
Missing	28		14			14		9		
Education										
- Secondary School/GED	861	(30.3)	236	(35.5)	**0.0044**	354	(30.4)	119	(41.2)	**0.0002**
- Associate/Technical Degree	505	(17.8)	133	(20.0)		218	(18.7)	61	(21.1)	
- Bachelor’s Degree	832	(29.3)	175	(26.4)		335	(28.8)	71	(24.6)	
- Post Bachelor’s Degree	645	(22.7)	120	(18.1)		258	(22.2)	38	(13.2)	
Missing	48		22			16		14		
Income										
- <$30,000	717	(24.8)	213	(31.1)	**0.0031**	311	(26.3)	93	(30.7)	0.52
- $30,000–$50,000	515	(17.8)	120	(17.5)		209	(17.7)	54	(17.8)	
- $50,001–$100,000	742	(25.7)	149	(21.7)		277	(23.5)	68	(22.4)	
- > $100,000	371	(12.8)	68	(9.9)		156	(13.2)	32	(10.6)	
- Unanswered/missing	546	(18.9)	136	(19.8)		228	(19.3)	56	(18.5)	
Employment										
- Employed	953	(33.0)	190	(27.7)	**0.0078**	411	(34.8)	87	(28.7)	**0.045**
- Unemployed/missing	1938	(67.1)	496	(72.3)		770	(65.2)	216	(71.3)	
Health insurance										
- Private	1248	(43.2)	261	(38.1)	**0.072**	511	(43.3)	121	(39.9)	0.65
- Private and public	898	(31.1)	233	(34.0)		354	(30.0)	91	(30.0)	
- Public	649	(22.5)	162	(23.6)		267	(22.6)	78	(25.7)	
- Uninsured	96	(3.3)	30	(4.4)		49	(4.12)	13	(4.3)	
Missing	0		0			0		0		

[a,b] Respondents missing NARCOMS Depression Scale in 2011 were excluded from analyses: depression cohort ([a] missing n=12); anxiety cohort ([b] missing n=3).

[c] Outcome provided in 2011 and 2012

[d] Outcome provided in 2011 but missing in 2012.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; USA – United States of America.

Table 11.B Distribution of respondents' baseline clinical characteristics, by response to the NARCOMS Depression Scale at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (n, column%, unless otherwise noted)

Baseline Clinical Characteristics (2011)	**Spring 2012 NARCOMS Depression Scale**									
	Depression Cohort[a] (n=3577)					**Anxiety Cohort**[b] (n=1481)				
	Provided[c] (n=2891)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1181)		Missing[d] (n=303)		*p*-value
Baseline NARCOMS Depression score										
- <2	1181	(40.9)	203	(29.6)	**<0.0001**	477	(40.4)	93	(30.7)	**0.0020**
- ≥2	1710	(59.2)	483	(70.4)		704	(59.6)	210	(69.3)	
Admission to overnight healthcare facility										
- Yes	257	(8.9)	86	(12.5)	**0.0035**	123	(10.4)	36	(11.9)	0.46
- No	2634	(91.1)	600	(87.5)		1058	(89.6)	267	(88.1)	
Self-rated health										
- Excellent/very good/good	1851	(64.4)	396	(58.2)	**0.0022**	723	(61.4)	174	(57.8)	0.26
- Fair/poor	1025	(35.6)	286	(41.9)		455	(38.6)	127	(42. 2)	
Missing	15		4			3		2		
Cognitive impairment										
- Minimal	1164	(40.5)	231	(33.8)	**0.0038**	431	(36.7)	98	(32.5)	0.21
- Moderate	1408	(49.0)	364	(53.3)		605	(51.5)	159	(52.7)	
- Severe	302	(10.5)	88	(12.9)		139	(11.8)	45	(14.9)	
Missing	17		3			6		1		
Fatigue										
- Minimal	426	(14.8)	86	(12.6)	**0.040**	177	(15.1)	35	(11.6)	0.19
- Moderate	1373	(47.8)	307	(45.0)		552	(46.9)	138	(45.9)	
- Severe	1076	(37.4)	290	(42.5)		447	(38.0)	128	(42.5)	
Missing	16		3			5		2		
Pain										
- Minimal	1213	(42.0)	257	(37.5)	**<0.0001**	447	(38.0)	102	(33.8)	**0.037**
- Moderate	1192	(41.3)	256	(37.4)		498	(42.3)	120	(39.7)	
- Severe	484	(16.8)	172	(25.1)		233	(19.8)	80	(26.5)	
Missing	2		1			3		1		
Disability (PDDS)										
- Mild	1037	(36.1)	219	(32.3)	0.15	490	(41.7)	123	(41.4)	0.99
- Moderate	912	(31.7)	221	(32.6)		395	(33.6)	101	(34.0)	
- Severe	926	(32.2)	238	(35.1)		291	(24.7)	73	(24.6)	
Missing	16		8			5		6		
MCS-12 (mean, SD)	41.7	(11.4)	38.9	(11.6)	**<0.0001**	40.4	(11.3)	37.5	(11.2)	**0.0001**
PCS-12 (mean, SD)	37.2	(11.1)	36.4	(11.0)	0.11	37.8	(11.6)	37.4	(11.4)	0.57
Missing (MCS-12 and PCS-12)	86		29			31		12		

[a,b] Respondents missing NARCOMS Depression Scale in 2011 were excluded from analyses: depression cohort ([a] missing n=12); anxiety cohort ([b] missing n=3).

[c] Outcome provided in 2011 and 2012. [d] Outcome provided in 2011 but missing in 2012. Bolded estimates indicate p<0.10. Abbreviations: MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; PCS – Physical Component Score; SD – standard deviation.

Table 11.C Distribution of respondents' baseline MS characteristics, by response to the NARCOMS Depression Scale at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (n, column%, unless otherwise noted)

Baseline MS Characteristics (2011)	**Spring 2012 NARCOMS Depression Scale**									
	Depression Cohort[a] (n=3577)					**Anxiety Cohort[b]** (n=1484)				
	Provided[c] (n=2891)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1181)		Missing[d] (n=303)		*p*-value
Age of MS symptom onset (years)										
- < 25	877	(30.8)	195	(29.6)	0.18	371	(31.8)	101	(34.5)	0.16
- 25–39	1474	(51.8)	329	(49.9)		605	(52.0)	135	(46.1)	
- ≥ 40	496	(17.4)	135	(20.5)		187	(16.1)	57	(19.5)	
Missing	45		27			18		10		
Year of MS onset										
- ≤ 1980	814	(28.6)	171	(26.0)	**0.0006**	276	(23.7)	64	(21.8)	**0.0007**
- 1981–1985	443	(15.6)	73	(11.1)		173	(14.9)	23	(7.9)	
- 1986–1990	470	(16.5)	108	(16.4)		204	(17.5)	42	(14.3)	
- 1991–1995	480	(16.9)	113	(17.2)		195	(16.8)	55	(18.8)	
- ≥1996	639	(22.4)	194	(29.4)		315	(27.1)	109	(37.2)	
Missing	44		27			18		10		
Age of MS diagnosis (years)										
- <30	545	(19.1)	124	(18.5)	0.51	246	(21.2)	69	(23.6)	0.83
- 30–39	1012	(35.4)	228	(34.1)		401	(34.5)	99	(33.9)	
- 40–49	960	(33.6)	223	(33.3)		384	(33.1)	92	(31.5)	
- ≥50	341	(11.9)	94	(14.1)		131	(11.3)	32	(11.0)	
Missing	33		17			19		11		
Year of MS diagnosis										
- ≤1990	783	(27.4)	177	(26.4)	**<0.0001**	257	(22.1)	58	(19.8)	**0.032**
- 1991–1995	560	(19.6)	90	(13.4)		193	(16.6)	36	(12.3)	
- 1996–2000	727	(25.4)	160	(23.9)		296	(25.5)	68	(23.2)	
- ≥2001	788	(27.6)	243	(36.3)		416	(35.8)	131	(44.7)	
Missing	33		16			19		10		
Disease duration (years)										
- ≤10	788	(27.6)	243	(36.3)	**<0.0001**	416	(35.8)	131	(44.9)	**0.016**
- 11–20	1287	(45.0)	249	(37.2)		489	(42.1)	103	(35.3)	
- ≥21	783	(27.4)	177	(26.5)		257	(22.2)	58	(19.9)	
Missing	33		17			19		11		
Year of enrolment in NARCOMS										
- ≤2000	1205	(41.7)	218	(32.0)	**<0.0001**	431	(36.5)	76	(25.3)	**0.0010**
- 2001–2004	897	(31.0)	212	(31.1)		338	(28.6)	95	(31.7)	
- ≥2005	789	(27.3)	252	(37.0)		411	(34.8)	129	(43.0)	
Missing	0		4			1		3		

[a,b] Respondents missing NARCOMS Depression Scale in 2011 were excluded: depression cohort ([a] missing n=12); anxiety cohort ([b] missing n=3). [c] Outcome provided in 2011 and 2012. [d] Outcome provided in 2011 but missing in 2012. Bolded estimates indicate p<0.10. Abbreviations: MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis.

Table 12.1 Unadjusted and adjusted associations between baseline depression treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with depression.

Baseline Characteristics (2011)	**Depression Cohort** (n=2891) Clinically Meaningful Depressive Symptoms[a] (2012)					
	Unadjusted			Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status[c]						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.65	(0.53, 0.80)	**<0.0001**	0.90	(0.70, 1.16)	0.41
Age in 2011						
- <45	0.85	(0.69, 1.05)	0.14	0.97	(0.74, 1.28)	0.85
- 45–64	1.0			1.0		
- ≥65	0.86	(0.69 1.07)	0.17	0.81	(0.61, 1.08)	0.15
Sex						
- Female	1.0			1.0		
- Male	1.20	(0.98, 1.46)	**0.072**	1.22	(0.96, 1.56)	0.11
Race						
- White	1.0			1.0		
- People of Colour/Other	1.52	(1.17, 1.97)	**0.0020**	1.42	(1.03, 1.95)	**0.032**
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.31	(1.12, 1.54)	**0.0008**	1.03	(0.83, 1.28)	0.79
Education						
- Secondary School/GED	1.54	(1.25, 1.89)	**<0.0001**	1.14	(0.88, 1.47)	0.33
- Associate/Technical Degree	1.83	(1.44, 2.32)	**<0.0001**	1.41	(1.06, 1.89)	**0.020**
- Bachelor's Degree	1.03	(0.84, 1.27)	0.77	0.89	(0.70, 1.15)	0.37
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	2.68	(2.07, 3.46)	**<0.0001**	1.74	(1.21, 2.50)	**0.0030**
- $30,000–$50,000	2.06	(1.57, 2.70)	**<0.0001**	1.52	(1.08, 2.15)	**0.017**
- $50,001–$100,000	1.54	(1.19, 1.97)	**0.0008**	1.43	(1.05, 1.94)	**0.023**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.68	(1.28, 2.19)	**0.0001**	1.28	(0.91, 1.79)	0.16
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.61	(1.38, 1.89)	**<0.0001**	1.06	(0.85, 1.33)	0.59
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	10.83	(9.09,12.90)	**<0.0001**	10.26	(8.55,12.32)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.59	(1.33, 1.90)	**<0.0001**	1.17	(0.94, 1.47)	0.17
- Severe	1.70	(1.42, 2.04)	**<0.0001**	1.30	(1.02, 1.66)	**0.037**
Disease duration (years)						
- ≤10	1.07	(0.88, 1.31)	0.50	1.19	(0.91, 1.56)	0.19
- 11–20	0.94	(0.79, 1.13)	0.52	0.93	(0.75, 1.17)	0.54
- ≥21	1.0			1.0		

[a] In 2012, 56.6% (1636/2891) of respondents with depression reported clinically meaningful symptoms (vs. 43.4%, 1255/2891 without).

[b] Adjusted for all variables listed in above table; missing n=118.

[c] Received treatment at baseline n=2440; did not receive treatment at baseline n=45.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio.

Table 12.2 Unadjusted and adjusted associations between baseline anxiety treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with anxiety.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1181) Clinically Meaningful Depressive Symptoms[a] (2012)					
	Unadjusted			Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status[c]						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.76	(0.58, 0.98)	**0.035**	1.18	(0.84, 1.66)	0.34
Age in 2011						
- <45	0.81	(0.61, 1.08)	0.14	1.04	(0.71, 1.54)	0.84
- 45–64	1.0			1.0		
- ≥65	0.75	(0.52, 1.09)	0.13	0.59	(0.36, 0.98)	**0.041**
Sex						
- Female	1.0			1.0		
- Male	1.39	(0.97, 1.98)	**0.0070**	1.63	(1.03, 2.57)	**0.037**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.33	(0.90, 1.97)	0.15	1.07	(0.65, 1.76)	0.78
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.31	(1.02, 1.68)	**0.032**	0.95	(0.67, 1.36)	0.78
Education						
- Secondary School/GED	1.46	(1.05, 2.01)	**0.024**	1.28	(0.84, 1.96)	0.26
- Associate/Technical Degree	1.58	(1.09, 2.28)	**0.015**	1.27	(0.79, 2.04)	0.32
- Bachelor’s Degree	0.92	(0.67, 1.28)	0.63	0.84	(0.56, 1.27)	0.41
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	3.38	(2.27, 5.05)	**<0.0001**	1.75	(0.97, 3.17)	**0.065**
- $30,000–$50,000	2.62	(1.71, 4.01)	**<0.0001**	1.60	(0.91, 2.83)	0.11
- $50,001–$100,000	1.55	(1.04, 2.30)	**0.032**	1.30	(0.78, 2.15)	0.32
- > $100,000	1.0			1.0		
- Unanswered/missing	1.99	(1.32, 3.02)	**0.0011**	1.26	(0.72, 2.18)	0.42
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	2.09	(1.64, 2.67)	**<0.0001**	1.34	(0.93, 1.92)	0.12
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	13.64	(10.28, 18.10)	**<0.0001**	13.13	(9.71, 17.77)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.93	(1.47, 2.53)	**<0.0001**	1.26	(0.89, 1.80)	0.20
- Severe	2.13	(1.58, 2.87)	**<0.0001**	1.56	(1.03, 2.36)	**0.036**
Disease duration (years)						
- ≤10	0.89	(0.65, 1.23)	0.49	0.99	(0.63, 1.53)	0.95
- 11–20	0.80	(0.59, 1.09)	0.16	0.76	(0.51, 1.13)	0.17
- ≥21	1.0			1.0		

[a] In 2012, 56.8% (671/1181) of respondents with anxiety reported clinically meaningful symptoms (vs. 43.2%, 510/1181 without).
[b] Adjusted for all variables listed in above table; missing n=48.
[c] Received treatment at baseline n=868; did not receive treatment at baseline n=313.
Bolded estimates indicate p<0.10.
Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

5.2.2 Objective 2B: What are the crude and adjusted associations between respondents' baseline mental health treatment status and mental and physical health-related quality of life scores at one-year follow-up?

A comparison of baseline characteristics among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety, by the presence or absence of the RAND-12 at one-year follow-up, are presented in Tables 13.A–C for sociodemographic, clinical and MS characteristics, respectively.

Relevant unadjusted and adjusted odds ratios derived from logistic regression models illustrating the crude and independent associations between baseline mental health treatment status and relevant confounders and a clinically meaningful decline in HRQOL are presented in Tables 14.1 and 14.2 for a decline in MCS-12 score (for the depression and anxiety cohorts, respectively), and Tables 15.1 and 15.2 for a decline in PCS-12 score (for the depression and anxiety cohorts, respectively). The association between baseline treatment status and a clinically meaningful decline in RAND-12 scores (2011 to 2012) was adjusting for age, sex, race, marital status, education, income, employment, depressive symptoms (for PCS-12 only) disability (for MCS-12 only), relevant RAND-12 score, and disease duration (all assessed at baseline).

Supplemental tables for this objective include: (i) the unadjusted associations between all baseline characteristics and a clinically meaningful decline in MCS-12 (Tables D1.A–C) and PCS-12 scores (Tables D2A–C), (ii) adjusted models excluding untreated respondents reporting need factors as their only barrier to mental health treatment at baseline, and (iii) adjusted models excluding baseline RAND-12 scores, and (iv) adjusted models using a modified Poisson regression to derive RRs. The supplemental models for a clinically meaningful decline in MCS-12 score (mental HRQOL) are provided in Tables D3.A–C and D4.A–C for the depression and anxiety cohorts, respectively. The supplemental models for a clinically meaningful decline in PCS-12 score (physical HRQOL) are provided in Tables D5.A–C and D6.A–C for the depression and anxiety cohorts, respectively.

Sociodemographic Characteristics & Missing RAND-12 Outcome (Table 13.A) – Among respondents diagnosed with depression, 80.2% (2784/3470) responded to the RAND-12 on both the Spring 2011 and 2012 surveys, and 19.8% (686/3470) responded at baseline only (including those who were missing for the survey and those who skipped the measure). Baseline mental health treatment status was not significantly different between those missing vs. not missing the

RAND-12 at one-year follow-up. Compared to those who responded to the RAND-12 on both surveys, those who were missing at follow-up were significantly more likely to be younger (born ≥1960), People of Colour/Other, single or living alone, unemployed (or missing employment), to reside in a residence with assistance, have the lowest levels of education (secondary school/GED) and annual family income (<$30,000) at baseline. Those who were missing (vs. not missing) the RAND-12 at follow-up were significantly less likely to have only private health insurance at baseline.

Among respondents diagnosed with anxiety, 79.0% (1140/1443) responded to the RAND-12 on both surveys, and 21.0% (303/1443) responded at baseline only. Baseline mental health treatment status was not significantly different between those missing vs. not missing the RAND-12 Depression Scale at one-year follow-up. Respondents missing the RAND-12 at follow-up (vs. not missing) were significantly more likely to be younger (aged <45 years; born ≥1960), People of Colour/Other, unemployed (or missing employment), and have the lowest level of education (secondary school/GED) at baseline.

<u>Clinical Characteristics & Missing RAND-12 Outcome (Table 13.B)</u> – Among respondents diagnosed with depression, those who were missing (vs. not missing) the RAND-12 at one-year follow-up were significantly more likely to have been admitted overnight to a healthcare facility, have clinically meaningful depressive symptoms, poorer self-rated health, moderate or severe cognitive impairment, severe fatigue, severe pain, severe disability and worse mental and physical HRQOL (lower MCS-12 and PCS-12 scores) at baseline.

Among respondents diagnosed with anxiety, those who were missing (vs. not missing) the RAND-12 at one-year follow-up were significantly more likely to have clinically meaningful depressive symptoms, poorer self-rated health (fair/poor), severe fatigue, severe pain, and worse mental HRQOL (lower MCS-12 scores) at baseline.

<u>MS Characteristics & Missing RAND-12 Outcome (Table 13.C)</u> – Among respondents diagnosed with depression, those who were missing (vs. not missing) the RAND-12 at one-year follow-up were significantly more likely to have a more recent year of MS onset (≥1996), MS diagnosis (≥2001), year of enrolment in NARCOMS (≥2005), and shorter disease duration (≤10 years) at baseline. Comparable findings were observed for respondents diagnosed with anxiety in relation to MS characteristics associated with missing responses at follow-up.

Logistic Regression Models for Mental HRQOL: Depression Cohort (Table 14.1) – Among respondents diagnosed with depression, 32.3% (898/2784) reported a clinically meaningful decline in MCS-12 score (i.e., decline of ≥3 points) between baseline and one-year follow-up. Baseline depression treatment status was not significantly associated with a clinically meaningful decline in MCS-12 score in either crude or adjusted analyses (adjOR=0.97; 95% CI=0.77, 1.24). After adjusting for key covariates, the baseline MCS-12 score showed the strongest association with the outcome, indicating that a one-unit increase in baseline MCS-12 score was associated with significantly higher odds of decline in MCS-12 score at one-year follow-up (i.e., better mental HRQOL in 2011 was associated with higher odds of decline in 2012) (adjOR=1.06, 95% CI=1.05, 1.07). Among other covariates, only sex remained significantly associated with the outcome at one-year follow-up, with higher odds of decline in mental HRQOL evident among males vs. females (adjOR=1.31, 95% CI=1.04, 1.64).

Findings from the original model (Table 14.1) remained largely consistent after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”) (Table D3.A), and after the baseline MCS-12 score was excluded from the adjusted model (Table D3.B).

Logistic Regression Models for Mental HRQOL: Anxiety Cohort (Table 14.2) – Among respondents diagnosed with anxiety, 31.9% (364/1140) showed a clinically meaningful decline in MCS-12 score (i.e., decline of ≥3 points) between baseline and follow-up surveys. Baseline anxiety treatment status was not significantly associated with a clinically meaningful decline in MCS-12 score in either crude or adjusted analyses (adjOR=1.02; 95% CI=0.76, 1.39). After adjusting for key covariates, the baseline MCS-12 score showed the strongest association with the outcome, indicating that a one-unit increase in baseline MCS-12 score was associated with significantly higher odds of a decline in MCS-12 score at one-year follow-up (i.e., better mental HRQOL in 2011 was associated with higher odds of decline in 2012) (adjOR=1.05, 95% CI=1.04, 1.06). Among other covariates, only disability remained significantly associated with the outcome at one-year follow-up, with higher odds of decline in mental HRQOL evident for those with severe disability (vs. mild) at baseline (adjOR=1.36, 95% CI=0.94, 1.96).

Findings from the original model (Table 14.2) remained largely consistent after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”) (Table D4.A), and after the baseline MCS-12 score was excluded from the adjusted model (Table D4.B). In the former, People of Colour/Other (vs. White) had significantly greater odds of a clinically meaningful decline in MCS-12 score at one-year follow-up. In the latter, participants with younger ages at baseline (<45 years vs. 45–64 years) had significantly lower odds of a clinically meaningful decline in MCS-12 score at one-year follow-up.

Logistic Regression Models for Physical HRQOL: Depression Cohort (Table 15.1) – Among respondents diagnosed with depression, 32.9% (915/2784) reported a clinically meaningful decline in PCS-12 score (i.e., decline of ≥3 points) between baseline and follow-up surveys. Baseline depression treatment status was not significantly associated with a clinically meaningful decline in PCS-12 score in either crude or adjusted analyses (adjOR=0.88; 95% CI=0.70, 1.12). After adjusting for key covariates, the baseline PCS-12 score showed the strongest association with the outcome, indicating that a one-unit increase in baseline PCS-12 score was associated with significantly higher odds of decline in PCS-12 score at one-year follow-up (i.e., better physical HRQOL in 2011 was associated with higher odds of decline in 2012) (adjOR=1.06, 95% CI=1.05, 1.07). Among other covariates, significantly lower odds of decline in PCS-12 score were observed for younger age (<45 years vs. 45–64 years), while significantly higher odds of decline in PCS-12 score were observed for lower income levels (e.g., <$30,000 vs. >$100,000), unemployment (vs. employed), and the presence of clinically meaningful depressive symptoms (vs. absence) (all assessed at baseline).

Findings from the original model (Table 15.1) remained largely consistent after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”) (Table D5.A). After the baseline PCS-12 score was excluded from the adjusted model (Table D5.B), younger age, lower income and unemployment were no longer statistically significant.

Logistic Regression Models for Physical HRQOL: Anxiety Cohort (Table 15.2) – Among respondents diagnosed with anxiety, 31.1% (354/1140) reported a clinically meaningful decline in PCS-12 score (i.e., decline of ≥3 points) between baseline and follow-up surveys. Baseline anxiety treatment status was not significantly associated with a clinically meaningful decline in PCS-12 score in either crude or adjusted analyses (adjOR=1.17; 95% CI=0.86, 1.60). After adjusting for key covariates, the baseline PCS-12 score showed the strongest association with the outcome, indicating that a one-unit increase in baseline PCS-12 score was associated with significantly higher odds of decline in PCS-12 score at one-year follow-up (i.e., better physical HRQOL in 2011 was associated with higher odds of decline in 2012) (adjOR=1.07, 95% CI=1.05, 1.08). Among other covariates, significantly higher odds of a clinically meaningful decline in PCS-12 score were observed for lower income levels (e.g., <$30,000 vs. >$100,000) and unemployment (vs. employed) (all assessed at baseline).

Findings from the original model (Table 15.2) remained largely consistent after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”) (Table D6.A). After the baseline PCS-12 score was excluded from the adjusted model, less consistent findings were observed for lower income, and no statistically significant association was found for unemployment (Table D6.B).

Table 13.A Distribution of respondents' baseline sociodemographic characteristics, by response to the RAND-12 at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety. (n, column%, unless otherwise noted)

Baseline Sociodemographic Characteristics (2011)	**Spring 2012 RAND-12 Aggregate Scores**									
	Depression Cohort[a] (n=3470)					**Anxiety Cohort**[b] (n=1443)				
	Provided[c] (n=2784)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1140)		Missing[d] (n=303)		*p*-value
Baseline treatment status										
- Receiving treatment	2361	(84.8)	590	(86.0)	0.43	840	(73.7)	227	(74.9)	0.66
- Not receiving treatment	423	(15.2)	96	(14.0)		300	(26.3)	76	(25.1)	
Country of Enrolment										
- USA	2757	(99.1)	672	(99.0)	0.68	1130	(99.3)	296	(98.7)	0.29
- Other	24	(0.9)	7	(1.0)		8	(0.7)	4	(1.3)	
Missing	3		7			2		3		
Year of birth										
- ≤1946	341	(12.3)	94	(13.8)	**0.0027**	112	(9.8)	24	(8.0)	**0.050**
- 1947–1953	767	(27.6)	140	(20.5)		246	(21.6)	52	(17.3)	
- 1954–1959	687	(24.7)	167	(24.5)		285	(25.0)	64	(21.3)	
- 1960–1966	566	(20.3)	161	(23.6)		252	(22.1)	79	(26.3)	
- ≥1967	422	(15.2)	120	(17.6)		243	(21.4)	81	(27.0)	
Missing	1		4			2		3		
Age in 2011 (years)										
- <45	422	(15.2)	120	(17.6)	0.12	243	(21.4)	81	(27.0)	**0.095**
- 45–64	2020	(72.6)	468	(68.6)		783	(68.8)	195	(65.0)	
- ≥65	341	(12.3)	94	(13.8)		112	(9.8)	24	(8.0)	
Missing	1		4			2		3		
Sex										
- Female	2311	(83.0)	577	(84.5)	0.37	993	(87.3)	256	(85.1)	0.31
- Male	472	(17.0)	106	(15.5)		145	(12.7)	45	(15.0)	
Missing	1		3			2		2		
Race										
- White	2520	(90.6)	555	(81.3)	**<0.0001**	1016	(89.3)	231	(77.0)	**<0.0001**
- People of Colour/Other	261	(9.4)	128	(18.7)		122	(10.7)	69	(23.0)	
Missing	3		3			2		37		
Marital status										
- Married/cohabitating	1877	(68.1)	418	(62.2)	**0.0038**	748	(66.3)	187	(63.2)	0.31
- Single/living alone	881	(31.9)	254	(37.8)		380	(33.7)	109	(36.8)	
Missing	26		14			12				
Residence										
- Private residence	2606	(94.5)	612	(91.2)	**0.0017**	1066	(94.6)	276	(93.9)	0.64
- Living with assistance	153	(5.6)	59	(8.8)		61	(5.4)	18	(6.1)	

Baseline Sociodemographic Characteristics (2011)	**Spring 2012 RAND-12 Aggregate Scores**									
	Depression Cohort[a] (n=3470)					**Anxiety Cohort**[b] (n=1443)				
	Provided[c] (n=2784)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1140)		Missing[d] (n=303)		*p*-value
Missing	25		15			13		9		
Education										
- Secondary School/GED	814	(29.7)	232	(35.0)	**0.0085**	338	(30.1)	113	(39.0)	**0.0037**
- Associate/Technical Degree	491	(17.9)	131	(19.8)		209	(18.6)	60	(20.7)	
- Bachelor's Degree	807	(29.5)	176	(26.6)		326	(29.0)	74	(25.5)	
- Post Bachelor's Degree	628	(22.9)	124	(18.7)		251	(22.3)	43	(14.8)	
Missing	44		23			16		13		
Income										
- <$30,000	676	(24.3)	214	(31.2)	**0.0005**	302	(26.5)	90	(29.7)	0.53
- $30,000–$50,000	494	(17.7)	127	(18.5)		200	(17.5)	68	(19.1)	
- $50,001–$100,000	729	(26.2)	152	(22.2)		270	(23.7)	72	(23.8	
- > $100,000	367	(13.2)	65	(9.5)		154	(13.5)	33	(10.9)	
- Unanswered/missing	518	(18.6)	128	(18.7)		214	(18.8)	50	(16.5)	
Employment										
- Employed	943	(33.9)	192	(28.0)	**0.0033**	409	(35.9)	87	(28.7)	**0.020**
- Unemployed/missing	1841	(66.1)	494	(72.0)		731	(64.1)	216	(71.3)	
Health insurance										
- Private	1229	(44.2)	260	(37.9)	**0.026**	505	(44.3)	119	(39.3)	0.26
- Private and public	856	(30.8)	234	(34.1)		336	(29.5)	91	(30.0)	
- Public	607	(21.8)	163	(23.8)		249	(21.8)	81	(26.7)	
- Uninsured	92	(3.3)	29	(4.2)		50	(4.4)	12	(4.0)	
Missing	0		0			0		0		

[a,b] Respondents missing RAND-12 in 2011 were excluded from analyses: depression cohort ([a] missing n=119); ([b] missing n=44).

[c] Outcome provided in 2011 and 2012

[d] Outcome provided in 2011 but missing in 2012.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; RAND – RAND Health Status Inventory scale (12-Item); USA – United States of America.

Table 13.B Distribution of respondents' baseline clinical characteristics, by response to the RAND-12 at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (n, column%, unless otherwise noted)

Baseline Clinical Characteristics (2011)	**Spring 2012 RAND-12 Aggregate Scores**									
	Depression Cohort[a] (n=3470)					**Anxiety Cohort**[b] (n=1443)				
	Provided[c] (n=2784)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1140)		Missing[d] (n=303)		*p*-value
Spring 2011 NARCOMS Depression score										
- <2	1139	(41.0)	208	(30.5)	**<0.0001**	458	(40.3)	94	(31.0)	**0.0033**
- ≥2	1641	(59.0)	474	(69.5)		680	(59.8)	209	(69.0)	
Missing	4		4			2		0		
Admission to overnight healthcare facility										
- Yes	244	(8.8)	84	(12.2)	**0.0053**	115	(10.1)	36	(11.9)	0.36
- No	2540	(91.2)	602	(87.8)		1025	(89.9)	267	(88.1)	
Self-rated health										
- Excellent/very good/good	1807	(64.9)	398	(58.0)	**0.0008**	712	(62.5)	172	(56.8)	**0.071**
- Fair/poor	977	(35.1)	288	(42.0)		428	(37.5)	131	(43.2)	
Missing	0		0			0		0		
Cognitive impairment										
- Minimal	1126	(40.7)	238	(35.1)	**0.0099**	417	(36.8)	102	(33.8)	0.12
- Moderate	1362	(49.2)	353	(52.0)		589	(51.9)	153	(50.7)	
- Severe	281	(10.2)	88	(13.0)		128	(11.3)	47	(15.6)	
Missing	15		7			6		1		
Fatigue										
- Minimal	417	(15.1)	85	(12.5)	**0.014**	174	(15.3)	35	(11.6)	**0.034**
- Moderate	1325	(47.9)	303	(44.6)		540	(47.6)	131	(43.5)	
- Severe	1027	(37.1)	292	(42.9)		421	(37.1)	135	(44.9)	
Missing	15		6			5		2		
Pain										
- Minimal	1177	(42.3)	257	(37.5)	**<0.0001**	437	(38.4)	100	(33.0)	**0.014**
- Moderate	1145	(41.2)	257	(37.5)		481	(42.3)	122	(40.3)	
- Severe	458	(16.5)	171	(25.0)		219	(19.3)	81	(26.7)	
Missing	4		1			3		0		
Disability (PDDS)										
- Mild	1024	(37.0)	219	(32.2)	**0.054**	488	(42.9)	120	(39.9)	0.61
- Moderate	872	(31.5)	222	(32.7)		377	(33.2)	103	(34.2)	
- Severe	874	(31.6)	239	(35.2)		272	(23.9)	78	(25.9)	
Missing	14		6			3		2		
MCS-12 (mean, SD)	41.7	(11.4)	39.0	(11.6)	**<0.0001**	40.4	(11.3)	37.5	(11.2)	**<0.0001**
PCS-12 (mean, SD)	37.3	(11.1)	36.2	(10.9)	**0.023**	37.9	(11.6)	36.9	(11.5)	0.15

[a,b] Respondents missing RAND-12 in 2011 were excluded from analyses ([a] missing n=119); ([b] missing n=44).[c] Provided both outcomes; [d] Missing Spring 2012 outcome. Bolded estimates indicate p<0.10. Abbreviations: MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; PCS – Physical Component Score; PDDS – Patient Determined Disease Step; RAND – RAND Health Status Inventory scale (12-Item); SD – standard deviation.

Table 13.C Distribution of respondents' baseline MS characteristics, by response to the RAND-12 at one-year follow-up, among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety. (n, column%, unless otherwise noted)

Baseline MS Characteristics (2011)	**Spring 2012 RAND-12 Aggregate Scores**									
	Depression Cohort[a] (n=3470)					**Anxiety Cohort**[b] (n=1443)				
	Provided[c] (n=2784)		Missing[d] (n=686)		*p*-value	Provided[c] (n=1140)		Missing[d] (n=303)		*p*-value
Age of MS symptom onset (years)										
- < 25	843	(30.7)	195	(29.6)	0.16	361	(32.2)	99	(33.6)	0.31
- 25–39	1425	(52.0)	329	(49.9)		582	(51.9)	140	(47.5)	
- ≥ 40	475	(17.3)	135	(20.5)		179	(16.0)	56	(19.0)	
Missing	41		27			18		8		
Year of MS onset										
- ≤ 1980	764	(27.9)	174	(26.4)	**0.0027**	256	(22.8)	68	(23.1)	**0.0002**
- 1981–1985	428	(15.6)	76	(11.5)		171	(15.2)	21	(7.1)	
- 1986–1990	460	(16.8)	104	(15.8)		202	(18.0)	41	(13.9)	
- 1991–1995	460	(16.8)	110	(16.8)		184	(16.4)	55	(18.6)	
- ≥1996	630	(23.0)	195	(29.6)		309	(27.5)	110	(37.3)	
Missing	42		27			18		8		
Age of MS diagnosis (years)										
- <30	522	(19.0)	126	(18.8)	0.29	242	(21.6)	66	(22.5)	0.99
- 30–39	981	(35.7)	219	(32.6)		387	(34.6)	101	(34.4)	
- 40–49	920	(33.4)	231	(34.4)		365	(32.6)	97	(32.0)	
- ≥50	328	(11.9)	95	(14.2)		126	(11.3)	33	(11.2)	
Missing	33		15			20		9		
Year of MS diagnosis										
- ≤1990	730	(26.5)	177	(26.3)	**<0.0001**	240	(21.4)	59	(20.0)	**0.087**
- 1991–1995	540	(19.6)	91	(13.5)		184	(16.4)	36	(12.2)	
- 1996–2000	700	(25.5)	162	(24.1)		282	(25.2)	69	(23.4)	
- ≥2001	781	(28.4)	242	(36.0)		414	(37.0)	131	(44.4)	
Missing	33		14			20		8		
Disease duration (years)										
- ≤10	781	(28.4)	242	(36.1)	**0.0001**	414	(37.0)	131	(44.6)	**0.052**
- 11–20	1240	(45.1)	252	(37.6)		466	(41.6)	104	(35.4)	
- ≥21	730	(26.5)	177	(26.4)		240	(21.4)	59	(20.1)	
Missing	33		15			20		9		
Year of enrolment in NARCOMS										
- ≤2000	1123	(40.4)	226	(33.1)	**<0.0001**	401	(35.2)	79	(26.3)	**0.0087**
- 2001–2004	884	(31.8)	204	(29.9)		330	(29.0)	92	(30.6)	
- ≥2005	776	(27.9)	253	(37.0)		407	(35.8)	130	(43.2)	
Missing	1		3			2		2		

[a,b] Respondents missing RAND-12 in 2011 were excluded from analyses ([a] missing n=119); ([b] missing n=44).[c] Provided both outcomes; [d] Missing outcome in Spring 2012. Bolded estimates indicate p<0.10. Abbreviations: MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; RAND – RAND Health Status Inventory scale (12-Item).

Table 14.1 Unadjusted and adjusted associations between baseline depression treatment status and a clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Unadjusted			Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status[c]						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.97	(0.78, 1.21)	0.78	0.97	(0.77, 1.24)	0.83
Age in 2011						
- <45	0.77	(0.61, 0.98)	**0.030**	0.88	(0.68, 1.14)	0.33
- 45–64	1.0			1.0		
- ≥65	1.15	(0.90, 1.46)	0.26	0.99	(0.75, 1.30)	0.93
Sex						
- Female	1.0			1.0		
- Male	1.23	(1.00, 1.51)	**0.054**	1.31	(1.04, 1.64)	**0.020**
Race						
- White	1.0			1.0		
- People of Colour/Other	0.90	(0.69, 1.19)	0.47	1.12	(0.83, 1.51)	0.44
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.94	(0.79, 1.12)	0.50	1.04	(0.84, 1.28)	0.74
Education						
- Secondary School/GED	1.07	(0.85, 1.33)	0.58	1.22	(0.95, 1.57)	0.12
- Associate/Technical Degree	1.09	(0.85, 1.41)	0.49	1.24	(0.94, 1.63)	0.13
- Bachelor's Degree	1.06	(0.85, 1.33)	0.60	1.08	(0.85, 1.38)	0.52
- Post Bachelor's Degree	1.0			1.0		
Income						
- <\$30,000	1.01	(0.77, 1.33)	0.95	1.15	(0.81, 1.63)	0.43
- \$30,000–\$50,000	1.04	(0.78, 1.39)	0.79	1.18	(0.85, 1.65)	0.32
- \$50,001–\$100,000	1.11	(0.85, 1.45)	0.45	1.17	(0.87, 1.56)	0.30
- > \$100,000	1.0			1.0		
- Unanswered/missing	1.03	(0.78, 1.38)	0.82	1.13	(0.82, 1.56)	0.47
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.10	(0.93, 1.31)	0.26	1.11	(0.90, 1.38)	0.32
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.10	(0.90, 1.34)	0.35	1.10	(0.89, 1.37)	0.39
- Severe	1.28	(1.06, 1.56)	**0.011**	1.18	(0.93, 1.49)	0.18
Baseline MCS-12 score	1.06	(1.05, 1.07)	**<0.0001**	1.06	(1.05, 1.07)	**<0.0001**
Disease duration (years)						
- ≤10	0.91	(0.73, 1.13)	0.39	1.13	(0.88, 1.45)	0.34
- 11–20	0.93	(0.77, 1.13)	0.47	1.00	(0.81, 1.24)	0.99
- ≥21	1.0			1.0		

[a] In 2012, 32.3% (898/2784) of respondents with depression reported a clinically meaningful decline in MCS-12 score (vs. 67.7%, 1886/2784 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=109.

[c] Received treatment at baseline n=2361; did not receive treatment at baseline n=423.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table 14.2 Unadjusted and adjusted associations between baseline anxiety treatment status and a clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Unadjusted			Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status[c]						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.09	(0.82, 1.45)	0.54	1.02	(0.76, 1.39)	0.88
Age in 2011 (years)						
- <45	0.73	(0.52, 1.00)	**0.051**	0.78	(0.54, 1.12)	0.17
- 45–64	1.0			1.0		
- ≥65	1.39	(0.93, 2.09)	0.11	1.06	(0.67, 1.69)	0.79
Sex						
- Female	1.0			1.0		
- Male	1.27	(0.88, 1.83)	0.20	1.23	(0.83, 1.83)	0.30
Race						
- White	1.0			1.0		
- People of Colour/Other	1.14	(0.77, 1.69)	0.53	1.35	(0.88, 2.06)	0.17
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.86	(0.66, 1.13)	0.28	0.93	(0.67, 1.28)	0.65
Education						
- Secondary School/GED	1.27	(0.90, 1.81)	0.18	1.33	(0.90, 1.97)	0.15
- Associate/Technical Degree	1.23	(0.83, 1.82)	0.31	1.24	(0.81, 1.89)	0.33
- Bachelor’s Degree	1.11	(0.78, 1.59)	0.57	1.03	(0.70, 1.50)	0.89
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	1.05	(0.69, 1.59)	0.84	1.04	(0.61, 1.77)	0.90
- $30,000–$50,000	1.11	(0.71, 1.75)	0.64	1.10	(0.66, 1.84)	0.72
- $50,001–$100,000	1.10	(0.72, 1.69)	0.65	1.08	(0.69, 1.71)	0.73
- > $100,000	1.0			1.0		
- Unanswered/missing	0.90	(0.57, 1.41)	0.65	0.79	(0.47, 1.31)	0.35
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.21	(0.93, 1.57)	0.16	1.21	(0.87, 1.69)	0.25
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	0.91	(0.68, 1.22)	0.53	0.88	(0.64, 1.22)	0.46
- Severe	1.51	(1.11, 2.06)	**0.0089**	1.36	(0.94, 1.96)	**0.099**
Baseline MCS-12 score	1.05	(1.03, 1.06)	**<0.0001**	1.05	(1.04, 1.06)	**<0.0001**
Disease duration (years)						
- ≤10	0.92	(0.66, 1.29)	0.62	1.02	(0.69, 1.50)	0.93
- 11–20	0.89	(0.64, 1.24)	0.48	0.93	(0.58, 1.18)	0.83
- ≥21	1.0			1.0		

[a] In 2012, 31.9% (364/1140) of respondents with anxiety reported a clinically meaningful decline in MCS-12 score (vs. 68.1%, 776/1140 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=46.

[c] Received treatment at baseline n=840; did not receive treatment at baseline n=300.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table 15.1 Unadjusted and adjusted associations between baseline depression treatment status and a clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in PCS-12 Score^{a} (2011 to 2012)					
	Unadjusted			Adjusted^{b}		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status^{c}						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.95	(0.76, 1.19)	0.65	0.88	(0.70, 1.12)	0.31
Age in 2011 (years)						
- <45	0.99	(0.79, 1.24)	0.99	0.76	(0.59, 0.98)	**0.033**
- 45–64	1.0			1.0		
- ≥65	0.92	(0.72, 1.18)	0.53	1.03	(0.78, 1.36)	0.84
Sex						
- Female	1.0			1.0		
- Male	0.89	(0.72, 1.10)	0.27	1.01	(0.81, 1.27)	0.92
Race						
- White	1.0			1.0		
- People of Colour/Other	1.28	(0.98, 1.66)	**0.068**	1.20	(0.90, 1.60)	0.21
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.03	(0.87, 1.22)	0.74	0.95	(0.77, 1.16)	0.59
Education						
- Secondary School/GED	0.89	(0.71, 1.11)	0.31	0.85	(0.66, 1.08)	0.17
- Associate/Technical Degree	1.01	(0.79, 1.29)	0.95	0.95	(0.73, 1.25)	0.72
- Bachelor’s Degree	0.89	(0.71, 1.11)	0.29	0.84	(0.67, 1.06)	0.15
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	1.30	(0.98, 1.71)	**0.067**	1.63	(1.15, 2.31)	**0.0059**
- $30,000–$50,000	1.23	(0.92, 1.66)	0.16	1.44	(1.04, 2.01)	**0.031**
- $50,001–$100,000	1.25	(0.95, 1.64)	0.11	1.37	(1.02, 1.84)	**0.038**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.34	(1.00, 1.79)	**0.051**	1.50	(1.08, 2.07)	**0.015**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.06	(0.90, 1.25)	0.50	1.76	(1.42, 2.18)	**<0.0001**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.21	(1.03, 1.43)	**0.020**	1.32	(1.10, 1.57)	**0.0024**
Baseline PCS-12 score	1.04	(1.04, 1.05)	**<0.0001**	1.06	(1.05, 1.07)	**<0.0001**
Disease duration (years)						
- ≤10	1.12	(0.91, 1.39)	0.29	1.13	(0.88, 1.44)	0.35
- 11–20	1.05	(0.87, 1.28)	0.60	1.06	(0.86, 1.31)	0.60
- ≥21	1.0			1.0		

[a] In 2012, 32.9% (915/2784) of respondents with depression reported a clinically meaningful decline in PCS-12 score (vs 67.1%, 1869/2784 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n= 101.

[c] Received treatment at baseline n=2361; did not receive treatment at baseline n=423.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table 15.2 Unadjusted and adjusted associations between baseline anxiety treatment status and a clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)					
	Unadjusted			Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status[c]						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.23	(0.93, 1.62)	0.15	1.17	(0.86, 1.60)	0.31
Age in 2011 (years)						
- <45	0.99	(0.72, 1.35)	0.94	0.80	(0.56, 1.14)	0.22
- 45–64	1.0			1.0		
- ≥65	0.83	(0.54, 1.29)	0.41	0.96	(0.59, 1.57)	0.87
Sex						
- Female	1.0			1.0		
- Male	0.82	(0.56, 1.21)	0.33	0.92	(0.60, 1.39)	0.68
Race						
- White	1.0			1.0		
- People of Colour/Other	1.19	(0.80, 1.76)	0.40	1.14	(0.74, 1.75)	0.55
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.00	(0.76, 1.30)	0.98	0.97	(0.70, 1.33)	0.83
Education						
- Secondary School/GED	0.82	(0.57, 1.16)	0.26	0.74	(0.50, 1.09)	0.13
- Associate/Technical Degree	0.87	(0.59, 1.30)	0.50	0.78	(0.51, 1.20)	0.26
- Bachelor's Degree	0.96	(0.68, 1.37)	0.83	0.88	(0.61, 1.29)	0.52
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.21	(0.78, 1.87)	0.39	2.14	(1.22, 3.77)	**0.0084**
- $30,000–$50,000	1.57	(0.99, 2.49)	**0.056**	2.15	(1.26, 3.68)	**0.0053**
- $50,001–$100,000	1.22	(0.78, 1.91)	0.38	1.65	(1.02, 2.69)	**0.043**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.45	(0.91, 2.29)	0.12	1.89	(1.12, 3.19)	**0.018**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	0.98	(0.76, 1.28)	0.89	1.85	(1.30, 2.63)	**<0.0001**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	0.99	(0.77 1.28)	0.94	1.10	(0.83, 1.47)	0.50
Baseline PCS-12 score	1.05	(1.04, 1.06)	**<0.0001**	1.07	(1.05, 1.08)	**<0.0001**
Disease duration (years)						
- ≤10	0.88	(0.63, 1.24)	0.47	0.90	(0.61. 1.33)	0.60
- 11–20	0.77	(0.55, 1.08)	0.12	0.77	(0.53, 1.11)	0.16
- ≥21	1.0			1.0		

[a] In 2012, 31.1% (354/1140) of respondents with anxiety reported a clinically meaningful decline in PCS-12 score (vs. 69.0%, 786/1140 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=45.

[c] Received treatment at baseline n=840; did not receive treatment at baseline n=300.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

6.0 Discussion

6.1 Summary of Key Findings

In Objective 1, this thesis utilized data from the NARCOMS Spring 2011 survey to explore the correlates and barriers associated with untreated depression and anxiety in MS patients. In Objective 2, this thesis examined the associations between baseline non-treatment and clinically meaningful depressive symptoms and a clinically meaningful decline in mental and physical HRQOL domains at one-year follow-up in a longitudinal sample of MS patients. The following sections highlight the key findings from Objectives 1 and 2.

6.1.1 Overview of Objectives 1A & 1B

In the NARCOMS Spring 2011 cohort, previous diagnoses of depression, anxiety and bipolar disorder were reported by 36%, 15%, and 2% of participants, respectively. Of those reporting a diagnosis of depression, anxiety or bipolar disorder, 15%, 26%, and 24% of participants were not receiving treatment at the time of survey response, respectively.

Multivariable regression analyses explored the correlates of untreated depression and anxiety; bipolar was not pursued due to small sample sizes. In both cohorts, older age was associated with greater odds of not receiving treatment. Younger age was associated with greater odds of untreated depression but not anxiety. Racialized participants had significantly higher odds of not receiving treatment for depression. This association followed a similar direction in the anxiety cohort but did not reach statistical significance. In both cohorts, participants with lower SES (uninsured or only one type of health insurance coverage for depression cohort; lower levels of education for anxiety cohort) had significantly higher odds of not receiving treatment. Participants with clinically meaningful depressive symptoms and those with more severe levels of disability (and moderate levels, for depression cohort only) had significantly lower odds of not receiving treatment for depression or anxiety.

6.1.2 Overview of Objectives 1C, 1D & Sensitivity Analyses for Objective 1B

Descriptive analyses explored the prevalence and correlates of mental health treatment barriers (i.e., predisposing, enabling and need factors). We acknowledge that the sociodemographic and clinical correlates assessed in descriptive analyses may also represent population characteristics under Andersen's Behavioural Model (e.g., age as a predisposing factor, health insurance as an enabling factor, depressive symptoms as a need factor) (Andersen, 1995). Andersen's Model is dynamic, and predisposing, enabling and need factors can influence each other (Andersen, 1995). As such, our descriptive analyses allowed us to explore the associations between correlates and barriers within similar domains (e.g., age and barriers representing predisposing factors) and between different domains (e.g., depressive symptoms and barriers representing predisposing factors).

Of those not receiving treatment for depression or anxiety, over half of participants were not receiving treatment due to need factors (i.e., “not having symptoms now”). Over one-third of participants reported predisposing factors as barriers to mental health treatment (i.e., “personal choice or decision,” followed by “did not know where to get care), while approximately 20% of participants were untreated due to enabling factors (e.g., cost-barriers, insurance-barriers, transportation/accessibility barriers).

Participants with younger ages (depression cohort only), lower levels of education (depression cohort only), clinically meaningful depressive symptoms and higher levels of fatigue were significantly more likely to report predisposing factors. Racialized participants (anxiety cohort only), those with lower levels of SES, clinically meaningful depressive symptoms, and more severe levels of impairment (cognitive impairment and fatigue) were significantly more likely to report enabling factors. Participants with earlier birth cohorts (anxiety cohort only), higher levels of SES, more mild levels of impairment (cognitive impairment and fatigue), as well as those without clinically meaningful depressive symptoms were significantly more likely to report need factors. These results indicated that our untreated samples contained a mix of participants: those who were untreated while currently exhibiting clinically meaningful depressive symptoms and those who were untreated and not currently exhibiting clinically meaningful depressive symptoms.

Given the mixed nature of our outcome group, we revisited our multivariable regression models by excluding participants who reported need factors (i.e., “not having symptoms now”) as their only reason for non-treatment. Upon excluding this group from adjusted regression analyses, key findings were generally consistent with our original models. Measures of low SES (uninsured for depression cohort; low levels of education for anxiety cohort) showed more pronounced associations with untreated outcomes. In the depression cohort, the association between clinically meaningful depressive symptoms reversed direction, though this association was not significant. Race (for depression cohort) and clinically meaningful depressive symptoms (for anxiety cohort) were no longer significantly associated with untreated outcomes.

6.1.3 Overview of Objective 1E

In descriptive analyses, we explored the prevalence and correlates of treatment modalities in those receiving treatment for depression or anxiety. Of those receiving treatment for depression or anxiety, less than one-third of participants were receiving the recommended combination of psychotherapy and medication. In both cohorts, participants who were single or living alone, those with younger ages, higher levels of education, clinically meaningful depressive symptoms, and more severe levels of cognitive impairment and fatigue were significantly more likely to be treated with both psychotherapy and medication. Uniquely, those who were unemployed (anxiety cohort only) and those with more mild levels of disability (depression cohort only) were more likely to be treated with both psychotherapy and medication. In the depression cohort, racialized participants were significantly less likely to be treated exclusively with medication relative to White participants. Of those receiving treatment for depression or anxiety, approximately two-thirds of participants had clinically meaningful depressive symptoms. These results suggest that depression and anxiety may have been sub-optimally treated in many of our participants.

6.1.4 Overview of Objective 2A

Longitudinally, this study investigated the temporal association between baseline mental health non-treatment and clinically meaningful depressive symptoms at one-year follow-up. Over half of baseline participants reported clinically meaningful depressive symptoms at one-year follow-up. Crude analyses indicated that baseline non-treatment for depression and anxiety were associated with lower odds of clinically meaningful depressive symptoms at one-year follow-up; however, these associations were no longer significant after adjusting for baseline depressive scores. Among model covariates, significantly greater odds of clinically meaningful depressive symptoms at one-year follow-up were observed for males (anxiety cohort only), racialized participants (depression cohort only), those with clinically meaningful depressive symptoms, lower levels of income and education (latter for depression cohort only), and severe disability at baseline. Significantly lower odds of clinically meaningful depressive symptoms at one-year follow-up were observed for participants with older ages at baseline (≥65 years vs. 45–64 years) in the anxiety cohort.

In sensitivity analyses, key findings were generally consistent with the original models after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”). In the depression cohort, older age at baseline (≥65 years vs. 45–64 years) was associated with significantly lower odds of clinically meaningful depressive symptoms at follow-up. After baseline NARCOMS Depression score was excluded from adjusted analyses, baseline non-treatment for depression was associated with significantly lower odds of clinically meaningful depressive symptoms at follow-up (finding not observed in the anxiety cohort). In both cohorts, many model covariates showed significant associations with the one-year outcome.

6.1.5 Overview of Objective 2B

Longitudinally, this study investigated the temporal association between baseline mental health non-treatment and a clinically meaningful decline (≥3 points) in mental and physical HRQOL scores at one-year follow-up. Approximately one-third of baseline participants reported a decline in physical or mental HRQOL at one-year follow-up. Contrary to our original hypotheses, baseline mental health treatment status was not associated with a clinically meaningful decline in mental or physical HRQOL at follow-up in crude or multivariable regression analyses. In adjusted analyses, participants with higher baseline MCS-12 and PCS-12 scores had significantly higher odds of a clinically meaningful decline in mental and physical HRQOL at one-year follow-up, respectively. Among other model covariates, significantly higher odds of a clinically meaningful decline in MCS-12 score were observed for males (depression cohort only) and those with severe disability at baseline (anxiety cohort only). Significantly higher odds of a clinically meaningful decline in PCS-12 score were observed for those with lower income levels, unemployed status, and clinically meaningful depressive symptoms (latter for the depression cohort only) at baseline. Significantly lower odds of a clinically meaningful decline in PCS-12 score were observed for those with younger ages (<45 years vs. 45–64 years) at baseline (depression cohort only).

In sensitivity analyses, key findings were generally consistent with the original models after excluding untreated respondents whose only reported treatment barrier at baseline was need factors (i.e., “not having symptoms now”). In the anxiety cohort, racialized participants had significantly greater odds of a decline in MCS-12 score at follow-up. Key findings for baseline treatment status did not change after excluding baseline RAND-12 scores from adjusted analyses. Model covariates were largely consistent compared to original models, with several expected changes.

6.2 Discussion of Key Findings

6.2.1 Prevalence & Treatment of Depression, Anxiety and Bipolar Disorder

A primary objective of this thesis was to explore the prevalence of untreated mental health comorbidities among persons with MS from the NARCOMS Registry. In 2011, participants were most commonly diagnosed with depression (37%), of which only 15% were untreated. While anxiety and bipolar disorder were less prevalent overall (15% and 2.0%, respectively), approximately one-quarter of participants were untreated. Of those receiving treatment for depression or anxiety, less than one-third of participants were receiving both psychotherapy and medication (i.e., recommended treatment). Approximately two-thirds of participants had clinically meaningful depressive symptoms.

Previous studies reported similar proportions of MS patients with depression to be receiving treatment (~85%) (Marrie, Patten, et al., 2018; Raissi et al., 2015). A Canadian study also found medication to be the most common type of depression treatment administered to MS patients (Raissi et al., 2015). Consistent with prior studies, we found that many participants treated for depression continued to report clinically meaningful depressive symptoms despite ongoing treatment (Marrie et al., 2018; Raissi et al., 2015). The persistence of depressive symptoms despite ongoing treatment suggests inadequate management (Koch et al., 2015; Marrie, Patten, et al., 2018; Raissi et al., 2015). Though NARCOMS did not assess the length of treatment, our findings suggest that depression was likely undertreated in many of our study participants.

Similar to the findings of a Canadian investigation, we found anxiety to be undertreated to a greater extent than depression in persons with MS (Marrie, Patten, et al., 2018). In their study, Marrie, Patten, et al. (2018) found many MS patients with anxiety to remain symptomatic despite receiving ongoing treatment. Though the NARCOMS Spring 2011 survey did not assess anxiety symptoms, approximately two-thirds of our participants treated for anxiety reported clinically meaningful depressive symptoms, and depression has been found to predict anxiety in MS patients (Korostil & Feinstein, 2007; Podda et al., 2020).

To date, very few studies have explored the adequacy of bipolar treatment in persons with MS. In a sample of MS patients with bipolar disorder (n=10), a 2017 investigation found that 50% of MS patients with bipolar disorder were receiving psychopharmacotherapies, while the other 50% were treated with antidepressants or antianxiety agents (i.e., not the recommended treatment for bipolar disorders in MS) (Jun-O'connell et al., 2017). Given that bipolar disorder can impair HRQOL to a greater extent than depression in MS patients (Carta, Moro, Lorefice, Picardi, et al., 2014), the undertreatment of bipolar disorder in MS patients presents a substantial cause for concern.

6.2.1.1 Barriers to Mental Health Treatment

We explored the barriers to mental health treatment captured by the NARCOMS survey using Andersen's Behavioural Model of Health Service Utilization. In general, participants who were untreated most commonly report need factors (i.e., "not having symptoms now"), followed by predisposing and enabling factors, as barriers to receiving mental health treatment.

Need Factors – Over half of untreated participants reported need factors (i.e., "not having symptoms now") as barriers to mental health treatment. Descriptive analyses indicated that participants without clinically meaningful depressive symptoms were significantly more likely to report need factors. Indeed, a prior Canadian investigation found elevated depressive symptoms to be a strong predictor of the perceived need for mental health treatment in MS patients (Orr et al., 2018). These findings suggest that participants with lower depressive symptoms may not have perceived a need for mental health treatment.

In descriptive analyses, we also identified a group of untreated participants who reported need factors despite reporting clinically meaningful depressive symptoms. There are several possible explanations for this finding. First, patients may have had difficulties distinguishing a need for mental health treatment due to the overlap between depression and MS symptoms (Methley, Campbell, et al., 2017). Participants' sociodemographic characteristics may have also played a role in this finding. For instance, in the general American population, studies have found the perceived need for mental health treatment to vary by age, race, ethnicity, gender, and SES (notably education) (Mojtabai et al., 2002; Villatoro et al., 2018). In MS patients, Orr et al. (2018) found younger age, but not socioeconomic status or gender, to be associated with greater odds of having a perceived need for mental health treatment. While we did not find age, race, or sex to be associated with need factors, our analyses were limited in size and racial heterogeneity. Future studies with larger, more heterogeneous samples should explore the association between sociodemographic characteristics and the perceived need for mental health treatment in MS patients.

Predisposing Factors – Of those reporting predisposing factors as barriers to mental health treatment, participants most commonly reported non-treatment due to a "personal choice or decision." Patient attitudes and beliefs towards mental health services may have influenced decision-making. Findings from qualitative studies in MS patients have revealed a trend of poor experiences when seeking mental health treatment (Marck et al., 2022; Methley, Chew-Graham, et al., 2017; Rintell et al., 2012). Many MS patients use their past experiences with healthcare providers when deciding to access health services; previous negative when seeking mental health care may deter MS patients from future help-seeking behaviour (Pétrin et al., 2020; Rintell et al., 2012). Sociodemographic characteristics, such as age, race, and gender, may have also influenced decision-making. In a sample of Americans with MS, Pimentel Maldonado et al. (2022) found that Black/African American participants were significantly less likely to believe that their mental health could influence their MS symptoms, and that their healthcare provider would understand their mental health concerns (relative to White MS patients) (Pimentel Maldonado et al., 2022). In general, males and younger adults also tend to have more negative attitudes toward mental health services (Gonzalez et al., 2005; C. S. Mackenzie et al., 2006). Descriptive analyses indicated that younger adults were more likely to report predisposing factors as barriers to depression treatment. Unfortunately, the NARCOMS Spring 2011 survey did not assess patient attitudes towards mental health services. Given that a large proportion of untreated participants chose not to receive treatment, these findings warrant further investigation.

Untreated participants also reported that they "did not know where to get care." A poor understanding of available mental health services could reflect lower levels of mental health literacy (Jorm, 2012). The NARCOMS Spring 2011 survey did not assess health literacy; however, a study using data from the Spring 2012 survey found male participants, those with younger ages, and lower levels of SES to have poorer levels of health literacy (Marrie et al., 2014). In our descriptive analyses, participants with younger age and lower education were more likely to report predisposing factors as barriers to depression treatment. As such, low levels of health literacy may have contributed to MS patients reporting predisposing factors as barriers to depression treatment; further investigation is needed to confirm this hypothesis.

Enabling Factors – Consistent with other MS studies, we found cost, health insurance coverage, and transportation/accessibility to be prominent barriers to accessing mental health treatment (Buchanan et al., 2006; Methley, Campbell, et al., 2017; Minden et al., 2007; Rintell et al., 2012). In this thesis, we found racialized participants (anxiety cohort only), those with low SES, clinically meaningful depressive symptoms, and greater physical limitations to be significantly more likely to report enabling factors. These results align with the findings of prior American studies. For instance, Stepleman et al. (2014) found that Black MS patients were less likely to be diagnosed with depression and to be treated with antidepressants. Other investigations have found Black and Latino MS patients to have lower SES and poorer health insurance coverage relative to White MS patients (Pimentel Maldonado et al., 2022; Wang et al., 2020). Further, prior studies have found MS patients with lower levels of SES (including health insurance and income) and worse levels of physical and mental health to experience greater difficulties accessing care (Minden et al., 2007; Wu et al., 2007). Cumulatively, these results highlight potential inequities in mental health service use among persons with MS.

6.2.2 Sociodemographic Correlates of Untreated Depression and Anxiety

In multivariable regression analyses, we explored the sociodemographic and clinical correlates of untreated depression and anxiety in MS patients. Among the sociodemographic correlates, we found low levels of SES (poor health insurance coverage for depression cohort, low education for anxiety cohort), race (significant for depression cohort only) and older age (and younger for depression cohort) to be significant correlates of untreated mental health comorbidities.

Health Insurance Coverage – Similar to the findings of Minden et al. (2007), we found participants with uninsured status or inadequate health insurance coverage to be more likely to have unmet mental health needs. Minden et al. (2007) found uninsured MS patients to have the most difficulties accessing health services, though MS patients with private health insurance still reported challenges accessing care due to inadequate coverage for mental health services. In general, Americans with MS who are uninsured tend to be Black, in worse health and have low SES (Minden et al., 2007; Wang et al., 2020). MS patients covered by public plans tend to perceive better coverage for health services relative to those with private plans (Pozniak et al., 2014); however, Black MS patients and those with greater levels of disability tend to have lower utilization of publicly funded services (namely Medicaid) (Fabius et al., 2019; McDoom et al., 2012). Disparities in health insurance coverage may present additional barriers to mental health treatment for disadvantaged MS patients.

Our sample was composed of almost entirely American respondents (99%). Given the differences in the structure of health systems between Canada and the United States, our findings may not be generalizable to the Canadian population. Findings from the Canadian general population indicate that long wait times for publicly funded mental health services and inadequate coverage for mental health services from private plans are common barriers to mental health care (Moroz et al., 2020). Nevertheless, future studies should assess the impact of health insurance coverage on the use of mental health services in Canadians with MS.

Education – Education level was not associated with depression treatment status in either crude or multivariable regression analyses. Conversely, a previous NARCOMS investigation found education to be the only significant predictor of untreated depression (Marrie et al., 2009). The difference in our findings could be due to differences in population characteristics. In their study, Marrie et al. (2009) examined the factors associated with untreated depression only in those with probable major depression (CESD scores ≥21), while our analyses were not restricted by depressive symptomology. Prior studies in MS populations have found education to have an inverse association with depressive symptoms (Simpson et al., 2019) and for depressive symptomology to predict the perceived need for mental health care (Orr et al., 2018). As previously mentioned, our untreated samples included a group of participants with relatively high SES whose only reported treatment barrier was need factors (i.e., “not having symptoms now”). In sensitivity analyses excluding these participants, we found the direction of association between lower education and untreated depression (though still not statistically significant) to be more consistent with the direction of those reported by Marrie et al. (2009).

On the other hand, lower education was a significant correlate of untreated anxiety. While there is limited evidence on the factors associated with untreated anxiety in MS, prior studies have generally reported a positive association between educational attainment and the use of mental health services (Garcia & Finlayson, 2009; Gromisch et al., 2020; Minden et al., 2013). Varying levels of mental health literacy may explain the difference in our results between our depression and anxiety cohorts. While mental health literacy has been largely unexplored in MS patients, a NARCOMS study found lower education to be associated with poorer health literacy in study participants (Marrie et al., 2014). Given that anxiety is underdiagnosed and undertreated to a greater extent than depression in MS patients (Marrie, Patten, et al., 2018), individuals with lower education may experience greater difficulty identifying a need for anxiety treatment and navigating available services. An investigation of mental health literacy in a sample of American students found that participants had a poorer recognition of anxiety disorders relative to depressive disorders (Paulus et al., 2015). Future studies could explore the association between mental health literacy and unmet mental health needs in MS patients.

Race – In this study, we found racialized MS patients to have significantly higher odds of untreated depression relative to White MS patients. While race was not a significant correlate of untreated anxiety in multivariable regression analyses, racialized MS patients were significantly more likely to report enabling factors as barriers to anxiety treatment. The association between race and mental health service use among MS patients varies across studies, likely due to differences in the sample population and the assessment of race and ethnicity. In this study, we assessed race as a binary outcome (White vs. People of Colour/Other) due to a lack of variability within our data; however, prior investigations have employed different approaches. For example, Marrie et al. (2009) assessed race as "White, Black, or Other" in NARCOMS participants, while Pimentel Maldonado et al. (2022) explored race (Black/African American vs. White) and ethnicity (Hispanic/Latino vs. Non-Hispanic/Latino) separately in a sample of American survey respondents. We acknowledge that our binary assessment of race is an oversimplified measure and likely does not capture the differences in mental health service use across racial and ethnic groups (Buchanan et al., 2010; Cook et al., 2017).

Despite these limitations, our results highlight racial disparities in the treatment of mental health comorbidities (associations more pronounced among those with depression relative to those with anxiety). Since mental health comorbidities are associated with disability progression (McKay, Tremlett, et al., 2018) and unmet needs adversely impact HRQOL and health behaviours (Ploughman et al., 2020; Ponzio et al., 2020), disparities in mental health treatment could worsen health outcomes for racialized MS patients. The racial disparities identified in this study are likely influenced by social, economic, and environmental factors (Amezcua et al., 2021). Further research is needed to more clearly identify and characterize racial disparities in mental health outcomes in persons with MS.

Age – In this study, MS patients with younger ages (<45 years) were more likely to be untreated for depression, while MS patients with older ages (≥65 years) were more likely to be untreated for both depression and anxiety. In our descriptive analyses, younger adults were more likely to report predisposing factors (depression cohort only), while older adults were more likely to report need factors (anxiety cohort only) as barriers to mental health treatment. These findings suggest that the barriers to mental health care may have differed between age groups.

Prior studies have generally found age and depressive symptoms tend to be inversely associated in MS patients (Beal et al., 2007; Chwastiak et al., 2002; Ensari et al., 2013). In a representative sample of Australians, a prior study found that older adults were less likely to have a perceived need for mental health care but were more likely to receive treatment if needed (Forbes et al., 2017). Indeed, a NARCOMS study found that younger adults with MS were significantly less likely to receive mental health services from a mental health provider (e.g., psychologist, psychiatrist, social worker) relative to older adults with MS (Buchanan et al., 2009). Patient satisfaction with the quality and accessibility of mental health care may also differ across age groups, as younger adults tend to report greater levels of dissatisfaction towards mental health services relative to older adults (Gonzalez et al., 2005; Iezzoni et al., 2002; C. S. Mackenzie et al., 2006). Taken together, it is possible that younger adults with MS may not have accessed mental health services due to more negative attitudes towards mental health services, while older adults may not have had a perceived need for mental health treatment due to lower depressive symptoms. Attitudes and satisfaction with mental health treatment should be further explored in younger adults with MS.

6.2.3 Clinical Correlates of Untreated Depression and Anxiety

In multivariable regression analyses, participants with clinically meaningful depressive symptoms and severe disability had significantly lower odds of mental health non-treatment.

Severity of Depressive Symptoms – A previous investigation found MS patients with more severe mental health symptoms to have an increased likelihood of receiving mental health treatment (Minden et al., 2013). Indeed, a previous investigation found elevated levels of depressive symptoms to be a strong predictor of the perceived need for mental health treatment in MS patients (Orr et al., 2018). Participants with more severe depressive symptoms may simply be more likely to seek out mental health care relative to those with more mild symptomology (Koch et al., 2015). That being said, we found that participants with clinically meaningful depressive symptoms were significantly more likely to report predisposing and enabling factors as barriers to receiving treatment for depression or anxiety. These results suggest that MS patients with clinically meaningful depressive symptoms also experienced greater barriers to mental health care. An American study found MS patients with lower mental HRQOL to report significantly greater difficulties accessing mental health care (Wu et al., 2007). In the general population, Americans with more severe mental illnesses are more likely to have lower SES, worse health, and greater difficulties accessing mental health care (Viron & Stern, 2010). As such, disadvantaged MS patients may experience greater barriers to mental health care despite reporting clinically meaningful depressive symptoms.

Disability – We found MS patients with more severe levels of disability to have a lower likelihood of untreated depression and anxiety. In general, MS patients with higher levels of physical impairment have greater health service utilization (Hansen et al., 2002; McKay, Marrie, et al., 2018; Pétrin et al., 2020). Depressive symptoms and level of physical impairment also tend to be positively correlated in MS patients (Chwastiak et al., 2002; Patten et al., 2005). MS patients with more severe disability may have less difficulty accessing mental health treatment given their elevated usage of general health services.

While more severe levels of impairment can act as barriers to care (Becker & Stuifbergen, 2004; Wu et al., 2007), we did not find disability to be associated with reporting mental health treatment barriers. Instead, participants with severe levels of cognitive impairment and fatigue were significantly more likely to report enabling factors as barriers to mental health care. These results suggest that other aspects of physical impairment, apart from disability, may impede access to mental health care in MS patients.

6.2.4 Predictors of Clinically Meaningful Depressive Symptoms at One-Year Follow-up

Longitudinally, this thesis explored the association between baseline mental health non-treatment and clinically meaningful depressive symptoms at one-year follow-up. The prevalence of clinically meaningful depressive symptoms at one-year follow-up (~56%) was similar to our baseline estimates (~60%); prior estimates range from 20% to 60%, depending on methodology (McGuigan & Hutchinson, 2006; Minden et al., 1987; Solaro et al., 2016). Previous longitudinal analyses have also found depressive symptoms to remain relatively consistent in their samples over time (Beal et al., 2007; Ensari et al., 2013; Koch et al., 2015). The persistence of elevated symptomology suggests that depression is largely chronic in persons with MS (Koch et al., 2015).

Baseline Mental Health Treatment Status & Depression Symptoms – We did not find baseline mental health treatment status to be a significant predictor of clinically meaningful depressive symptomology after adjusting for baseline depressive symptoms and other confounders. A longitudinal study in MS patients found consistent antidepressant use to be associated with greater odds of depression at multiple timepoints over four years (Koch et al., 2015). Consistent with the findings of Koch et al. (2015), we found baseline depressive symptoms to be the strongest predictor of later depressive symptomology in MS patients. MS patients with more severe symptoms tend to have a greater perceived need for mental health treatment, so they may be more likely to seek out mental health treatment (Koch et al., 2015; Orr et al., 2018). The inadequate management of depression may also contribute to persistent depressive symptoms in MS patients over time (Koch et al., 2015). Due to the wording of the NARCOMS survey, we only had one measure of treatment status. Future longitudinal studies should assess treatment status at multiple timepoints to more clearly identify the association between unmet mental health needs (e.g., undertreated, untreated) and depressive symptoms in MS patients.

Other Model Covariates – The predictors in this study vary from other longitudinal studies due in part to differences in population characteristics, and methodological and modelling approaches (e.g., MS patients with probable vs. physician-diagnosed depression, adjusting vs. not adjusting for baseline scores, variability in model confounders). Nevertheless, the direction of association of our predictors was generally consistent with prior studies. Similar to previous literature, we found racialized MS patients, those with lower levels of SES, and those with more severe disability to have higher odds of clinically meaningful depressive symptoms at follow-up (Chwastiak et al., 2002; Ensari et al., 2013; Kister et al., 2021; Patten et al., 2005; Wang et al., 2020). While prior studies have generally not found sex to be associated with more severe depressive symptomology (Beiske et al., 2008; Chwastiak et al., 2002), we found males to have greater odds of severe depressive symptomology at one-year follow-up (particularly for the anxiety cohort). Since males tend to experience a more rapid disease progression relative to females (in those with a relapsing-remitting phenotype) (Confavreux & Vukusic, 2014; Manouchehrinia et al., 2016; Ribbons et al., 2017) and prior studies have generally found higher levels of disability to be associated with severe depressive symptoms (Chwastiak & Ehde, 2007; Ormel et al., 1999; Patten et al., 2005), higher levels of physical impairment in males (as suggested by our descriptive findings for sex and physical HRQOL scores) may have contributed to worse depressive outcomes.

6.2.5 Predictors of Decline in Health-Related Quality Life at One-Year Follow-up

Longitudinally, this thesis also explored the association between baseline mental health non-treatment and a decline in mental and physical HRQOL at one-year follow-up. Approximately one-third of our baseline participants reported a clinically meaningful decline in mental or physical HRQOL at one-year follow-up. Prior studies using similar methods of assessing change in HRQOL scores (i.e., decrease of ≥3 points in RAND-12/36 HRQOL aggregate scores) reported similar estimates in MS patients (Janzen et al., 2013; Marrie, Bernstein, et al., 2023). For instance, a 2013 NARCOMS investigation found that 36% and 40% of participants declined in mental and physical HRQOL, respectively, over five years (Janzen et al., 2013).

Baseline Mental Health Treatment Status – We did not find baseline treatment status to be associated with a clinically meaningful decline in mental or physical HRQOL at one-year follow-up. Due to the nature of the data used in this investigation, we could not assess participants' prior treatment status or their continuation of treatment following their initial survey response. As such, it is understandable that a singular assessment of mental health treatment, without any indication of continuation, may be less likely to show a significant association with a decline in mental and physical HRQOL after one year.

Baseline HRQOL Scores – We found baseline HRQOL scores to have the strongest association with a clinically meaningful decline in mental and physical HRQOL at one-year follow-up. Baseline HRQOL scores are important predictors of later health status (D. M. Miller et al., 2003). Consistent with a prior NARCOMS investigation, we found that participants with higher mental and physical HRQOL scores at baseline were more likely to decline over time (Janzen et al., 2013). MS is a progressive neurologic condition, so it is reasonable that disability and symptomatic burden will increase over time (Kister et al., 2021). Participants with better mental and physical HRQOL may simply have had more room to decline over time compared to those with poorer HRQOL at baseline.

Other Model Covariates – As expected, our baseline HRQOL scores were strongly associated with many of our model covariates, so our findings for other model covariates may differ from other longitudinal studies that did not adjust for baseline HRQOL scores. Nevertheless, our model predictors generally showed a consistent direction of association with poor mental and physical HRQOL outcomes relative to prior studies (Hopman et al., 2007;

Janzen et al., 2013; Lo et al., 2021; O'Mahony et al., 2022; Wu et al., 2007). In this study, we found the male sex to predict a later decline in mental HRQOL (among those with depression). A prior Italian found that the impact of disability on mental HRQOL was more substantial in males than females, indicating that males were more likely to have lower mental HRQOL as levels of physical impairment increased (Casetta et al., 2009). Younger age was associated with lower odds of decline in physical HRQOL (significant for depression cohort only); previous investigations in MS patients have found physical impairment to worsen with age (Buchanan et al., 2009; Kister et al., 2013, 2021). Consistent with previous studies, we found low levels of SES (income, unemployment status) and elevated depressive symptoms at baseline (depression cohort only) to be significantly associated with worse physical HRQOL outcomes (Hopman et al., 2007; Janzen et al., 2013; Lo et al., 2021).

6.3 Implications

6.3.1 Implications for Future Research

In exploring the prevalence and correlates of unmet mental health needs, this project helped to characterize mental health service use among MS patients diagnosed with depression and anxiety, identify common barriers to mental health care, and explore the longitudinal health consequences of untreated mental health comorbidities. The results and limitations of this study helped to identify opportunities for future investigation.

We did not pursue analyses in those with bipolar disorder due to small sample sizes; however, our findings indicate that bipolar disorder may be undertreated to a greater extent than depression. Bipolar disorder in MS has been poorly researched to date, though a prior study indicated that bipolar disorder may be underdiagnosed in MS patients (Carta, Moro, Lorefice, Trincas, et al., 2014). As bipolar disorder has been associated with even greater impairments in HRQOL than depression (Carta, Moro, Lorefice, Picardi, et al., 2014), future studies should explore the prevalence and correlates of bipolar disorders in MS.

Due to the wording of the NARCOMS survey, we could not explore the barriers to mental health treatment in those without a prior psychiatric diagnosis. Receiving a psychiatric diagnosis can be a barrier itself; racialized MS patients and those with lower levels of SES, more severe mental health concerns, and greater levels of physical impairment may have been underrepresented in our sample (Marrie et al., 2009; Moroz et al., 2020; Stepleman et al., 2014; Wu et al., 2007). While this study highlighted general racial disparities in the use of mental health services in NARCOMS participants with a prior psychiatric diagnosis, the lack of racial diversity was evident in our samples. Prior studies have found that attitudes toward mental health services and help-seeking behaviours can vary between Black and Latino persons with MS (Buchanan et al., 2010; Pimentel Maldonado et al., 2022). As such, identifying the disparities in mental health outcomes for MS patients representing racial and ethnic minorities could help to inform more strategic and culturally-sensitive public health initiatives. To capture a more representative sample of MS patients, future studies should explore the barriers and correlates of mental health service use in participants with and without a prior psychiatric diagnosis, and use better measurements of race and ethnicity.

In our second objective, we did not find untreated mental health comorbidities to be associated with depressive symptoms or with changes in mental and physical HRQOL status at one-year follow-up. That being said, prior studies have found psychological and pharmacological interventions to improve current levels of HRQOL (Hart et al., 2005; McCabe et al., 2009). In addition, a recent cross-sectional study assessed the impact of untreated and undertreated depression on health behaviours and HRQOL (Ploughman et al., 2020). To build on findings from this study, future longitudinal studies could assess the mental and physical HRQOL of MS patients who are untreated, undertreated, or receiving the recommended treatment for depression at multiple timepoints to explore the impact of unmet mental health needs on the trajectory of HRQOL over time.

6.3.2 Implications for Clinical Care

This study identified predisposing, enabling, and need factors as barriers to mental health treatment in persons with MS. Targeting the common barriers to care could help providers better meet the needs of their patients. In MS patients, past experiences with healthcare providers strongly influence future help-seeking behaviour (Pétrin et al., 2020). Negative experiences can act as strong deterrents to care, while positive experiences can improve patient satisfaction, promote greater participation in their treatment, and facilitate easier access to care (Methley, Campbell, et al., 2017; Pétrin et al., 2020; Yorkston et al., 2005). Educational interventions targeted toward healthcare providers to promote a collaborative, patient-centred approach could help to improve mental health outcomes for their patients (Yorkston et al., 2005).

Further, providing MS patients with earlier interventions to promote emotional and psychological skills could improve health outcomes (Tan-Kristanto & Kiropoulos, 2015).

Promoting emotional resilience and adaptive coping skills early on in the disease course can help MS patients better manage symptoms of depression and anxiety (Tan-Kristanto & Kiropoulos, 2015). Encouraging MS patients to engage in positive life experiences and to practice self-compassion could help to improve their mental well-being and their overall quality of life (McCabe et al., 2009; Nery-Hurwit et al., 2018; Pakenham & Cox, 2009; Phillips & Stuifbergen, 2008; Silverman et al., 2017). While sociodemographic and clinical risk factors can still influence mental health outcomes, resilience is a modifiable and targetable skill that can be developed through interventions (Silverman et al., 2017). Prior studies have found telehealth services to be a feasible and affordable method of delivering resilience-based interventions and support groups to MS patients (Halstead et al., 2020; Leavitt et al., 2019).

6.3.3 Implications for Public Policy

Current results suggest that targeting predisposing, enabling and need factors could improve access for MS patients. For instance, interventions focused on improving the health literacy of MS patients could help them to better navigate health services (Bonabi et al., 2016). Since MS patients with low SES tend to have worse health literacy (Marrie et al., 2014), these strategies could help promote help-seeking behaviour in economically disadvantaged MS patients. Improving the health literacy of MS patients could also help to reduce adverse health behaviours and decrease the frequency of emergency room visits (Marrie et al., 2014), which may reduce the healthcare expenditures associated with mental health comorbidities (Bhattacharjee et al., 2021). A prior study found that Black MS patients were less likely to agree that mental health concerns could worsen their MS (Pimentel Maldonado et al., 2021); thus, collaboration with community-based resources, such as local chapters of national MS societies, could be useful for developing accessible and culturally sensitive resources for racialized MS patients to improve access to care.

Interventions targeted toward healthcare providers may help to increase their skills in detecting mental health comorbidities in MS, as well as improve their awareness of existing mental health services and potential barriers to these services for vulnerable subgroups of the population (Methley, Chew-Graham, et al., 2017). Providing healthcare professionals with additional resources and training on facilitating culturally appropriate care could help to build trust with racialized MS patients (Pimentel Maldonado et al., 2022). Increasing provider knowledge could help to facilitate easier access to mental health treatment for their patients (Methley, Chew-Graham, et al., 2017).

Future initiatives targeting enabling factors (i.e., access barriers) could help to increase the availability and accessibility of mental health treatment for MS patients. Strategies focused on integrating mental health services into existing MS centers could facilitate easier access to care for Black and Latino MS patients (Pimentel Maldonado et al., 2022), improve the coordination of care between providers (Minden et al., 2013), and improve mental health outcomes for patients (Cimpean & Drake, 2011). Offering more community-based resources, such as support groups, could be used to improve mental health outcomes (Wakefield et al., 2013). More long-term initiatives could work to increase the availability of culturally competent mental health services and foster greater diversity in MS care to address racial disparities in health outcomes (Charleston & Ovbiagele, 2021; Pimentel Maldonado et al., 2022). Telehealth resources are a valuable tool for expediting care, improving access to health services, particularly for those with greater physical limitations, and reducing travel-related costs for patients (Chen et al., 2022). Given that telehealth services for mental health care have expanded following the COVID-19 pandemic (Chen et al., 2022), continuing to invest and develop telehealth services with various offerings (e.g., providing both phone and video chats, developing video tutorials to help patients navigate virtual spaces, offering services in multiple languages, promoting culturally-competent care) could help to increase the accessibility of mental health treatment for MS patients (Nouri et al., 2020).

While targeting inequities in patients MS will require system-level interventions across the healthcare continuum (Amezcua et al., 2021), identifying, and subsequently addressing, the barriers to mental health may improve access to care and mental health outcomes for persons with MS. Better meeting the mental health needs of MS patients may reduce the adverse health and economic consequences associated with mental health comorbidities (Bhattacharjee et al., 2021; Ponzio et al., 2020).

6.4 Strengths and Limitations

6.4.1 Study Strengths

This study had multiple strengths. First, this study used data collected by NARCOMS, a registry that has been validated for self-reported MS diagnoses and other patient-reported outcomes (Marrie, Cutter, et al., 2008; Marrie et al., 2007; Nortvedt et al., 2000). This study also had a large cohort size, which allowed us to explore the correlates of untreated depression and anxiety separately. We assessed multiple measures of SES, health status, and disease state to comprehensively describe our cohorts. In our multivariable regression analyses, model covariates were purposely selected to provide meaningful adjustments for potential confounding. Exploring the barriers to mental health treatment helped to contextualize the results of our regression analyses. Our sensitivity analyses provided additional insight into the effect of need factors on treatment outcomes and highlighted the robustness of model covariates.

The longitudinal component of this study provided insight into health disparities in depressive and HRQOL outcomes over time. Our multivariable regression analyses adjusted for baseline scores to more accurately assess the impact of baseline covariates on subsequent health outcomes (D. M. Miller et al., 2003). Taken together, the results from this study helped address previous knowledge gaps in the literature and defined important next steps for future research.

6.4.2 Study Limitations

This study had several limitations. First, the NARCOMS is a volunteer-based, self-reported registry. NARCOMS is not representative of the general MS population in the United States (Marrie, Cutter, et al., 2021). The nature of registry data introduces potential sources of bias, notably in the underrepresentation of racial and ethnic minorities, patients who are economically disadvantaged, and patients with the most severe disease states (Rooney et al., 2017). In this study, our cross-sectional sample lacked heterogeneity for key characteristics (e.g., race, ethnicity), and the participants in our longitudinal sample differed from non-respondents on many sociodemographic, clinical, and disease-related characteristics.

The lack of racial and ethnic diversity in our sample is reflective of greater issues in MS research, as minority groups are consistently underrepresented in clinical trials (Avasarala, 2014; Khan et al., 2015). In 2023, an international workshop of stakeholders and specialists recommended that multi-level strategies should be employed to enhance diversity in MS clinical trials (Marrie, Chataway, et al., 2023). Among the recommendations, future steps in MS research should consider broadening inclusion criteria, promoting community engagement and education initiatives, and facilitating culturally competent training for researchers (Marrie, Chataway, et al., 2023). Given the characteristics of our sample population, our findings may be limited in their generalizability to larger MS populations, notably those representing minority groups, with lower SES, and more severe clinical phenotypes. In addition, our findings may not be generalizable to

MS patients in Canada due to differences in the healthcare systems and the health insurance landscape. To capture a more representative sample of persons with MS, future studies could utilize administrative data sources and medical records in conjunction with registry data.

Second, this study used self-reported data to assess mental health comorbidities. Participants may not have remembered receiving a previous psychiatric diagnosis, which could have led to an underestimation of our prevalence estimates. That being said, prior studies support the validity of self-reported diagnoses of depression, anxiety, and bipolar disorder (Cluss et al., 1999; Roemer et al., 1995; Sangha et al., 2003). Current treatment status, a key variable in this study, was also self-reported. Participants may have misreported or misremembered their current treatment status, particularly among participants reporting more than one condition. To minimize this concern, we assessed multiple responses to assign participants to the most relevant treatment group (diagnostic status, treatment type, and self-reported barriers, if necessary), and we excluded participants missing a discernable treatment status. While misclassification remains a potential concern, we do not believe it presents a serious limitation to this study.

In addition, the NARCOMS Spring 2011 survey did not assess anxiety symptoms, so we could not assess the association between clinically meaningful anxiety symptoms and untreated anxiety. A previous study found clinically meaningful depressive symptoms to predict clinically meaningful anxiety symptoms in MS (Podda et al., 2020). It is possible that depressive and anxiety symptoms were similar among study participants; however, we cannot confirm this finding.

Finally, the data used in this study were collected in 2011, which may limit the relevance of these findings. While the estimates reported in this study are consistent with studies using more recent data (Methley, Campbell, et al., 2017; Minden et al., 2013; Raissi et al., 2015; Rintell et al., 2012), the shift towards telehealth services during the COVID-19 pandemic may have reduced barriers to care for many MS patients (Chen et al., 2022). As such, the prevalence of untreated depression and anxiety in MS patients may have decreased in recent years. Recent studies have still reported disparities in telehealth services, notably in racial and ethnic minorities, older adults, those with lower SES, and those with disease-related impairments (e.g., visual impairments) (Marrie et al., 2022; Rivera, Aldridge, et al., 2021). The results of this thesis are likely still relevant; however, future studies should use more recent data (2020 onwards) to identify disparities in mental health service use following the COVID-19 pandemic.

6.5 Conclusion

Depression, anxiety, and bipolar disorder are common in persons living with MS. These comorbidities present substantial health and economic challenges for patients and health systems; however, they are frequently undertreated. By assessing the correlates of untreated mental health comorbidities in a large sample of persons with MS, this study identified sociodemographic disparities in the treatment of mental health comorbidities. While baseline unmet health needs were not associated with health outcomes at one-year follow-up, the results of longitudinal analyses identified possible sociodemographic and clinical predictors of depressive symptomology and HRQOL status in MS patients with a prior psychiatric diagnosis. Targeting the predisposing, enabling and need factors identified in this study may improve access to mental health care and subsequent health outcomes for disadvantaged MS patients. The findings of this study add to the literature by identifying important sociodemographic and clinical correlates of mental health service use to be considered in future research. Future studies can build upon this research by exploring disparities in mental health service use across racial and ethnic groups, as well as exploring how the ongoing undertreatment, and the lack of treatment, of mental health comorbidities influence trajectories of depression and HRQOL over time.

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Appendices

Appendix A Description and Coding of Key Variables

Table A1 Description and Coding of Mental Health Treatment Barriers using Andersen's Behavioural Model of Health Service Use.

Barrier Groupings	
Predisposing Factors	Based on the structure provided by Andersen (1995),predisposing factors are composed of **demographic factors** (age, gender), **social structure** (an individual's status within a community [race, education, employment], ability to cope with presenting problems, ability to find resources to deal with presenting issues etc.), and **health beliefs** (attitudes, values and knowledge that an individual has regarding health and health services that can influence decision-making).
Enabling Factors	Based on the structure provided by Andersen (1995), enabling resources are composed of **community/organizational factors** (health services are available and accessible for those seeking services) and **personal factors** (means and ability to access health services, e.g., health insurance, income, regular source of care, travel, waiting times)
Need Factors	Based on the structure provided by Andersen (1995),need factors are composed of **perceived need** (an individual's assessment of their own health status based on by the severity of symptomology and/or their disease state) and **evaluated need** (health professional's assessment about an individual's health status and need for services).
Barriers Captured by NARCOMS Spring 2011 Survey	
Barrier	**Grouping and Reasoning**
Did not know where to go to get care	Predisposing factors → captures "ability to find resources and to deal with presenting issues" under social structure
Chose not to or personal decision	Predisposing factor → captures health beliefs
Could not afford care	Enabling factors → captures "income" under personal factors
Insurance would not approve or pay for care	Enabling factors → captures "insurance" under personal factors
Doctor refused to accept insurance plan	Enabling factors → captures "availability and accessibility of health services" under community/organizational factors
Problems getting to doctor's office	Enabling factors → captures "travel" under personal factors
Could not get time off of work	Enabling factors → captures "means and ability to access health services" under personal factors
Did not have time or took too long	Enabling factors → captures "wait times" under personal factors
Could not get child care	Enabling factors → captures "means and ability to access health services" under personal factors
Was refused services	Enabling factors → captures "availability and accessibility of health services" under community/organizational factors
Not having symptoms now	Need Factors → captures "perceived need"

Table A2 Description and Coding of Baseline Characteristics

Baseline Characteristics		
Variable	**Description/Notes**	**Levels**
Country[a]	Distribution of country at the time of enrolment: USA (n=3884); Canada (n=23); Other (n=10). Canada and 'Other' were grouped together.	1. USA (reference) 2. Other
Age in 2011[a]	Age was first investigated as a 5-level variable based on quintiles; ages between 45–64 years were collapsed as they showed a similar associations with outcome variables. Levels were grouped based on standardized age groupings for adults vs. older adults (<65 vs. ≥65 years) (Statistics Canada, 2021). Level 2 (ages 45–64) was used as the reference level as it was the largest level and respondents in this age-cohort reported the highest proportion of mental health treatment. Age was also investigated as a continuous measure in initial descriptive analyses (Objective 1A).	1. <45 years 2. 45–64 years (reference) 3. ≥65 years
Year of birth[a]	Year of birth was grouped so that the years corresponded with age in 2011. Year of birth was retained as a five-level variable to provide additional information regarding respondents born between 1947 and 1966 (aged 45–64 years). Level 3 (1954–1959) was used as the reference level to maintain consistency with the reference group used for the age variable.	1. ≤1946 2. 1947–1953 3. 1954–1959 (reference) 4. 1960–1966 5. ≥1967
Sex[a]	Same coding as provided by NARCOMS Data Center.	1. Female (reference) 2. Male
Race[a]	Distribution of racial/ethnic groups among full NARCOMS baseline sample: American Indian (n=18); Arabic (n=10); Asian (n=3); Black/African American (n=68); Hispanic/Latino (n=39); Multi-ethnic (n=45); Native Hawaiian/Other Pacific Islander (n=1); Other/Unknown (n=251); White/Caucasian (n=3485). All racial groups other than White/Caucasian were recoded as "People of Colour/Other".	1. White (reference) 2. People of Colour/Other
Marital status[b]	Due to small cell sizes, the following levels were grouped together: Married/cohabitating/domestic partner vs. never married/divorced/widowed/separated.	1. Married/cohabitating (reference) 2. Single/living alone
Residence[a]	Due to small cell sizes, the following levels were grouped together: Private home/apartment/condo vs. private home with home health aide/assisted living/nursing home.	1. Private residence (reference) 2. Living with assistance
Education[a]	Due to small cell sizes, technical degree was grouped with associate degree.	1. Secondary School/GED 2. Associate/Technical Degree 3. Bachelor's Degree 4. Post-Bachelor's Degree (reference)
Annual Family Income[b]	Levels <$15,000 and $15,001–$30,000 were collapsed due to similar associations with the outcome.	1. <$30,000 2. $30-000–$50,000 3. $50,001–$100,000 4. >$100,000 (reference) 5. I do not wish to answer/missing
Employment[a]	Investigated as a binary variable; "unemployed" and "missing" were grouped together as they showed similar associations with outcome variables.	1. Employed (reference) 2. Unemployed/missing
Health insurance[b]	Respondents were grouped according to their reported health insurance coverage (yes/no), and their	1. Private

Baseline Characteristics		
Variable	**Description/Notes**	**Levels**
	reported type of health insurance (private/public/both). Respondents could select their type(s) of insurance and/or write-in additional coverages. The write-in responses were examined and categorized as either "private/supplementary" or "public" based on descriptions of their respective websites or from governmental resources. Among respondents who were missing for health insurance, those who did not select any type of coverage were coded as "uninsured". The coding for the mutually exclusive health insurance variable is as followed: - Private health insurance: yes health insurance + at least one type of private/supplementary coverage - Public health insurance: yes health insurance + at least one of Medicare, Medicaid, Veteran's/Military Plans, Universal Health Care, or other publicly funded plans. - Private and public health insurance: yes health insurance + at least one private and/or one public plan - Uninsured: no health insurance + no coverages reported. Private and public health insurance was used as the reference level as respondents in this group showed the highest proportion of mental health treatment.	2. Private and public (reference) 3. Public 4. Uninsured
Severity of depressive symptoms[b]	NARCOMS Depression Scale was available at baseline and at one-year follow-up; the CES-D20 was only available at baseline. Scores above the clinical cut-points were used to determine the presence of clinically meaningful depressive symptoms: NARCOMS Depression Scale (<2 vs. ≥2); CES-D20 (<16 vs. ≥16) (Marrie, Cutter, et al., 2008; Pandya et al., 2005; Weissman et al., 1977).	1. Without clinically meaningful depressive symptoms (reference) 2. With clinically meaningful depressive symptoms
Admission to overnight healthcare facility[b]	Admission to overnight healthcare facility in the past 6 months for any reason. Those who skipped the question were recoded as "no".	1. Yes 2. No (reference)
Self-rated health[b]	Assessed using RAND-12. Self-rated health was dichotomized using common groupings: excellent/very good/good vs. fair/poor (Zajacova & Dowd, 2011).	1. Excellent/very good/good (reference) 2. Fair/poor
Cognitive impairment & fatigue[b]	Both variables were assessed using Performance Scales©. Levels of impairment were collapsed based on the distribution of the data and groupings used by Salter et al. (2019): minimal (levels 0–1); moderate (levels 2–3); severe (levels 4–5).	1. Minimal (reference) 2. Moderate 3. Severe
Pain[b]	Assessed using the NARCOMS pain assessment. Pain was assessed as an ordinal variable using the same groupings as the cognitive impairment and fatigue variable (Salter et al., 2019).	1. Minimal (reference) 2. Moderate 3. Severe
Disability[b]	Assessed using Patient Determined Disease Steps (PDDS). PDDS scores were grouped together based on the distribution of the data and groupings used by Reider et al. (2017): Mild (PDDS ≤2), moderate (PDDS 3–4) and severe (PDDS ≥5).	1. Mild (reference) 2. Moderate 3. Severe
RAND-12[b]	Mental Component Score (MCS-12) and Physical Component Score (PCS-12) measures were kept as continuous when included in regression analyses as covariates (assessed as binary measures when examined as outcome variables).	
Age of MS symptom onset[a]	Continuous variable that was categorized according to findings from Esbjerg et al. (1999). Level 2 (25–39 years) was selected as the reference level as it was the largest level.	1. <25 years 2. 25–39 years (reference) 3. ≥40 years

Baseline Characteristics		
Variable	**Description/Notes**	**Levels**
Year of MS symptom onset[a]	Continuous variable that was categorized according to quintiles. Shorter disease duration (i.e., more recent MS onset) has been associated with elevated depressive symptoms among MS patients (Bamer et al., 2008; Beiske et al., 2008; Chwastiak et al., 2002; Patten et al., 2003). As such, the cohort with the longest time since MS onset (years ≤1980) was selected as the reference group.	1. ≤ 1980 (reference) 2. 1981–1985 3. 1986–1990 4. 1991–1995 5. ≥1996
Age of MS diagnosis[a]	Continuous variable that was categorized based on the distribution of the data and corresponding 10-year age increments. Since younger age at MS onset has been associated with more severe depressive symptoms (Beiske et al., 2008), the cohort with the oldest age at MS onset (≥50 years) was selected as the reference group.	1. <30 years 2. 30–39 years 3. 40–49 years 4. ≥50 years (reference)
Year of MS diagnosis[a]	Continuous variable that was categorized based on the distribution of the data and corresponding 5-year increments. Shorter disease duration has been associated with elevated depressive symptoms among MS patients (Bamer et al., 2008; Beiske et al., 2008; Chwastiak et al., 2002; Patten et al., 2003). As such, the cohort with the longest disease duration (i.e., longest time since MS diagnosis; ≤1990) was selected as the reference group.	1. ≤1990 (reference) 2. 1991–1995 3. 1996–2000 4. ≥2001
Disease duration[a]	Continuous variable that was categorized according to the distribution of the data and corresponding 10-year increments. The cohort with the longest disease duration (≥20 years) was selected as the reference level (see explanation in Year of MS onset for justification).	1. <10 years 2. 11–20 years 3. ≥20 years (reference)
Year of Enrolment in NARCOMS[a]	Continuous variable that was categorized into terciles according to the distribution of the data.	1. ≤2000 (reference) 2. 2001–2004 3. ≥2005

[a] Item captured on enrolment survey and/or previous survey response.

[b] Item captured on the NARCOMS Spring 2011 survey.

Appendix B Objective 1 Supplementary Tables

Table B1.A Unadjusted associations between respondents' baseline sociodemographic characteristics and not receiving treatment among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (row %, unless otherwise noted)

Baseline Sociodemographic Characteristics	**Depression Cohort** (n=3589)				**Anxiety Cohort** (n=1487)			
	% Not Treated	OR	(95% CI)	*p*-value	% Not Treated	OR	(95% CI)	*p*-value
Year of birth								
- ≤1946	16.1	1.08	(0.80, 1.47)	0.61	31.3	1.36	(0.89, 2.07)	0.15
- 1947–1953	13.2	0.86	(0.66, 1.12)	0.27	23.5	0.91	(0.64, 1.30)	0.62
- 1954–1959	15.1	1.0			25.1	1.0		
- 1960–1966	14.0	0.92	(0.70, 1.21)	0.54	27.7	1.14	(0.81, 1.60)	0.45
- ≥1967	19.3	1.35	(1.02, 1.79)	**0.035**	25.7	1.03	(0.73, 1.45)	0.87
Age in 2011 (years)								
- <45	19.3	1.47	(1.15, 1.86)	**0.0018**	25.7	1.01	(0.76, 1.34)	0.94
- 45–64	14.1	1.0			25.5	1.0		
- ≥65	16.1	1.17	(0.90, 1.53)	0.25	31.3	1.34	(0.92, 1.94)	0.13
Sex								
- Female	15.0	1.0			26.6	1.0		
- Male	16.1	1.09	(0.86, 1.39)	0.49	23.1	0.83	(0.58, 1.18)	0.30
Race								
- White	14.7	1.0			25.4	1.0		
- People of Colour/Other	18.4	1.31	(1.00, 1.71)	**0.054**	30.2	1.27	(0.91, 1.77)	0.16
Marital status								
- Married/cohabitating	15.1	1.0			26.6	1.0		
- Single/living alone	15.5	1.03	(0.85, 1.25)	0.76	24.3	0.88	(0.69, 1.13)	0.32
Residence								
- Private residence	15.4	1.0			26.8	1.0		
- Living with assistance	13.6	0.87	(0.59, 1.28)	0.47	13.1	0.41	(0.22, 0.78)	**0.0069**
Education								
- Secondary School/GED	14.7	0.92	(0.71, 1.19)	0.53	25.2	1.15	(0.82, 1.63)	0.41
- Associate/Technical Degree	14.7	0.92	(0.69, 1.23)	0.56	29.3	1.42	(0.98, 2.07)	**0.066**
- Bachelor's Degree	15.6	0.98	(0.76, 1.27)	0.90	27.6	1.31	(0.92, 1.85)	0.13
- Post Bachelor's Degree	15.8	1.0			22.7	1.0		
Income								
- <$30,000	15.4	1.10	(0.85, 1.42)	0.48	24.9	1.02	(0.73, 1.42)	0.92
- $30,000–$50,000	13.6	0.95	(0.71, 1.28)	0.74	24.2	0.97	(0.67, 1.41)	0.89
- $50,001–$100,000	14.2	1.0			24.6	1.0		0.25
- > $100,000	16.6	1.2	(0.88, 1.64)	0.26	29.3	1.27	(0.85, 1.88)	0.20
- Unanswered/missing	16.7	1.21	(0.92, 1.59)	0.18	29.2	1.26	(0.89, 1.80)	
Employment								
- Employed	18.6	1.0			31.9	1.0		
- Unemployed/missing	13.6	0.69	(0.57, 0.83)	**0.0001**	23.2	0.65	(0.51, 0.82)	**0.0003**
Health insurance								
- Private	17.2	1.51	(1.21, 1.88)	**0.0003**	29.1	1.38	(1.05, 1.83)	**0.023**
- Private and public	12.1	1.0			22.9	1.0		

Baseline Sociodemographic Characteristics	**Depression Cohort** (n=3589)				**Anxiety Cohort** (n=1487)			
	% Not Treated	OR	(95% CI)	*p*-value	% Not Treated	OR	(95% CI)	*p*-value
- Public	14.9	1.27	(0.98, 1.65)	**0.076**	23.1	1.01	(0.73, 1.42)	0.93
- Uninsured	20.6	1.89	(1.83, 3.01)	**0.0077**	35.5	1.86	(1.05, 3.27)	**0.032**

Among both cohorts, all listed variables were missing no more than 3%.
Bolded estimates indicate p<0.10.
Abbreviations: CI confidence interval; GED – General Educational Development; OR – odds ratio.

Table B1.B Unadjusted associations between respondents' baseline clinical characteristics and not receiving treatment among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (row %, unless otherwise noted)

Baseline Clinical Characteristics	**Depression Cohort** (n=3589)				**Anxiety Cohort** (n=1487)			
	% Not Treated	OR	(95% CI)	*p*-value	% Not Treated	OR	(95% CI)	*p*-value
NARCOMS Depression Scale								
- <2	20.0	1.0			33.0	1.0		
- ≥2	12.1	0.55	(0.46, 0.66)	**<0.0001**	21.8	0.57	(0.45, 0.72)	**<0.0001**
CES-D20 score								
- <16	16.5	1.0			29.8	1.0		
- ≥16	13.9	0.81	(0.67, 0.98)	**0.026**	23.6	0.73	(0.57, 0.93)	**0.0082**
Admission to overnight healthcare facility								
- Yes	9.3	0.54	(0.37, 0.79)	**0.0014**	17.6	0.58	(0.38, 0.88)	**0.011**
- No	15.8	1.0			27.1	1.0		
Self-rated health								
- Excellent/very good/good	16.1	1.0			28.6	1.0		
- Fair/poor	13.6	0.82	(0.68, 1.00)	**0.044**	22.5	0.72	(0.57, 0.92)	**0.0087**
Cognitive impairment								
- Minimal	16.0	1.0			28.1	1.0		
- Moderate	15.5	0.97	(0.80, 1.17)	0.72	26.7	0.93	(0.73, 1.19)	0.57
- Severe	11.0	0.65	(0.46, 0.92)	**0.015**	18.4	0.58	(0.38, 0.88)	**0.011**
Fatigue								
- Minimal	22.9	1.0			33.0	1.0		
- Moderate	14.7	0.58	(0.45, 0.74)	**<0.0001**	28.3	0.80	(0.57, 1.12)	0.18
- Severe	13.1	0.51	(0.39, 0.66)	**<0.0001**	21.1	0.54	(0.38, 0.77)	**0.0006**
Pain								
- Minimal	16.6	1.0			28.8	1.0		
- Moderate	14.5	0.85	(0.70, 1.04)	0.11	26.2	0.88	(0.68, 1.14)	0.32
- Severe	13.7	0.80	(0.62, 1.04)	**0.095**	20.8	0.65	(0.46, 0.90)	**0.010**
Disability (PDDS)								
- Mild	19.8	1.0			29.8	1.0		
- Moderate	13.2	0.62	(0.50, 0.77)	**<0.0001**	26.0	0.83	(0.64, 1.08)	0.16
- Severe	12.2	0.56	(0.45, 0.70)	**<0.0001**	20.3	0.60	(0.44, 0.82)	**0.0011**
MCS-12	-	1.01	(1.00, 1.01)	0.23	-	1.02	(1.01, 1.04)	**<0.0001**
PCS-12	-	1.02	(1.01, 1.03)	**<0.0001**	-	1.01	(1.00, 1.02)	**0.028**

Among both cohorts, CESD20 scores were missing 6% and RAND-12 outcomes (i.e., MCS-12, PCS-12) were missing 3%. All other variables were missing no more than 1%.
Bolded estimates indicate p<0.10.
Abbreviations: CES-D20 – Centre for Epidemiological Studies Depression Scale (20-items); CI confidence interval; MCS-12 – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS-12 – Physical Component Score; PDDS – Patient Determined Disease Steps.

Table B1.C Unadjusted associations between respondents' baseline MS characteristics and not receiving treatment among NARCOMS Spring 2011 respondents diagnosed with depression or anxiety (row %, unless otherwise noted)

Baseline MS Characteristics	**Depression Cohort** (n=3589)				**Anxiety Cohort** (n=1487)			
	% Not Treated	OR	(95% CI)	*p*-value	% Not Treated	OR	(95% CI)	*p*-value
Age of MS symptom onset (years)								
- < 25	17.2	1.24	(1.01, 1.53)	**0.040**	28.6	1.15	(0.88, 1.48)	0.30
- 25–39	14.3	1.0			25.9	1.0		
- ≥ 40	14.1	0.98	(0.76, 1.27)	0.88	22.0	0.80	(0.57, 1.13)	0.21
Year of MS onset								
- ≤ 1980	15.6	1.0			28.2	1.0		
- 1981–1985	12.7	0.79	(0.58, 1.07)	0.13	23.9	0.80	(0.53, 1.19)	0.27
- 1986–1990	15.9	1.02	(0.77, 1.36)	0.87	30.0	1.09	(0.76, 1.56)	0.65
- 1991–1995	15.5	0.99	(0.75, 1.31)	0.95	23.5	0.78	(0.54, 1.14)	0.20
- ≥1996	15.3	0.97	(0.75, 1.26)	0.83	24.8	0.84	(0.61, 1.16)	0.28
Age at MS diagnosis (years)								
- <30	17.0	1.17	(0.84, 1.63)	0.35	27.3	0.99	(0.65, 1.52)	0.97
- 30–39	14.5	0.97	(0.71, 1.32)	0.85	26.0	0.93	(0.62, 1.38)	0.71
- 40–49	14.6	0.98	(0.72, 1.34)	0.90	25.2	0.89	(0.60, 1.33)	0.56
- ≥50	14.9	1.0			27.4	1.0		
Year of MS diagnosis								
- ≤1990	14.0	1.0			26.6	1.0		
- 1991–1995	15.0	1.09	(0.82, 1.47)	0.55	27.1	1.03	(0.70, 1.51)	0.90
- 1996-2000	14.8	1.08	(0.83, 1.39)	0.60	27.4	1.04	(0.74, 1.46)	0.81
- ≥2001	16.3	1.20	(0.94, 1.53)	0.15	24.6	0.90	(0.66, 1.24)	0.53
Disease duration (years)								
- ≤10	16.3	1.20	(0.94, 1.53)	0.94	24.6	0.90	(0.66, 1.24)	0.53
- 11–20	14.9	1.08	(0.86, 1.36)	0.15	27.3	1.04	(0.76, 1.41)	0.81
- ≥21	14.0	1.0			26.6	1.0		

Among both cohorts, all listed variables were missing no more than 2%.
Bolded estimates indicate p<0.10.
Abbreviations: CI – confidence interval; MS – multiple sclerosis; OR – odds ratio.

Table B2.A Bivariate associations between respondents' baseline characteristics and mental health treatment modality among NARCOMS Spring 2011 respondents diagnosed with depression who were receiving treatment, stratified by depressive symptoms (n, row%, unless otherwise noted)

Baseline Characteristics	**Depression Cohort[a]** Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=3044)													
	NARCOMS Depression score <2 (n=1107)							**NARCOMS Depression score ≥2** (n=1927)						
	TxA[c] (n=32)		TxB[c] (n=903)		TxC[c] (n=151)		*p*-value	TxA[c] (n=87)		TxB[c] (n=1343)		TxC[c] (n=459)		*p*-value
Year of birth														
- ≤1946	2	(1.3)	136	(90.1)	13	(8.6)	**0.017**	4	(1.8)	174	(78.0)	45	(20.2)	**0.0086**
- 1947–1953	9	(3.0)	260	(86.4)	32	(10.6)		26	(5.3)	361	(73.4)	105	(21.3)	
- 1954–1959	9	(3.5)	205	(79.8)	43	(16.7)		16	(3.4)	342	(71.9)	118	(24.8)	
- 1960–1966	4	(1.9)	177	(83.9)	30	(14.2)		20	(4.8)	282	(67.0)	119	(28.3)	
- ≥1967	8	(4.9)	124	(75.2)	33	(20.0)		20	(7.3)	183	(66.6)	72	(26.2)	
Age in 2011 (years)														
- <45	8	(4.9)	124	(75.2)	33	(20.0)	**0.011**	20	(7.3)	183	(66.6)	72	(26.2)	**0.014**
- 45–64	22	(2.9)	642	(83.5)	105	(13.7)		62	(4.5)	985	(70.9)	342	(24.6)	
- ≥65	2	(1.3)	136	(90.1)	13	(8.6)		4	(1.8)	174	(78.0)	45	(20.2)	
Sex														
- Female	25	(2.7)	774	(84.0)	123	(13.3)	0.21	76	(4.9)	1113	(71.0)	378	(24.1)	0.52
- Male	7	(4.3)	128	(78.5)	28	(17.2)		11	(3.4)	229	(71.3)	81	(25.2)	
Race														
- White	24	(2.4)	827	(83.6)	138	(14.0)	**0.0043**	72	(4.3)	1198	(72.0)	394	(23.7)	**0.037**
- People of Colour/Other	8	(8.4)	74	(77.9)	13	(13.7)		15	(6.7)	143	(64.1)	65	(29.2)	
Marital status														
- Married/cohabitating	21	(2.8)	643	(84.1)	101	(13.2)	0.50	43	(3.6)	888	(74.1)	267	(22.3)	**0.0001**
- Single/living alone	11	(3.6)	250	(81.2)	47	(15.3)		44	(6.6)	438	(65.5)	187	(28.0)	
Residence														
- Private residence	29	(2.9)	846	(83.4)	140	(13.8)	0.55	81	(4.6)	1249	(71.6)	414	(23.7)	0.14
- Living with assistance	3	(5.2)	46	(79.3)	9	(15.5)		6	(4.8)	79	(63.7)	39	(31.5)	
Education														
- Secondary School/GED	5	(1.7)	256	(87.7)	31	(10.6)	**0.048**	27	(4.4)	468	(75.5)	125	(20.2)	**0.001**
- Associate/Technical Degree	3	(1.7)	150	(82.9)	28	(15.5)		14	(3.9)	270	(75.6)	73	(20.5)	
- Bachelor's Degree	10	(3.1)	272	(82.9)	46	(14.0)		28	(5.5)	331	(64.2)	149	(29.3)	
- Post Bachelor's Degree	13	(4.9)	204	(77.6)	46	(17.5)		18	(4.9)	245	(66.6)	105	(28.5)	
Income														
- <$30,000	4	(1.9)	183	(85.1)	28	(13.0)	0.72	22	(4.0)	401	(73.4)	123	(22.5)	0.20
- $30,000–$50,000	3	(1.7)	151	(85.3)	23	(13.0)		19	(5.2)	259	(70.2)	91	(24.7)	
- $50,001–$100,000	13	(4.3)	245	(80.1)	48	(15.7)		22	(4.9)	318	(70.8)	109	(24.3)	
- > $100,000	5	(2.8)	152	(83.5)	25	(13.7)		7	(4.0)	110	(62.5)	59	(33.5)	
- Unanswered/missing	7	(3.4)	172	(83.5)	27	(13.1)		17	(4.9)	255	(73.1)	77	(22.1)	
Employment														
- Employed	15	(3.6)	346	(82.8)	57	(13.6)	0.61	31	(6.1)	354	(70.0)	121	(23.9)	0.16
- Unemployed/missing	17	(2.5)	557	(83.4)	94	(14.1)		56	(4.1)	989	(71.5)	338	(24.4)	
Health insurance														
- Private	18	(3.3)	445	(84.0)	69	(12.7)	0.86	41	(5.9)	493	(70.6)	164	(23.5)	0.58

Baseline Characteristics	**Depression Cohort**[a] Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=3044)													
	NARCOMS Depression score <2 (n=1107)							**NARCOMS Depression score ≥2** (n=1927)						
	TxA[c] (n=32)		TxB[c] (n=903)		TxC[c] (n=151)		*p*-value	TxA[c] (n=87)		TxB[c] (n=1343)		TxC[c] (n=459)		*p*-value
- Private and public	8	(2.5)	261	(82.1)	49	(15.4)		24	(3.7)	467	(71.3)	164	(25.0)	
- Public	6	(3.0)	166	(82.2)	3	(14.9)		20	(4.3)	332	(71.1)	115	(24.6)	
- Uninsured	0	(0.0)	21	(87.5)	3	(12.5)		2	(2.9)	51	(73.9)	16	(23.2)	
Cognitive impairment														
- Minimal	24	(3.7)	538	(82.6)	89	(13.7)	0.20	32	(6.4)	364	(72.4)	107	(21.3)	**0.029**
- Moderate	8	(2.2)	311	(84.5)	49	(13.3)		45	(4.1)	783	(71.3)	270	(24.6)	
- Severe	0	(0.0)	51	(79.7)	13	(20.3)		8	(2.9)	187	(68.0)	80	(29.1)	
Fatigue														
- Minimal	11	(3.9)	236	(83.1)	37	(13.0)	0.29	9	(8.7)	66	(63.5)	29	(27.9)	0.12
- Moderate	19	(3.4)	473	(83.3)	76	(13.4)		38	(4.5)	611	(72.7)	191	(22.7)	
- Severe	2	(0.9)	191	(82.7)	38	(16.5)		38	(4.1)	658	(70.6)	236	(25.3)	
Disability (PDDS)														
- Mild	16	(3.6)	360	(80.9)	69	(15.5)	0.29	33	(6.0)	361	(65.8)	155	(28.2)	**0.0060**
- Moderate	5	(1.5)	278	(85.8)	41	(12.7)		29	(4.5)	457	(71.0)	158	(24.5)	
- Severe	10	(3.2)	262	(84.0)	40	(12.8)		25	(3.7)	516	(75.4)	143	(20.9)	
Age of MS symptom onset (years)														
- < 25	10	(3.3)	246	(80.1)	15	(16.6)	**0.085**	24	(4.2)	401	(70.6)	143	(25.2)	0.92
- 25–39	18	(2.3)	459	(82.7)	78	(14.1)		48	(5.0)	684	(71.3)	227	(23.7)	
- ≥ 40	2	(1.0)	186	(89.0)	21	(10.1)		14	(4.4)	228	(71.0)	79	(23.6)	

[a] Among those receiving treatment for depression (n=3044), treatment modality was missing for n=59 respondents, and NARCOMS Depression score was missing for n=10 respondents.

[b] Mental health treatment modalities were captured generally for respondents with one or more diagnosed mental health comorbidity who were receiving treatment for at least one condition at the time of survey response.

[c] TxA – Psychotherapy; TxB – Medication; TxC – Combination. Treatment modalities among stratified subgroups are mutually exclusive. Respondents receiving both psychotherapy and medication are listed under “combination”.

Among both subgroups, all listed variables were missing no more than 4%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; PDDS – Patient Determined Disease Steps.

Table B2.B Bivariate associations between respondents' baseline characteristics and mental health treatment modality among NARCOMS Spring 2011 respondents diagnosed with anxiety who were receiving treatment, stratified by depressive symptoms (n, row%, unless otherwise noted)

Baseline Characteristics	**Anxiety Cohort**[a] Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=1099)													
	NARCOMS Depression score <2 (n=382)							**NARCOMS Depression score ≥2** (n=715)						
	TxA[c] (n=17)		TxB[c] (n=293)		TxC[c] (n=66)		*p*-value	TxA[c] (n=42)		TxB[c] (n=415)		TxC[c] (n=238)		*p*-value
Year of birth[d]														
- ≤1946	0	(0.0)	31	(81.6)	7	(18.4)	0.59	3	(5.3)	35	(61.4)	19	(33.3)	**0.098**
- 1947–1967	11	(4.4)	196	(78.7)	42	(16.9)		21	(4.4)	289	(60.2)	170	(35.4)	
- ≥1967	6	(6.8)	66	(75.0)	16	(18.2)		16	(10.3)	90	(58.1)	49	(31.6)	
Age in 2011 (years)														
- <45	6	(6.8)	66	(75.0)	16	(18.2)	0.59	16	(10.3)	90	(58.1)	49	(31.6)	**0.098**
- 45–64	11	(4.4)	196	(78.7)	42	(16.9)		21	(4.4)	289	(60.2)	170	(35.4)	
- ≥65	0	(0.0)	31	(81.6)	7	(18.4)		3	(5.3)	35	(61.4)	19	(33.3)	
Sex														
- Female	14	(4.3)	253	(78.1)	57	(17.6)	0.85	39	(6.4)	360	(60.2)	199	(33.3)	0.12
- Male	3	(5.9)	40	(78.4)	8	(15.7)		2	(2.1)	54	(56.8)	39	(41.1)	
Race														
- White	15	(4.5)	262	(78.0)	59	(17.6)	0.93	35	(5.8)	360	(59.9)	206	(34.3)	0.96
- People of Colour/Other	2	(5.1)	31	(79.5)	6	(15.4)		6	(6.5)	54	(58.7)	32	(34.8)	
Marital status														
- Married/cohabitating	14	(5.3)	207	(77.8)	45	(16.9)	0.51	21	(5.0)	271	(64.4)	129	(30.6)	**0.0043**
- Single/living alone	3	(2.8)	83	(77.6)	21	(19.6)		21	(7.8)	139	(51.9)	108	(40.3)	
Residence														
- Private residence	16	(4.5)	280	(78.2)	62	(17.3)	0.49	37	(5.9)	381	(60.3)	214	(33.9)	0.33
- Living with assistance	1	(6.3)	11	(68.8)	4	(25.0)		5	(9.4)	27	(50.9)	21	(39.6)	
Education[d]														
- ≤ Bachelor's degree	2	(1.1)	148	(84.1)	26	(14.8)	**0.0026**	18	(5.0)	231	(64.2)	111	(30.8)	**0.038**
- ≥ Bachelor's degree	15	(7.7)	140	(72.2)	39	(20.1)		23	(7.1)	176	(54.7)	123	(38.2)	
Income[d]														
- <$30,000	2	(2.8)	57	(79.2)	13	(18.1)	0.99	15	(6.8)	127	(57.5)	79	(35.8)	0.38
- $30,000–$100,000	9	(5.2)	135	(78.0)	29	(16.8)		13	(4.6)	172	(61.4)	95	(33.9)	
- > $100,000	3	(4.4)	54	(78.3)	12	(17.4)		5	(8.2)	30	(49.2)	26	(42.6)	
- Unanswered/missing	3	(4.8)	47	(75.8)	12	(19.4)		9	(6.8)	86	(64.7)	38	(28.6)	
Employment														
- Employed	9	(5.7)	127	(80.4)	22	(13.9)	0.21	15	(8.3)	103	(57.2)	62	(34.4)	0.31
- Unemployed/missing	8	(3.7)	166	(76.2)	44	(20.2)		27	(5.2)	312	(60.6)	176	(34.2)	
Health insurance[d]														
- Private or public	14	(5.0)	218	(78.1)	47	(16.9)	0.61	29	(6.9)	247	(58.4)	147	(34.8)	0.76
- Private and public	3	(3.4)	67	(75.3)	19	(21.4)		11	(4.5)	150	(61.7)	82	(33.7)	
- Uninsured	0	(0.0)	8	(100)	0	(0.0)		2	(6.9)	18	(62.1)	9	(31.0)	
Cognitive impairment														
- Minimal	13	(5.8)	171	(76.7)	39	(17.5)	0.64	14	(9.3)	95	(62.9)	42	(27.8)	0.12
- Moderate	4	(3.1)	105	(80.2)	22	(16.8)		22	(5.3)	248	(59.6)	146	(35.1)	

Baseline Characteristics	**Anxiety Cohort**[a] Receiving Treatment for a Diagnosed Mental Health Comorbidity[b] (n=1099)													
	NARCOMS Depression score <2 (n=382)							**NARCOMS Depression score ≥2** (n=715)						
	TxA[c] (n=17)		TxB[c] (n=293)		TxC[c] (n=66)		*p*-value	TxA[c] (n=42)		TxB[c] (n=415)		TxC[c] (n=238)		*p*-value
- Severe	0	(0.0)	16	(76.2)	5	(23.8)		5	(4.0)	70	(56.5)	49	(39.5)	
Fatigue														
- Minimal	5	(4.8)	80	(76.9)	19	(18.3)	0.61	5	(13.9)	19	(52.8)	12	(33.3)	0.14
- Moderate	8	(4.1)	158	(80.6)	30	(15.3)		18	(6.2)	182	(62.8)	90	(31.0)	
- Severe	4	(5.3)	54	(72.0)	17	(22.7)		18	(4.9)	213	(58.4)	134	(26.7)	
Disability (PDDS)														
- Mild	9	(4.8)	144	(77.4)	33	(17.7)	0.88	17	(7.0)	135	(55.8)	90	(37.2)	0.56
- Moderate	5	(4.8)	83	(79.8)	16	(15.4)		13	(5.2)	153	(61.0)	85	(33.9)	
- Severe	2	(2.4)	65	(78.3)	16	(19.3)		12	(6.1)	124	(62.9)	61	(31.0)	
Age of MS symptom onset (years)														
- < 25	7	(7.0)	69	(69.0)	24	(24.0)	0.12	12	(5.2)	137	(59.3)	82	(35.5)	0.95
- 25–39	7	(3.6)	159	(81.1)	30	(15.3)		20	(5.9)	203	(60.2)	114	(33.8)	
- ≥ 40	2	(2.7)	62	(83.8)	10	(13.5)		8	(7.1)	68	(60.2)	37	(32.7)	

[a] Among those receiving treatment for anxiety (n=1099), treatment modality was missing for n=26 respondents, and NARCOMS Depression score was missing for n=2 respondents.

[b] Mental health treatment modalities were captured generally for respondents with one or more diagnosed mental health comorbidity who were receiving treatment for at least one condition at the time of survey response.

[c] TxA – Psychotherapy; TxB – Medication; TxC – Combination. Treatment modalities among stratified subgroups are mutually exclusive. Respondents receiving both psychotherapy and medication are listed under "combination".

[d] Variables collapsed due to small cells.

Among those with NARCOMS Depression score <2, all listed variables were missing no more than 4%.

Among those with NARCOMS Depression score ≥2, education, age of MS symptom onset and residence were missing <5%. All other variables were missing no more than 4%.

Bolded estimates indicate p<0.10.

Abbreviations: GED – General Educational Development; MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; PDDS – Patient Determined Disease Steps.

Appendix C Objective 2A Supplementary Tables

Table C1.A Bivariate and unadjusted associations between respondents' baseline sociodemographic characteristics and Spring 2012 NARCOMS Depression score among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Depressive Symptoms^{a} (2012)**									
	Depression Cohort^{b} (n=2891)					**Anxiety Cohort^{b}** (n=1181)				
	Crosstabulation with Outcome		**Crude OR**			**Crosstabulation with Outcome**		**Crude OR**		
	<2^{c}	≥2^{c}	OR	95% CI	*p*-value	<2^{d}	≥2^{d}	OR	95% CI	*p*-value
Baseline treatment status										
- Receiving treatment	41.8	58.2	1.0			41.4	58.6	1.0		
- Not receiving treatment	52.3	47.7	0.65	(0.53, 0.80)	**<0.0001**	48.2	51.8	0.76	(0.57, 0.98)	**0.035**
Year of birth										
- ≤1946	46.1	53.9	0.87	(0.68, 1.12)	0.28	48.4	51.6	0.72	(0.47, 1.09)	0.12
- 1947–1953	42.9	57.1	0.99	(0.81, 1.22)	0.95	42.0	58.0	0.93	(0.66, 1.31)	0.68
- 1954–1959	42.7	57.3	1.0			40.3	59.7	1.0		
- 1960–1966	41.2	58.8	1.06	(0.85, 1.33)	0.58	41.6	58.4	0.95	(0.67, 1.33)	0.74
- ≥1967	46.2	53.8	0.87	(0.68, 1.10)	0.24	46.5	53.5	0.78	(0.55, 1.09)	0.14
Age in 2011 (years)										
- <45	46.2	53.8	0.85	(0.69, 1.05)	0.14	46.5	53.5	0.81	(0.61, 1.08)	0.14
- 45–64	42.3	57.7	1.0			41.3	58.7	1.0		
- ≥65	46.1	53.9	0.86	(0.69 1.07)	0.17	48.4	51.6	0.75	(0.52, 1.09)	0.13
Sex										
- Female	44.2	55.8	1.0			44.1	55.9	1.0		
- Male	39.7	60.3	1.20	(0.98, 1.46)	**0.072**	36.2	63.8	1.39	(0.97, 1.98)	**0.0070**
Race										
- White	44.4	55.6	1.0			43.8	56.2	1.0		
- People of Colour/Other	34.5	65.5	1.52	(1.17, 1.97)	**0.0020**	37.0	63.0	1.33	(0.90, 1.97)	0.15
Marital status										
- Married/cohabitating	45.7	54.3	1.0			45.5	54.5	1.0		
- Single/living alone	39.1	60.9	1.31	(1.12, 1.54)	**0.0008**	38.9	61.1	1.31	(1.02, 1.68)	**0.032**
Residence										
- Private residence	43.9	56.1	1.0			44.5	55.5	1.0		
- Living with assistance	37.8	62.2	1.29	(0.93, 1.78)	0.12	27.7	72.3	2.09	(1.20, 3.64)	**0.0094**
Education										
- Secondary School/GED	38.9	61.1	1.54	(1.25, 1.89)	**<0.0001**	38.1	61.9	1.46	(1.05, 2.01)	**0.024**
- Associate/Technical Degree	34.9	65.2	1.83	(1.44, 2.32)	**<0.0001**	36.2	63.8	1.58	(1.09, 2.28)	**0.015**
- Bachelor's Degree	48.7	51.3	1.03	(0.84, 1.27)	0.77	49.3	50.8	0.92	(0.67, 1.28)	0.63
- Post Bachelor's Degree	49.5	50.5	1.0			47.3	52.7	1.0		
Income										
- <$30,000	33.8	66.3	2.68	(2.07, 3.46)	**<0.0001**	31.5	68.5	3.38	(2.27, 5.05)	**<0.0001**
- $30,000–$50,000	39.8	60.2	2.06	(1.57, 2.70)	**<0.0001**	37.2	62.7	2.62	(1.71, 4.01)	**<0.0001**
- $50,001–$100,000	47.0	53.0	1.54	(1.19, 1.97)	**0.0008**	50.2	49.8	1.55	(1.04, 2.30)	**0.032**
- > $100,000	57.7	42.3	1.0			60.9	39.1	1.0		
- Unanswered/missing	44.9	55.1	1.68	(1.28, 2.19)	**0.0001**	43.9	56.1	1.99	(1.32, 3.02)	**0.0011**

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Depressive Symptoms**[a] **(2012)**									
	Depression Cohort[b] (n=2891)					**Anxiety Cohort**[b] (n=1181)				
	Crosstabulation with Outcome		**Crude OR**			**Crosstabulation with Outcome**		**Crude OR**		
	<2[c]	≥2[c]	OR	95% CI	*p*-value	<2[d]	≥2[d]	OR	95% CI	*p*-value
Employment										
- Employed	51.3	48.7	1.0			55.0	45.0	1.0		
- Unemployed/missing	39.5	60.5	1.61	(1.38, 1.89)	**<0.0001**	36.9	63.1	2.09	(1.64, 2.67)	**<0.0001**
Health insurance										
- Private	50.6	49.4	0.64	(0.53, 0.75)	**<0.0001**	52.1	48.0	0.59	(0.45, 0.78)	**0.0002**
- Private and public	39.2	60.8	1.0			39.0	61.0	1.0		
- Public	37.0	63.0	1.10	(0.89, 1.35)	0.38	34.5	65.5	1.22	(0.87, 1.69)	0.25
- Uninsured	33.3	66.7	1.29	(0.83, 2.01)	0.26	28.6	71.4	1.60	(0.83, 3.08)	0.16

[a] Clinically meaningful depressive symptoms on NARCOMS Spring 2012 survey: depression cohort 56.6% (1636/2891); anxiety cohort 56.8% (671/1181).

[b] Includes respondents who provided outcome at baseline and follow-up.

[c] Depression cohort: <2 (n=1255); ≥2 (n=1636).

[d] Anxiety cohort: <2 (n=510); ≥2 (n=671).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; USA – United States of America.

Table C1.B Bivariate and unadjusted associations between respondents' baseline clinical characteristics and Spring 2012 NARCOMS Depression score among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Clinical Characteristics (2011)	**Clinically Meaningful Depressive Symptoms (2012)**									
	Depression Cohort[a] (n=2891)					**Anxiety Cohort**[a] (n=1181)				
	Crosstabulation with Outcome		**Crude OR**			**Crosstabulation with Outcome**		**Crude OR**		
	<2[d]	≥2[d]	OR	95% CI	*p*-value	<2[e]	≥2[e]	OR	95% CI	*p*-value
Spring 2011 NARCOMS Depression score										
- <2	74.9	25.1	1.0			77.4	22.6	1.0		
- ≥2	21.6	78.4	10.83	(9.09, 12.90)	**<0.0001**	20.0	80.0	13.64	(10.28,18.10)	**<0.0001**
Admission to overnight healthcare facility										
- Yes	33.9	66.2	1.56	(1.19, 2.04)	**0.0013**	38.2	61.8	1.26	(0.86, 1.85)	0.24
- No	44.3	55.7	1.0			43.8	56.2	1.0		
Self-rated health										
- Excellent/very good/good	51.5	48.5	1.0			52.1	47.9	1.0		
- Fair/poor	28.7	71.3	2.64	(2.25, 3.11)	**<0.0001**	29.2	70.8	2.64	(2.06, 3.39)	**<0.0001**
Cognitive impairment										
- Minimal	61.8	38.2	1.0			65.9	34.1	1.0		
- Moderate	32.7	67.3	3.32	(2.82, 3.90)	**<0.0001**	33.9	66.1	3.77	(2.90, 4.89)	**<0.0001**
- Severe	22.5	77.5	5.56	(4.14, 7.47)	**<0.0001**	14.4	85.6	11.49	(6.87, 19.21)	**<0.0001**
Fatigue										
- Minimal	75.1	25.9	1.0			75.7	24.3	1.0		
- Moderate	47.3	52.7	3.37	(2.64, 4.30)	**<0.0001**	48.4	51.6	3.33	(2.27, 4.87)	**<0.0001**
- Severe	26.0	74.0	8.58	(6.63, 11.11)	**<0.0001**	24.2	75.8	9.78	(6.52, 14.68)	**<0.0001**
Pain										
- Minimal	57.9	42.1	1.0			58.4	41.6	1.0		
- Moderate	37.3	62.8	2.31	(1.97, 2.73)	**<0.0001**	38.2	61.9	2.28	(1.75, 2.95)	**<0.0001**
- Severe	22.3	77.7	4.78	(3.75, 6.10)	**<0.0001**	24.9	75.1	4.23	(2.98, 6.02)	**<0.0001**
Disability (PDDS)										
- Mild	51.3	48.7	1.0			53.1	46.9	1.0		
- Moderate	39.9	60.1	1.59	(1.33, 1.90)	**<0.0001**	37.0	63.0	1.93	(1.47, 2.53)	**<0.0001**
- Severe	38.2	61.8	1.70	(1.42, 2.04)	**<0.0001**	34.7	65.3	2.13	(1.58, 2.87)	**<0.0001**
MCS-12 (mean)	47.8	37.0	0.90	(0.89, 0.91)	**<0.0001**	46.7	35.5	0.90	(0.88, 0.91)	**<0.0001**
PCS-12 (mean)	39.2	35.7	0.97	(0.97, 0.98)	**<0.0001**	40.2	36.0	0.97	(0.96, 0.98)	**<0.0001**

[a] Clinically meaningful depressive symptoms on NARCOMS Spring 2012 survey: depression cohort 56.6% (1636/2891); anxiety cohort 56.8% (671/1181).

[b] Includes respondents who provided outcome at baseline and follow-up.

[c] Depression cohort: <2 (n=1255); ≥2 (n=1636).

[d] Anxiety cohort: <2 (n=510); ≥2 (n=671).

Among both cohorts, all listed variables were missing no more than 3%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; RAND – RAND Health Status Inventory scale (12-Item); PCS – Physical Component Score; PDDS – Patient Determined Disease Steps.

Table C1.C Bivariate and unadjusted associations between respondents' baseline MS characteristics and Spring 2012 NARCOMS Depression score among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline MS Characteristics (2011)	**Clinically Meaningful Depressive Symptoms[a] (2012)**									
	Depression Cohort[b] (n=2891)					**Anxiety Cohort[b]** (n=1181)				
	Crosstabulation with Outcome		**Crude OR**			**Crosstabulation with Outcome**		**Crude OR**		
	<2[c]	≥2[c]	OR	95% CI	*p*-value	<2[d]	≥2[d]	OR	95% CI	*p*-value
Age of MS symptom onset (years)										
- < 25	41.1	59.0	1.17	(0.99, 1.38)	**0.073**	39.4	60.7	1.28	(0.98, 1.66)	**0.069**
- 25–39	44.8	55.2	1.0			45.3	54.7	1.0		
- ≥ 40	44.4	55.7	1.02	(0.83, 1.25)	0.85	44.9	55.1	1.02	(0.73, 1.41)	0.93
Year of MS onset										
- ≤ 1980	42.5	57.5	1.0			40.9	59.1	1.0		
- 1981–1985	40.9	59.1	1.07	(0.85, 1.25)	0.57	42.2	57.8	0.95	(0.65, 1.40)	0.79
- 1986–1990	44.5	55.5	0.92	(0.73, 1.16)	0.49	45.1	54.9	0.84	(0.59, 1.22)	0.36
- 1991–1995	45.6	54.4	0.88	(0.70, 1.11)	0.27	42.6	57.4	0.94	(0.65, 1.36)	0.73
- ≥1996	44.6	55.4	0.92	(0.75, 1.13)	0.42	45.1	54.9	0.85	(0.61, 1.17)	0.31
Age at MS diagnosis (years)										
- <30	46.1	53.9	0.86	(0.65, 1.13)	0.27	44.7	55.3	1.18	(0.77, 1.81)	0.44
- 30–39	43.6	56.4	0.95	(0.74, 1.21)	0.66	44.4	55.6	1.20	(0.81, 1.78)	0.37
- 40–49	42.4	57.6	0.99	(0.77, 1.28)	0.96	39.3	60.7	1.47	(0.99, 2.20)	**0.057**
- ≥50	42.2	57.8	1.0			48.9	51.2	1.0		
Year of MS diagnosis										
- ≤1990	43.3	56.7	1.0			40.1	59.9	1.0		
- 1991–1995	46.3	53.8	0.89	(0.71, 1.10)	0.28	46.6	53.4	0.77	(0.53, 1.12)	0.16
- 1996-2000	43.6	56.4	0.99	(0.81, 1.21)	0.99	44.6	55.4	0.83	(0.59, 1.17)	0.28
- ≥2001	41.6	58.4	1.07	(0.88, 1.31)	0.50	42.8	57.2	0.89	(0.65, 1.23)	0.49
Disease duration (years)										
- ≤10	41.6	58.4	1.07	(0.88, 1.31)	0.50	42.8	57.2	0.89	(0.65, 1.23)	0.49
- 11–20	44.8	55.2	0.94	(0.79, 1.13)	0.52	45.4	54.6	0.80	(0.59, 1.09)	0.16
- ≥21	43.3	56.7	1.0			40.1	59.1	1.0		

[a] Clinically meaningful depressive symptoms on NARCOMS Spring 2012 survey: depression cohort 56.6% (1636/2891); anxiety cohort 56.8% (671/1181).

[b] Includes respondents who provided outcome at baseline and follow-up.

[c] Depression cohort: <2 (n=1255); ≥2 (n=1636).

[d] Anxiety cohort: <2 (n=510); ≥2 (n=671).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence Interval; MS – multiple sclerosis; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; RAND – RAND Health Status Inventory scale (12-Item).

Table C2.A Adjusted associations between baseline depression treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with depression, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors

Baseline Characteristics (2011)	**Depression Cohort** Clinically Meaningful Depressive Symptoms[a] (2012)					
	Full Cohort (n=2891) Adjusted[c]			**Restricted Cohort**[b] (n=2691) Adjusted[d]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.90	(0.70, 1.16)	0.41	1.19	(0.86, 1.65)	0.29
Age in 2011						
- <45	0.97	(0.74, 1.28)	0.85	0.94	(0.71 1.24)	0.66
- 45–64	1.0			1.0		
- ≥65	0.81	(0.61, 1.08)	0.15	0.78	(0.58, 1.04)	**0.091**
Sex						
- Female	1.0			1.0		
- Male	1.22	(0.96, 1.56)	0.11	1.21	(0.94, 1.56)	0.14
Race						
- White	1.0			1.0		
- People of Colour/Other	1.42	(1.03, 1.95)	**0.032**	1.43	(1.02, 2.00)	**0.036**
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.03	(0.83, 1.28)	0.79	1.02	(0.81, 1.27)	0.89
Education						
- Secondary School/GED	1.14	(0.88, 1.47)	0.33	1.16	(0.89, 1.52)	0.28
- Associate/Technical Degree	1.41	(1.06, 1.89)	**0.020**	1.47	(1.09, 1.99)	**0.012**
- Bachelor's Degree	0.89	(0.70, 1.15)	0.37	0.89	(0.69, 1.16)	0.39
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.74	(1.21, 2.50)	**0.0030**	1.82	(1.25, 2.65)	**0.0017**
- $30,000–$50,000	1.52	(1.08, 2.15)	**0.017**	1.57	(1.10, 2.24)	**0.012**
- $50,001–$100,000	1.43	(1.05, 1.94)	**0.023**	1.45	(1.05, 1.98)	**0.022**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.28	(0.91, 1.79)	0.16	1.31	(0.93, 1.86)	0.13
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.06	(0.85, 1.33)	0.59	1.09	(0.87 1.37)	0.45
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	10.26	(8.55,12.32)	**<0.0001**	9.49	(7.86,11.45)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.17	(0.94, 1.47)	0.17	1.21	(0.96, 1.53)	0.11
- Severe	1.30	(1.02, 1.66)	**0.037**	1.29	(1.00, 1.66)	**0.048**
Disease duration (years)						
- ≤10	1.19	(0.91, 1.56)	0.19	1.18	(0.90, 1.56)	0.24
- 11–20	0.93	(0.75, 1.17)	0.54	0.92	(0.73, 1.16)	0.47
- ≥21	1.0			1.0		

[a] Among full depression cohort, 56.6% (16362891) reported clinically meaningful depressive symptoms (2012).

[b] Excludes respondents whose only reported treatment barrier at baseline was "not having symptoms now" (200/451).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=118; [d] missing, n=108).

Bolded estimates indicate p<0.10.

Abbreviations: CI –confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio.

Table C2.B Adjusted associations between baseline depression treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with depression, adjusting vs. not adjusting for Spring 2011 NARCOMS Depression score

Baseline Characteristics (2011)	**Depression Cohort** (n=2891) Clinically Meaningful Depressive Symptoms[a]					
	Including Baseline Score Adjusted[b]			**Excluding Baseline Score** Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.90	(0.70, 1.16)	0.41	0.69	(0.56, 0.85)	**0.0006**
Age in 2011 (years)						
- <45	0.97	(0.74, 1.28)	0.85	1.01	(0.8, 1.28)	0.91
- 45–64	1.0			1.0		
- ≥65	0.81	(0.61, 1.08)	0.15	0.73	(0.57, 0.92)	**0.0092**
Sex						
- Female	1.0			1.0		
- Male	1.22	(0.96, 1.56)	0.11	1.25	(1.02, 1.55)	**0.036**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.42	(1.03, 1.95)	**0.032**	1.45	(1.10, 1.90)	**0.0089**
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.03	(0.83, 1.28)	0.79	1.07	(0.88, 1.29)	0.50
Education						
- Secondary School/GED	1.14	(0.88, 1.47)	0.33	1.28	(1.03, 1.60)	**0.029**
- Associate/Technical	1.41	(1.06, 1.89)	**0.020**	1.52	(1.18, 1.95)	**0.0011**
- Bachelor’s	0.89	(0.70, 1.15)	0.37	0.97	(0.78, 1.20)	0.75
- Post Bachelor’s	1.0			1.0		
Income						
- <\$30,000	1.74	(1.21, 2.50)	**0.0030**	1.93	(1.41, 2.63)	**<0.0001**
- \$30,000–\$50,000	1.52	(1.08, 2.15)	**0.017**	1.73	(1.28, 2.33)	**0.0003**
- \$50,001–\$100,000	1.43	(1.05, 1.94)	**0.023**	1.38	(1.06, 1.79)	**0.017**
- > \$100,000	1.0			1.0		
- Unanswered/missing	1.28	(0.91, 1.79)	0.16	1.35	(1.01, 1.81)	**0.041**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.06	(0.85, 1.33)	0.59	1.23	(1.01, 1.48)	**0.035**
Baseline NARCOMS Depression score						
- <2	1.0					
- ≥2	10.26	(8.55,12.32)	**<0.0001**			
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.17	(0.94, 1.47)	0.17	1.34	(1.10, 1.63)	**0.0032**
- Severe	1.30	(1.02, 1.66)	**0.037**	1.43	(1.16, 1.77)	**0.0009**
Disease duration (years)						
- ≤10	1.19	(0.91, 1.56)	0.19	1.18	(0.94, 1.48)	0.16
- 11–20	0.93	(0.75, 1.17)	0.54	0.96	(0.79, 1.16)	0.68
- ≥21	1.0			1.0		

[a] Among depression cohort, 56.6% (1636/2891) reported clinically meaningful depressive symptoms on Spring 2012 survey.

[b] Model adjusted for all variables listed above in table (missing n=118).

[c] Model adjusted for variables listed above in table, apart from baseline NARCOMS Depression score (missing n=118).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table C2.C Adjusted associations between baseline depression treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with depression, assessed with logistic regression vs. modified Poisson regression

Baseline Characteristics (2011)	**Depression Cohort** (n=2891) Clinically Meaningful Depressive Symptoms[a] (2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	RR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.90	(0.70, 1.16)	0.41	0.99	(0.96, 1.02)	0.40
Age in 2011						
- <45	0.97	(0.74, 1.28)	0.85	1.00	(0.97, 1.03)	0.92
- 45–64	1.0			1.0		
- ≥65	0.81	(0.61, 1.08)	0.15	0.98	(0.95, 1.01)	0.16
Sex						
- Female	1.0			1.0		
- Male	1.22	(0.96, 1.56)	0.11	1.02	(0.99, 1.05)	0.12
Race						
- White	1.0			1.0		
- People of Colour	1.42	(1.03, 1.95)	**0.032**	1.04	(1.00, 1.07)	**0.029**
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.03	(0.83, 1.28)	0.79	1.00	(0.98, 1.03)	0.73
Education						
- Secondary School/GED	1.14	(0.88, 1.47)	0.33	1.01	(0.99, 1.04)	0.32
- Associate/Technical Degree	1.41	(1.06, 1.89)	**0.020**	1.04	(1.00, 1.07)	**0.024**
- Bachelor's Degree	0.89	(0.70, 1.15)	0.37	0.99	(0.96, 1.02)	0.37
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.74	(1.21, 2.50)	**0.0030**	1.07	(1.02, 1.11)	**0.0025**
- $30,000–$50,000	1.52	(1.08, 2.15)	**0.017**	1.05	(1.01, 1.11)	**0.0133**
- $50,001–$100,000	1.43	(1.05, 1.94)	**0.023**	1.04	(1.01, 1.08)	**0.022**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.28	(0.91, 1.79)	0.16	1.03	(0.99, 1.07)	0.13
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.06	(0.85, 1.33)	0.59	1.01	(0.98, 1.03)	0.57
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	10.26	(8.55,12.32)	**<0.0001**	1.41	(1.38, 1.44)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.17	(0.94, 1.47)	0.17	1.02	(0.99, 1.05)	0.15
- Severe	1.30	(1.02, 1.66)	**0.037**	1.03	(1.00, 1.06)	**0.034**
Disease duration (years)						
- ≤10	1.19	(0.91, 1.56)	0.19	1.02	(0.99, 1.05)	0.21
- 11–20	0.93	(0.75, 1.17)	0.54	0.99	(0.97, 1.02)	0.54
- ≥21	1.0			1.0		

[a] In 2012, 56.6% (1636/2891) of respondents with depression reported clinically meaningful symptoms (vs. 43.4%, 1255/2891 without).

[b] Adjusted for all variables listed in above table; missing n=118.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps; RR – relative risk.

Table C3.A Adjusted associations between baseline anxiety treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with anxiety, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors

Baseline Characteristics (2011)	**Anxiety Cohort** Clinically Meaningful Depressive Symptoms[a] (2012)					
	Full Cohort (n=1181) Adjusted[c]			**Restricted Cohort[b]** (n=1026) Adjusted[d]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.18	(0.84, 1.66)	0.34	1.25	(0.80, 1.96)	0.32
Age in 2011						
- <45	1.04	(0.71, 1.54)	0.84	1.05	(0.69, 1.60)	0.82
- 45–64	1.0			1.0		
- ≥65	0.59	(0.36, 0.98)	**0.041**	0.44	(0.25, 0.77)	**0.0036**
Sex						
- Female	1.0			1.0		
- Male	1.63	(1.03, 2.57)	**0.037**	1.70	(1.03, 2.77)	**0.036**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.07	(0.65, 1.76)	0.78	1.21	(0.70, 2.09)	0.50
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.67, 1.36)	0.78	0.76	(0.52, 1.11)	0.16
Education						
- Secondary School/GED	1.28	(0.84, 1.96)	0.26	1.18	(0.74, 1.87)	0.48
- Associate/Technical Degree	1.27	(0.79, 2.04)	0.32	1.33	(0.79, 2.22)	0.29
- Bachelor’s Degree	0.84	(0.56, 1.27)	0.41	0.73	(0.47, 1.15)	0.17
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	1.75	(0.97, 3.17)	**0.065**	2.24	(1.17, 4.29)	**0.015**
- $30,000–$50,000	1.60	(0.91, 2.83)	0.11	1.65	(0.89, 3.09)	0.11
- $50,001–$100,000	1.30	(0.78, 2.15)	0.32	1.39	(0.80, 2.43)	0.25
- > $100,000	1.0			1.0		
- Unanswered/missing	1.26	(0.72, 2.18)	0.42	1.35	(0.74, 2.47)	0.33
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.34	(0.93, 1.92)	0.12	1.30	(0.88, 1.92)	0.19
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	13.13	(9.71, 17.77)	**<0.0001**	12.89	(9.28, 17.92)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.26	(0.89, 1.80)	0.20	1.33	(0.91, 1.96)	0.14
- Severe	1.56	(1.03, 2.36)	**0.036**	1.71	(1.10, 2.68)	**0.018**
Disease duration (years)						
- ≤10	0.99	(0.63, 1.53)	0.95	0.88	(0.55, 1.42)	0.60
- 11–20	0.76	(0.51, 1.13)	0.17	0.71	(0.46, 1.10)	0.13
- ≥21	1.0			1.0		

[a] Among full anxiety cohort, 56.8% (671/1181) reported clinically meaningful depressive symptoms on Spring 2012 survey.

[b] Excludes respondents whose only reported treatment barrier at baseline was “not having symptoms now” (157/313).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=48; [d] missing, n=41).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table C3.B Adjusted associations between baseline anxiety treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with anxiety, adjusting vs. not adjusting for Spring 2011 NARCOMS Depression score

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1181) Clinically Meaningful Depressive Symptoms[a]					
	Including Baseline Score Adjusted[b]			**Excluding Baseline Score** Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.18	(0.84, 1.66)	0.34	0.88	(0.66, 1.16)	0.35
Age in 2011 (years)						
- <45	1.04	(0.71, 1.54)	0.84	1.09	(0.79, 1.51)	0.61
- 45–64	1.0			1.0		
- ≥65	0.59	(0.36, 0.98)	**0.041**	0.49	(0.32, 0.75)	**0.0010**
Sex						
- Female	1.0			1.0		
- Male	1.63	(1.03, 2.57)	**0.037**	1.48	(1.01, 2.19)	**0.046**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.07	(0.65, 1.76)	0.78	1.23	(0.81, 2.19)	0.34
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.67, 1.36)	0.78	0.98	(0.73, 1.32)	0.88
Education						
- Secondary School/GED	1.28	(0.84, 1.96)	0.26	1.09	(0.76, 1.56)	0.64
- Associate/Technical Degree	1.27	(0.79, 2.04)	0.32	1.22	(0.82, 1.81)	0.33
- Bachelor's Degree	0.84	(0.56, 1.27)	0.41	0.87	(0.62, 1.23)	0.44
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.75	(0.97, 3.17)	**0.065**	2.38	(1.45, 3.92)	**0.0006**
- $30,000–$50,000	1.60	(0.91, 2.83)	0.11	2.11	(1.31, 3.39)	**0.0022**
- $50,001–$100,000	1.30	(0.78, 2.15)	0.32	1.33	(0.87, 2.03)	0.18
- > $100,000	1.0			1.0		
- Unanswered/missing	1.26	(0.72, 2.18)	0.42	1.50	(0.95, 2.38)	**0.085**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.34	(0.93, 1.92)	0.12	1.48	(1.09, 1.99)	**0.0049**
Baseline NARCOMS Depression score						
- <2	1.0					
- ≥2	13.13	(9.71, 17.77)	**<0.0001**			
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.26	(0.89, 1.80)	0.20	1.53	(1.14, 2.05)	**0.0049**
- Severe	1.56	(1.03, 2.36)	**0.036**	1.73	(1.23, 2.45)	**0.0019**
Disease duration (years)						
- ≤10	0.99	(0.63, 1.53)	0.95	0.92	(0.64, 1.32)	0.64
- 11–20	0.76	(0.51, 1.13)	0.17	0.78	(0.56, 1.10)	0.15
- ≥21	1.0			1.0		

[a] Among anxiety cohort, 56.8% (671/1181) reported clinically meaningful depressive symptoms on Spring 2012 survey.

[b] Model adjusted for all variables listed above in table (missing n=48).

[c] Model adjusted for variables listed above in table, apart from baseline NARCOMS Depression score (missing n=48).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table C3.C Adjusted associations between baseline anxiety treatment status and clinically meaningful depressive symptoms at one-year follow-up among NARCOMS Spring 2011 respondents diagnosed with anxiety, assessed with logistic regression vs. modified Poisson regression

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1181) Clinically Meaningful Depressive Symptoms[a] (2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.18	(0.84, 1.66)	0.34	1.02	(0.98, 1.05)	0.30
Age in 2011						
- <45	1.04	(0.71, 1.54)	0.84	1.00	(0.97, 1.05)	0.82
- 45–64	1.0			1.0		
- ≥65	0.59	(0.36, 0.98)	**0.041**	0.95	(0.90, 1.00)	**0.055**
Sex						
- Female	1.0			1.0		
- Male	1.63	(1.03, 2.57)	**0.037**	1.05	(1.01, 1.09)	**0.026**
Race						
- White	1.0			1.0		
- People of Colour	1.07	(0.65, 1.76)	0.78	1.01	(0.96, 1.05)	0.78
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.67, 1.36)	0.78	1.00	(0.96, 1.03)	0.87
Education						
- Secondary School/GED	1.28	(0.84, 1.96)	0.26	1.03	(0.98, 1.07)	0.27
- Associate/Technical Degree	1.27	(0.79, 2.04)	0.32	1.02	(0.97, 1.07)	0.40
- Bachelor's Degree	0.84	(0.56, 1.27)	0.41	0.98	(0.94, 1.03)	0.40
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.75	(0.97, 3.17)	**0.065**	1.06	(1.00, 1.13)	**0.060**
- $30,000–$50,000	1.60	(0.91, 2.83)	0.11	1.05	(0.99, 1.12)	**0.096**
- $50,001–$100,000	1.30	(0.78, 2.15)	0.32	1.03	(0.98, 1.09)	0.27
- > $100,000	1.0			1.0		
- Unanswered/missing	1.26	(0.72, 2.18)	0.42	1.03	(0.97, 1.10)	0.36
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.34	(0.93, 1.92)	0.12	1.03	(0.99, 1.07)	0.10
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	13.13	(9.71, 17.77)	**<0.0001**	1.44	(1.39, 1.50)	**<0.0001**
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.26	(0.89, 1.80)	0.20	1.03	(0.99, 1.07)	0.17
- Severe	1.56	(1.03, 2.36)	**0.036**	1.05	(1.00, 1.09)	**0.034**
Disease duration (years)						
- ≤10	0.99	(0.63, 1.53)	0.95	1.00	(0.96, 1.04)	0.95
- 11–20	0.76	(0.51, 1.13)	0.17	0.97	(0.93, 1.01)	0.14
- ≥21	1.0			1.0		

[a] In 2012, 56.8% (671/1181) of respondents with anxiety reported clinically meaningful symptoms (vs. 43.2%, 510/1181 without).

[b] Adjusted for all variables listed in above table; missing n=48.

Bolded estimates indicate p<0.10.

Abbreviations: CI– Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps; RR – relative risk.

Appendix D Objective 2B Supplementary Tables

Table D1.A Bivariate and unadjusted associations between respondents' baseline sociodemographic characteristics and clinically meaningful decline in MCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome[c]**		**Crude OR**		
	MCS1a[d]	MCS1b[d]	OR	95% CI	*p*-value	MCS2a[d]	MCS2b[d]	OR	95% CI	*p*-value
Baseline treatment status										
- Receiving treatment	67.7	32.4	1.0			68.6	31.4	1.0		
- Not receiving treatment	68.3	31.7	0.97	(0.78, 1.21)	0.78	66.7	33.3	1.09	(0.82, 1.45)	0.54
Year of birth										
- ≤1946	64.2	35.8	1.22	(0.92, 1.60)	0.16	59.8	40.2	1.61	(1.02, 2.54)	**0.041**
- 1947–1953	66.3	33.8	1.11	(0.89, 1.39)	0.35	67.1	32.9	1.18	(0.81, 1.70)	0.39
- 1954–1959	68.6	31.4	1.0			70.5	29.5	1.0		
- 1960–1966	67.3	32.7	1.06	(0.83, 1.34)	0.64	64.3	35.7	1.33	(0.93, 1.91)	0.12
- ≥1967	72.8	27.3	0.82	(0.63, 1.07)	0.14	74.1	25.9	0.84	(0.57, 1.23)	0.37
Age in 2011 (years)										
- <45	72.8	27.3	0.77	(0.61, 0.98)	**0.030**	74.1	25.9	0.73	(0.52, 1.00)	**0.051**
- 45–64	67.3	32.7	1.0			67.4	32.6	1.0		
- ≥65	64.2	35.8	1.15	(0.90, 1.46)	0.26	59.8	40.2	1.39	(0.93, 2.09)	0.11
Sex										
- Female	68.5	31.5	1.0			68.8	31.2	1.0		
- Male	64.0	36.0	1.23	(1.00, 1.51)	**0.054**	63.5	36.6	1.27	(0.88, 1.83)	0.20
Race										
- White	67.5	32.5	1.0			68.4	31.6	1.0		
- People of Colour/Other	69.7	30.3	0.90	(0.69, 1.19)	0.47	64.6	43.3	1.14	(0.77, 1.69)	0.53
Marital status										
- Married/cohabitating	67.4	32.6	1.0			66.8	33.2	1.0		
- Single/living alone	68.7	31.3	0.94	(0.79, 1.12)	0.50	70.0	30.0	0.86	(0.66, 1.13)	0.28
Residence										
- Private residence	68.1	31.9	1.0			68.1	31.9	1.0		
- Living with assistance	62.8	37.3	1.27	(0.91, 1.78)	0.17	63.9	36.1	1.21	(0.70, 2.06)	0.50
Education										
- Secondary School/GED	67.6	32.4	1.07	(0.85, 1.33)	0.58	65.7	34.3	1.27	(0.90, 1.81)	0.18
- Associate/Technical Degree	67.0	33.0	1.09	(0.85, 1.41)	0.49	66.5	33.5	1.23	(0.83, 1.82)	0.31
- Bachelor's Degree	67.7	32.3	1.06	(0.85, 1.33)	0.60	68.7	31.3	1.11	(0.78, 1.59)	0.57
- Post Bachelor's Degree	69.0	31.1	1.0			70.9	29.1	1.0		
Income										
- <$30,000	68.5	31.5	1.01	(0.77, 1.33)	0.95	67.9	32.2	1.05	(0.69, 1.59)	0.84
- $30,000–$50,000	67.8	32.2	1.04	(0.78, 1.39)	0.79	66.5	33.5	1.11	(0.71, 1.75)	0.64
- $50,001–$100,000	66.4	33.6	1.11	(0.85, 1.45)	0.45	66.7	33.3	1.10	(0.72, 1.69)	0.65
- > $100,000	68.7	31.3	1.0			68.8	31.2	1.0		

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome[c]**		**Crude OR**		
	MCS1a[d]	MCS1b[d]	OR	95% CI	*p*-value	MCS2a[d]	MCS2b[d]	OR	95% CI	*p*-value
- Unanswered/missing	68.0	32.1	1.03	(0.78, 1.38)	0.82	71.0	29.0	0.90	(0.57, 1.41)	0.65
Employment										
- Employed	69.1	30.9	1.0			70.7	29.3	1.0		
- Unemployed/missing	67.0	33.0	1.10	(0.93, 1.31)	0.26	66.6	33.4	1.21	(0.93, 1.57)	0.16
Health insurance										
- Private	69.7	33.4	0.82	(0.68, 0.99)	**0.037**	71.1	28.9	0.73	(0.55, 0.98)	**0.038**
- Private and public	65.3	34.7	1.0			64.3	35.7	1.0		
- Public	67.4	32.6	0.91	(0.73, 1.14)	0.41	67.1	32.9	0.88	(0.63, 1.25)	0.48
- Uninsured	67.4	32.6	0.91	(0.58, 1.44)	0.69	68.0	32.0	0.85	(0.45, 1.60)	0.61

[a] Decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in MCS-12 score (2011 to 2012): [b] depression cohort: 32.3% (898/2784); [c] anxiety cohort 31.9% (364/1140).

[d] MCS1a = improved/no decline (n=1886); MCS1b = declined (n=898); MCS2a = improved/no decline (n=776); MCS2b = declined (n=364).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; OR – odds ratio; USA – United States of America.

Table D1.B Bivariate and unadjusted associations between respondents' baseline clinical characteristics and clinically meaningful decline in MCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Clinical Characteristics (2011)	**Clinically Meaningful Decline in MCS-12 Score (2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome**[c]		**Crude OR**		
	MCS1a[d]	MCS1b[d]	OR	95% CI	*p*-value	MCS2a[d]	MCS2b[d]	OR	95% CI	*p*-value
Spring 2011 NARCOMS Depression score										
- <2	64.2	35.8	1.0			65.5	34.5	1.0		
- ≥2	70.3	29.7	0.76	(0.65, 0.89)	**0.0007**	69.9	30.2	0.82	(0.64, 1.06)	0.12
Admission to overnight healthcare facility										
- Yes	64.3	35.7	1.18	(0.90, 1.56)	0.23	60.0	40.0	1.48	(1.00, 2.20)	**0.051**
- No	68.1	31.9	1.0			69.0	31.0	1.0		
Self-rated health										
- Excellent/very good/good	66.7	33.3	1.0			68.3	31.7	1.0		
- Fair/poor	69.6	30.4	0.88	(0.74, 1.04)	0.12	67.8	32.2	1.02	(0.79, 1.32)	0.86
Cognitive impairment										
- Minimal	67.0	33.0	1.0			68.4	31.7	1.0		
- Moderate	68.9	31.1	0.92	(0.77, 1.09)	0.31	68.8	31.2	0.98	(0.75, 1.29)	0.89
- Severe	65.1	34.9	1.09	(0.82, 1.43)	0.56	63.3	36.7	1.25	(0.83, 1.90)	0.29
Fatigue										
- Minimal	68.1	31.9	1.0			67.2	32.8	1.0		
- Moderate	66.6	33.4	1.07	(0.85, 1.35)	0.58	68.3	31.7	0.95	(0.66, 1.37)	0.79
- Severe	69.0	31.0	0.96	(0.75 1.22)	0.73	67.9	32.1	0.97	(0.66, 1.41)	0.87
Pain										
- Minimal	67.9	32.1	1.0			68.9	31.1	1.0		
- Moderate	67.7	32.3	1.01	(0.85, 1.20)	0.92	68.2	31.8	1.03	(0.78, 1.37)	0.82
- Severe	67.9	32.1	1.00	(0.79, 1.26)	0.99	66.7	33.3	1.11	(0.78, 1.57)	0.57
Disability (PDDS)										
- Mild	70.2	29.8	1.0			69.7	30.3	1.0		
- Moderate	68.2	31.8	1.10	(0.90, 1.34)	0.35	71.6	28.4	0.91	(0.68, 1.22)	0.53
- Severe	64.8	35.2	1.28	(1.06, 1.56)	**0.011**	60.3	39.7	1.51	(1.11, 2.06)	**0.0089**
MCS-12 (mean)	39.5	46.3	1.06	(1.05, 1.07)	**<0.0001**	38.6	44.2	1.05	(1.03, 1.06)	**<0.0001**
PCS-12 (mean)	38.1	35.5	0.98	(0.97, 0.99)	**<0.0001**	38.9	35.8	0.98	(0.97, 0.99)	**<0.0001**

[a] Decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in MCS-12 score (2011 to 2012): [b] depression cohort: 32.3% (898/2784); [c] anxiety cohort 31.9% (364/1140).

[d] MCS1a = improved/no decline (n=1886); MCS1b = declined (n=898); MCS2a = improved/no decline (n=776); MCS 2b = declined (n=364).

Among both cohorts, all listed variables were missing no more than 1%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table D1.C Bivariate and unadjusted associations between respondents' baseline MS characteristics and clinically meaningful decline in MCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline MS Characteristics (2011)	**Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome[c]**		**Crude OR**		
	MCS1a[d]	MCS1b[d]	OR	95% CI	*p*-value	MCS2a[d]	MCS2b[d]	OR	95% CI	*p*-value
Age of MS symptom onset (years)										
- < 25	69.0	31.0	0.93	(0.78, 1.12)	0.45	68.4	31.6	1.06	(0.80, 1.40)	0.71
- 25–39	67.5	32.5	1.0			69.6	30.4	1.0		
- ≥ 40	65.9	34.1	1.08	(0.86, 1.34)	0.52	62.0	38.0	1.40	(0.99, 1.99)	**0.058**
Year of MS onset										
- ≤ 1980	65.6	34.4	1.0			64.1	35.9	1.0		
- 1981–1985	65.4	34.6	1.01	(0.79, 1.29)	0.96	68.4	31.6	0.82	(0.55, 1.24)	0.35
- 1986–1990	68.5	31.5	0.88	(0.69, 1.12)	0.30	68.8	31.2	0.81	(0.55, 1.20)	0.29
- 1991–1995	69.6	30.4	0.83	(0.65, 1.07)	0.15	70.7	29.4	0.74	(0.49, 1.11)	0.15
- ≥1996	69.8	30.2	0.82	(0.66, 1.03)	**0.091**	68.6	31.4	0.82	(0.57, 1.16)	0.25
Age at MS diagnosis (years)										
- <30	69.2	30.8	0.78	(0.59, 1.05)	0.10	73.6	26.5	0.57	(0.36, 0.89)	**0.015**
- 30–39	68.0	32.0	0.83	(0.64, 1.07)	0.15	65.4	34.6	0.83	(0.55, 1.26)	0.39
- 40–49	68.5	31.5	0.82	(0.62, 1.05)	0.12	69.6	30.4	0.69	(0.45, 1.05)	**0.081**
- ≥50	63.7	36.3	1.0			61.1	38.9	1.0		
Year of MS diagnosis										
- ≤1990	66.6	33.4	1.0			66.3	33.8	1.0		
- 1991–1995	65.4	34.6	1.06	(0.83, 1.33)	0.65	64.7	35.3	1.07	(0.72, 1.61)	0.74
- 1996-2000	70.3	29.7	0.84	(0.67, 1.05)	0.13	71.6	28.4	0.78	(0.54, 1.13)	0.19
- ≥2001	68.6	31.4	0.91	(0.73, 1.13)	0.39	68.1	31.9	0.92	(0.66, 1.29)	0.62
Disease duration (years)										
- ≤10	68.6	31.4	0.91	(0.73, 1.13)	0.39	68.1	31.9	0.92	(0.66, 1.29)	0.62
- 11–20	68.2	31.9	0.93	(0.77, 1.13)	0.47	68.9	31.1	0.89	(0.64, 1.24)	0.48
- ≥21	66.6	33.4	1.0			66.3	33.8	1.0		

[a] Decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in MCS-12 score (2011 to 2012): [b] depression cohort: 32.3% (898/2784); [c] anxiety cohort 31.9% (364/1140).

[d] MCS1a = improved/no decline (n=1886); MCS1b = declined (n=898); MCS2a = improved/no decline (n=776); MCS2b = declined (n=364).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; MCS – Mental Component Score; MS – multiple sclerosis; OR – odds ratio.

Table D2.A Bivariate and unadjusted associations between respondents' baseline sociodemographic characteristics and clinically meaningful decline in PCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Decline in PCS-12 Score**[a] **(2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome**[c]		**Crude OR**		
	PCS1a[d]	PCS1b[d]	OR	95% CI	*p*-value	PCS2a[d]	PCS2b[d]	OR	95% CI	*p*-value
Baseline treatment status										
- Receiving treatment	66.7	33.0	1.0			70.1	29.9	1.0		
- Not receiving treatment	68.1	31.9	0.95	(0.76, 1.19)	0.65	65.7	34.3	1.23	(0.93, 1.62)	0.15
Year of birth										
- ≤1946	68.6	31.4	0.87	(0.66, 1.15)	0.34	72.3	27.7	0.72	(0.45, 1.16)	0.18
- 1947–1953	68.6	31.4	0.88	(0.70, 1.09)	0.23	67.5	32.5	0.91	(0.62, 1.30)	0.59
- 1954–1959	65.7	34.4	1.0			65.3	34.7	1.0		
- 1960–1966	66.1	33.9	0.98	(0.78, 1.24)	0.87	73.0	27.0	0.69	(0.48, 1.01)	**0.053**
- ≥1967	67.1	32.9	0.94	(0.73, 1.21)	0.63	68.7	31.3	0.86	(0.59, 1.23)	0.40
Age in 2011 (years)										
- <45	67.1	32.9	0.99	(0.79, 1.24)	0.94	68.7	31.3	0.99	(0.72, 1.35)	0.94
- 45–64	66.9	33.1	1.0			68.5	31.6	1.0		
- ≥65	68.6	31.4	0.92	(0.72, 1.18)	0.53	72.3	27.7	0.83	(0.54, 1.29)	0.41
Sex										
- Female	66.7	33.3	1.0			68.4	31.6	1.0		
- Male	69.3	30.7	0.89	(0.72, 1.10)	0.27	72.4	27.6	0.82	(0.56, 1.21)	0.33
Race										
- White	67.7	32.3	1.0			69.3	30.7	1.0		
- People of Colour/Other	62.1	37.9	1.28	(0.98, 1.66)	**0.068**	65.6	34.4	1.19	(0.80, 1.76)	0.40
Marital status										
- Married/cohabitating	67.5	32.5	1.0			69.1	30.9	1.0		
- Single/living alone	66.9	33.1	1.03	(0.87, 1.22)	0.74	69.2	30.8	1.00	(0.76, 1.30)	0.98
Residence										
- Private residence	67.3	32.7	1.0			69.1	30.9	1.0		
- Living with assistance	64.7	35.3	1.13	(0.80, 1.58)	0.50	70.5	29.5	0.94	(0.53, 1.65)	0.83
Education										
- Secondary School/GED	68.3	31.7	0.89	(0.71, 1.11)	0.31	71.3	28.7	0.82	(0.57, 1.16)	0.26
- Associate/Technical Degree	65.6	34.4	1.01	(0.79, 1.29)	0.95	69.9	30.1	0.87	(0.59, 1.30)	0.50
- Bachelor's Degree	68.4	31.6	0.89	(0.71, 1.11)	0.29	67.8	32.2	0.96	(0.68, 1.37)	0.83
- Post Bachelor's Degree	65.8	34.2	1.0			66.9	33.1	1.0		
Income										
- <$30,000	66.1	33.9	1.30	(0.98, 1.71)	**0.067**	70.2	39.8	1.21	(0.78, 1.87)	0.39
- $30,000–$50,000	67.2	32.8	1.23	(0.92, 1.66)	0.16	64.5	35.5	1.57	(0.99, 2.49)	**0.056**
- $50,001–$100,000	66.9	33.1	1.25	(0.95, 1.64)	0.11	70.0	30.0	1.22	(0.78, 1.91)	0.38
- > $100,000	71.7	28.3	1.0			74.0	26.0	1.0		

Baseline Sociodemographic Characteristics (2011)	**Clinically Meaningful Decline in PCS-12 Score**[a] **(2011 to 2012)**									
	Depression Cohort (n=2784)					**Anxiety Cohort** (n=1140)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome**[c]		**Crude OR**		
	PCS1a[d]	PCS1b[d]	OR	95% CI	*p*-value	PCS2a[d]	PCS2b[d]	OR	95% CI	*p*-value
- Unanswered/missing	65.4	34.6	1.34	(1.00, 1.79)	**0.051**	66.4	33.6	1.45	(0.91, 2.29)	0.12
Employment										
- Employed	68.0	32.0	1.0			68.7	31.3	1.0		
- Unemployed/missing	66.7	33.3	1.06	(0.90, 1.25)	0.50	69.1	30.9	0.98	(0.76, 1.28)	0.89
Health insurance										
- Private	66.4	33.6	1.10	(0.91, 1.32)	0.32	66.5	33.5	1.26	(0.92, 1.70)	0.13
- Private and public	68.5	31.5	1.0			71.4	28.6	1.0		
- Public	67.1	33.0	1.07	(0.85, 1.33)	0.57	72.3	27.7	0.96	(0.67, 1.38)	0.82
- Uninsured	65.2	34.8	1.16	(0.74, 1.82)	0.53	60.0	40.0	1.67	(0.90, 3.08)	0.11

[a] Decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in PCS-12 score (2011 to 2012): [b] depression cohort: 32.9% (915/2784); [c] anxiety cohort 31.1% (354/1140).

[d] PCS1a = improved/no decline (n=1869); PCS1b = declined (n=915); PCS2a = improved/no decline (n=786); PCS2b = declined (n=354).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; OR – odds ratio; PCS – Physical Component Score; USA – United States of America.

Table D2.B Bivariate and unadjusted associations between respondents' baseline clinical characteristics and clinically meaningful decline in PCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline Clinical Characteristics (2011)	**Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)**									
	Depression Cohort (n=2784)					**Depression Cohort** (n=2784)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome[c]**		**Crude OR**		
	PCS1a[d]	PCS1b[d]	OR	95% CI	*p*-value	PCS2a[d]	PCS2b[d]	OR	95% CI	*p*-value
Spring 2011 NARCOMS Depression score										
- <2	69.6	30.4	1.0			68.8	31.2	1.0		
- ≥2	65.4	34.6	1.21	(1.03, 1.43)	**0.020**	69.0	31.0	0.99	(0.77 1.28)	0.94
Admission to overnight healthcare facility										
- Yes	68.0	32.0	0.96	(0.72, 1.27)	0.76	72.2	27.8	0.84	(0.66, 1.29)	0.43
- No	67.1	33.0	1.0			68.6	31.4	1.0		
Self-rated health										
- Excellent/very good/good	64.0	36.0	1.0			65.0	35.0	1.0		
- Fair/poor	73.0	27.0	0.66	(0.55. 0.78)	**<0.0001**	75.5	24.5	0.61	(0.46, 0.79)	**0.0002**
Cognitive impairment										
- Minimal	69.1	30.9	1.0			68.6	31.4	1.0		
- Moderate	66.6	33.4	1.12	(0.95, 1.33)	0.18	70.3	29.7	0.92	(0.70, 1.21)	0.56
- Severe	61.9	38.1	1.38	(1.05, 1.80)	**0.022**	63.3	36.7	1.27	(0.84, 1.92)	0.26
Fatigue										
- Minimal	69.5	30.5	1.0			67.8	32.2	1.0		
- Moderate	66.3	33.7	1.16	(0.92, 1.47)	0.21	67.4	32.6	1.02	(0.71, 1.47)	0.92
- Severe	67.3	32.7	1.11	(0.87, 1.42)	0.40	71.3	28.7	0.85	(0.58, 1.25)	0.40
Pain										
- Minimal	63.4	36.6	1.0			62.9	37.1	1.0		
- Moderate	68.6	31.4	0.79	(0.67, 0.94)	**0.0085**	70.1	29.9	0.73	(0.55, 0.96)	**0.022**
- Severe	73.1	26.9	0.64	(0.50, 0.81)	**0.0002**	78.5	21.5	0.46	(0.92, 0.68)	**<0.0001**
Disability (PDDS)										
- Mild	67.3	32.7	1.0			67.4	32.6	1.0		
- Moderate	63.7	36.4	1.18	(0.97, 1.42)	**0.097**	65.5	34.5	1.09	(0.82, 1.45)	0.56
- Severe	70.5	29.5	0.86	(0.71, 1.05)	0.14	76.1	23.9	0.65	(0.46, 0.91)	**0.012**
MCS-12 (mean)	43.1	38.9	0.97	(0.96, 0.98)	**<0.0001**	41.7	37.5	0.97	(0.96, 0.98)	**<0.0001**
PCS-12 (mean)	35.6	40.7	1.04	(1.04, 1.05)	**<0.0001**	36.0	42.2	1.05	(1.04, 1.06)	**<0.0001**

[a] Decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in PCS-12 score (2011 to 2012): [b] depression cohort: 32.9% (915/2784); [c] anxiety cohort 31.1% (354/1140).

[d] PCS1a = improved/no decline (n=1869); PCS1b = declined (n=915); PCS2a = improved/no decline (n=786); PCS2b = declined (n=354).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – confidence interval; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score; PDDS – Patient Determined Disease Steps.

Table D2.C Bivariate and unadjusted associations between respondents' baseline MS characteristics and clinically meaningful decline in PCS-12 score between NARCOMS Spring 2011 and 2012 follow-up surveys among respondents diagnosed with depression or anxiety (n, row% for crosstabulations, unless otherwise noted)

Baseline MS Characteristics (2011)	**Clinically Meaningful Decline in PCS-12 Score (2011 to 2012)**									
	Depression Cohort (n=2784)					**Depression Cohort** (n=2784)				
	Crosstabulation with Outcome[b]		**Crude OR**			**Crosstabulation with Outcome**[c]		**Crude OR**		
	PCS1a[d]	PCS1b[d]	OR	95% CI	*p*-value	PCS2a[d]	PCS2b[d]	OR	95% CI	*p*-value
Age of MS symptom onset (years)										
- < 25	66.1	33.9	1.10	(0.92, 1.32)	0.29	69.5	30.5	1.01	(0.76, 1.35)	0.94
- 25–39	68.2	31.8	1.0			69.8	30.2	1.0		
- ≥ 40	66.3	33.7	1.09	(0.87, 1.36)	0.44	66.5	33.5	1.16	(0.81, 1.66)	0.41
Year of MS onset										
- ≤ 1980	67.7	32.3	1.0			69.8	31.3	1.0		
- 1981–1985	65.0	35.1	1.13	(0.88, 1.45)	0.34	69.0	31.0	0.99	(0.65, 1.50)	0.96
- 1986–1990	67.0	44.0	1.03	(0.81, 1.32)	0.80	71.8	28.2	0.87	(0.58, 1.30)	0.48
- 1991–1995	69.4	30.7	0.93	(0.72, 1.19)	0.64	70.7	29.4	0.91	(0.61, 1.38)	0.67
- ≥1996	67.0	33.0	1.03	(0.82, 1.29)	0.79	67.3	32.7	1.07	(0.75, 1.52)	0.72
Age at MS diagnosis (years)										
- <30	66.1	33.9	1.12	(0.83, 1.51)	0.45	69.4	30.6	1.15	(0.71, 1.84)	0.57
- 30–39	68.1	31.9	1.02	(0.78, 1.34)	0.87	69.8	30.2	1.13	(0.72, 1.76)	0.60
- 40–49	66.5	33.5	1.10	(0.84, 1.44)	0.49	67.4	32.6	1.26	(0.80, 1.97)	0.31
- ≥50	68.6	31.4	1.0			72.2	27.8	1.0		
Year of MS diagnosis										
- ≤1990	68.5	31.5	1.0			65.8	34.2	1.0		
- 1991–1995	67.8	32.2	1.03	(0.81, 1.31)	0.79	73.9	26.1	0.68	(0.45, 1.04)	**0.074**
- 1996-2000	67.0	33.0	1.07	(0.86, 1.34)	0.55	69.9	30.1	0.83	(0.58, 1.20)	0.33
- ≥2001	65.9	34.1	1.12	(0.91, 1.39)	0.29	68.6	31.4	0.88	(0.63, 1.24)	0.47
Disease duration (years)										
- ≤10	65.9	34.1	1.12	(0.91, 1.39)	0.29	68.6	31.4	0.88	(0.63, 1.24)	0.47
- 11–20	67.3	32.7	1.05	(0.87, 1.28)	0.60	71.5	28.5	0.77	(0.55, 1.08)	0.12
- ≥21	68.5	31.5	1.0			65.8	34.2	1.0		

[a] Decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys.

[b,c] Clinically meaningful decline in PCS-12 score (2011 to 2012): [b] depression cohort: 32.9% (915/2784); [c] anxiety cohort 31.1% (354/1140).

[d] PCS1a = improved/no decline (n=1869); PCS1b = declined (n=915); PCS2a = improved/no decline (n=786); PCS 2b = declined (n=354).

Among both cohorts, all listed variables were missing no more than 2%.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; MS – multiple sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table D3.A Adjusted associations between baseline depression treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors.

Baseline Characteristics (2011)	**Depression Cohort** Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Full Cohort (n=2784) Adjusted[c]			**Restricted Cohort**[b] (n=2594) Adjusted[d]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.97	(0.77, 1.24)	0.83	1.10	(0.80, 1.51)	0.57
Age in 2011						
- <45	0.88	(0.68, 1.14)	0.33	0.85	(0.65, 1.12)	0.25
- 45–64	1.0			1.0		
- ≥65	0.99	(0.75, 1.30)	0.93	0.92	(0.69, 1.23)	0.58
Sex						
- Female	1.0			1.0		
- Male	1.31	(1.04, 1.64)	**0.020**	1.35	(1.07, 1.70)	**0.012**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.12	(0.83, 1.51)	0.44	1.22	(0.90, 1.66)	0.20
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.04	(0.84, 1.28)	0.74	1.08	(0.87, 1.34)	0.51
Education						
- Secondary School/GED	1.22	(0.95, 1.57)	0.12	1.18	(0.91, 1.53)	0.23
- Associate/Technical Degree	1.24	(0.94, 1.63)	0.13	1.22	(0.92, 1.63)	0.17
- Bachelor's Degree	1.08	(0.85, 1.38)	0.52	1.02	(0.79, 1.31)	0.87
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.15	(0.81, 1.63)	0.43	1.21	(0.84, 1.74)	0.30
- $30,000–$50,000	1.18	(0.85, 1.65)	0.32	1.24	(0.88, 1.75)	0.22
- $50,001–$100,000	1.17	(0.87, 1.56)	0.30	1.18	(0.87, 1.60)	0.30
- > $100,000	1.0			1.0		
- Unanswered/missing	1.13	(0.82, 1.56)	0.47	1.19	(0.85, 1.67)	0.32
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.11	(0.90, 1.38)	0.32	1.15	(0.92, 1.44)	0.21
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.10	(0.89, 1.37)	0.39	1.09	(0.87, 1.36)	0.47
- Severe	1.18	(0.93, 1.49)	0.18	1.16	(0.91, 1.48)	0.22
Baseline MCS-12 score	1.06	(1.05, 1.07)	**<0.0001**	1.07	(1.06, 1.07	**<0.0001**
Disease duration (years)						
- ≤10	1.13	(0.88, 1.45)	0.34	1.05	(0.81, 1.36)	0.74
- 11–20	1.00	(0.81, 1.24)	0.99	0.92	(0.73, 1.14)	0.44
- ≥21				1.0		

[a] Among full depression cohort, 32.3% (898/2784) reported clinically meaningful decline in MCS-12 score (decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Excludes respondents whose only reported treatment barrier at baseline was "not having symptoms now" (190/432).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=109; [d] missing, n=99).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table D3.B Adjusted associations between baseline depression treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, adjusting vs. not adjusting for Spring 2011 MCS-12 score.

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Including Baseline Score Adjusted[b]			**Excluding Baseline Score** Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.97	(0.77, 1.24)	0.83	1.04	(0.82, 1.30)	0.77
Age in 2011 (years)						
- <45	0.78	(0.54, 1.12)	0.17	0.81	(0.83, 1.40)	0.10
- 45–64	1.0			1.0		
- ≥65	1.06	(0.67, 1.69)	0.79	1.07	(0.97, 1.49)	0.59
Sex						
- Female	1.0			1.0		
- Male	1.31	(1.04, 1.64)	**0.020**	1.20	(0.97, 1.49)	**0.094**
Race						
- White	1.0			1.0		
- People of Colour/Other	1.12	(0.83, 1.51)	0.44	0.98	(0.74, 1.30)	0.90
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.04	(0.84, 1.28)	0.74	0.96	(0.79, 1.17)	0.68
Education						
- Secondary School/GED	1.22	(0.95, 1.57)	0.12	1.09	(0.86, 1.39)	0.46
- Associate/Technical Degree	1.24	(0.94, 1.63)	0.13	1.12	(0.86, 1.45)	0.40
- Bachelor's Degree	1.08	(0.85, 1.38)	0.52	1.07	(0.85, 1.34)	0.58
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.15	(0.81, 1.63)	0.43	0.96	(0.69, 1.34)	0.82
- $30,000–$50,000	1.18	(0.85, 1.65)	0.32	1.01	(0.74, 1.38)	0.95
- $50,001–$100,000	1.17	(0.87, 1.56)	0.30	1.11	(0.84, 1.47)	0.46
- > $100,000	1.0			1.0		
- Unanswered/missing	1.13	(0.82, 1.56)	0.47	0.99	(0.72, 1.35)	0.93
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.11	(0.90, 1.38)	0.32	0.97	(0.79, 1.19)	0.77
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.10	(0.89, 1.37)	0.39	1.07	(0.87, 1.32)	0.5
- Severe	1.18	(0.93, 1.49)	0.18	1.24	(1.00 1.56)	**0.056**
Baseline MCS-12 score	1.06	(1.05, 1.07)	**<0.0001**			
Disease duration (years)						
- ≤10	1.13	(0.88, 1.45)	0.34	1.06	(0.83, 1.35)	0.64
- 11–20	1.00	(0.81, 1.24)	0.99	0.98	(0.80, 1.20)	0.84
- ≥21	1.0			1.0		

[a] Among depression cohort, 32.3% (898/2784) reported clinically meaningful decline in MCS-12 score (decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Model adjusted for all variables listed above in table (missing n=109).

[c] Model adjusted for variables listed above in table, apart from baseline MCS-12 score (missing n=109).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table D3.C Adjusted associations between baseline depression treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, assessed with logistic regression vs. modified Poisson regression.

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.97	(0.77, 1.24)	0.83	1.00	(0.96, 1.03)	0.81
Age in 2011						
- <45	0.88	(0.68, 1.14)	0.33	0.98	(0.95, 1.02)	0.32
- 45–64	1.0			1.0		
- ≥65	0.99	(0.75, 1.30)	0.93	1.00	(0.96, 1.04)	0.93
Sex						
- Female	1.0			1.0		
- Male	1.31	(1.04, 1.64)	**0.020**	1.04	(1.01, 1.08)	**0.024**
Race						
- White	1.0			1.0		
- People of Colour	1.12	(0.83, 1.51)	0.44	1.02	(0.97, 1.06)	0.47
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	1.04	(0.84, 1.28)	0.74	1.01	(0.98, 1.04)	0.66
Education						
- Secondary School/GED	1.22	(0.95, 1.57)	0.12	1.03	(0.99, 1.07)	0.12
- Associate/Technical Degree	1.24	(0.94, 1.63)	0.13	1.03	(0.99, 1.08)	0.14
- Bachelor's Degree	1.08	(0.85, 1.38)	0.52	1.01	(0.98, 1.05)	0.54
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.15	(0.81, 1.63)	0.43	1.02	(0.97, 1.07)	0.46
- $30,000–$50,000	1.18	(0.85, 1.65)	0.32	1.02	(0.97, 1.08)	0.34
- $50,001–$100,000	1.17	(0.87, 1.56)	0.30	1.02	(0.98, 1.07)	0.31
- > $100,000	1.0			1.0		
- Unanswered/missing	1.13	(0.82, 1.56)	0.47	1.02	(0.97, 1.07)	0.48
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.11	(0.90, 1.38)	0.32	1.02	(0.98, 1.05)	0.33
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	1.10	(0.89, 1.37)	0.39	1.01	(0.98, 1.05)	0.38
- Severe	1.18	(0.93, 1.49)	0.18	1.03	(0.99, 1.06)	0.17
Baseline MCS-12 score	1.06	(1.05, 1.07)	**<0.0001**	1.01	(1.01, 1.01)	**<0.0001**
Disease duration (years)						
- ≤10	1.13	(0.88, 1.45)	0.34	1.02	(0.98, 1.06)	0.35
- 11–20	1.00	(0.81, 1.24)	0.99	1.00	(0.97, 1.03)	0.99
- ≥21	1.0			1.0		

[a] In 2012, 32.3% (898/2784) of respondents with depression reported a clinically meaningful decline in MCS-12 score (vs. 67.7%, 1886/2784 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=109.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps; RR – relative risk.

Table D4.A Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors.

Baseline Characteristics (2011)	**Anxiety Cohort** Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Full Cohort (n=1140) Adjusted[c]			**Restricted Cohort**[b] (n=987) Adjusted[d]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.02	(0.76, 1.39)	0.88	0.90	(0.59, 1.37)	0.61
Age in 2011 (years)						
- <45	0.78	(0.54, 1.12)	0.17	0.84	(0.57, 1.24)	0.39
- 45–64	1.0			1.0		
- ≥65	1.06	(0.67, 1.69)	0.79	1.04	(0.63, 1.73)	0.88
Sex						
- Female	1.0			1.0		
- Male	1.23	(0.83, 1.83)	0.30	1.30	(0.85, 2.00)	0.22
Race						
- White	1.0			1.0		
- People of Colour/Other	1.35	(0.88, 2.06)	0.17	1.52	(0.96, 2.43)	**0.077**
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.93	(0.67, 1.28)	0.65	0.93	(0.66, 1.32)	0.68
Education						
- Secondary School/GED	1.33	(0.90, 1.97)	0.15	1.31	(0.86, 2.01)	0.21
- Associate/Technical Degree	1.24	(0.81, 1.89)	0.33	1.35	(0.85, 2.15)	0.20
- Bachelor's Degree	1.03	(0.70, 1.50)	0.89	0.92	(0.61, 1.41)	0.71
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.04	(0.61, 1.77)	0.90	1.01	(0.55, 1.82)	0.99
- $30,000–$50,000	1.10	(0.66, 1.84)	0.72	0.95	(0.54, 1.69)	0.86
- $50,001–$100,000	1.08	(0.69, 1.71)	0.73	1.14	(0.68, 1.90)	0.62
- > $100,000	1.0			1.0		
- Unanswered/missing	0.79	(0.47, 1.31)	0.35	0.78	(0.89, 1.85)	0.40
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.21	(0.87, 1.69)	0.25	1.28	(0.89, 1.85)	0.19
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	0.88	(0.64, 1.22)	0.46	0.83	(0.58, 1.18)	0.30
- Severe	1.36	(0.94, 1.96)	**0.099**	1.36	(0.92, 2.01)	0.12
Baseline MCS-12 score	1.05	(1.04, 1.06)	**<0.0001**	1.05	(1.04, 1.07)	**<0.0001**
Disease duration (years)						
- ≤10	1.02	(0.69, 1.50)	0.93	0.95	(0.63, 1.44)	0.81
- 11–20	0.93	(0.58, 1.18)	0.83	0.75	(0.51, 1.11)	0.15
- ≥21	1.0			1.0		

[a] Among full anxiety cohort, 31.9% (364/1140) reported clinically meaningful decline in MCS-12 score (decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Excludes respondents whose only reported treatment barrier at baseline was "not having symptoms now" (153/300).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=46; [d] missing, n=38).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table D4.B Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, adjusting vs. not adjusting for Spring 2011 MCS-12 score.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Including Baseline Score Adjusted[b]			**Excluding Baseline Score** Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.02	(0.76, 1.39)	0.88	1.14	(0.85, 1.53)	0.39
Age in 2011 (years)						
- <45	0.78	(0.54, 1.12)	0.17	0.73	(0.52, 1.03)	**0.075**
- 45–64	1.0			1.0		
- ≥65	1.06	(0.67, 1.69)	0.79	1.25	(0.80, 1.94)	0.33
Sex						
- Female	1.0			1.0		
- Male	1.23	(0.83, 1.83)	0.30	1.20	(0.82, 1.76)	0.35
Race						
- White	1.0			1.0		
- People of Colour/Other	1.35	(0.88, 2.06)	0.17	1.25	(0.83, 1.89)	0.28
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.93	(0.67, 1.28)	0.65	0.88	(0.64, 1.20)	0.41
Education						
- Secondary School/GED	1.33	(0.90, 1.97)	0.15	1.26	(0.86, 1.84)	0.23
- Associate/Technical Degree	1.24	(0.81, 1.89)	0.33	1.18	(0.78, 1.79)	0.44
- Bachelor's Degree	1.03	(0.70, 1.50)	0.89	1.09	(0.75, 1.57)	0.66
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.04	(0.61, 1.77)	0.90	0.89	(0.53, 1.50)	0.66
- $30,000–$50,000	1.10	(0.66, 1.84)	0.72	0.92	(0.56, 1.51)	0.74
- $50,001–$100,000	1.08	(0.69, 1.71)	0.73	1.01	(0.65, 1.57)	0.98
- > $100,000	1.0			1.0		
- Unanswered/missing	0.79	(0.47, 1.31)	0.35	0.71	(0.43, 1.16)	0.16
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.21	(0.87, 1.69)	0.25	1.06	(0.77, 1.46)	0.73
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	0.88	(0.64, 1.22)	0.46	0.86	(0.64, 1.18)	0.34
- Severe	1.36	(0.94, 1.96)	**0.099**	1.38	(0.97, 1.18)	**0.076**
Baseline MCS-12 score	1.05	(1.04, 1.06)	**<0.0001**			
Disease duration (years)						
- ≤10	1.02	(0.69, 1.50)	0.93	1.09	(0.75, 1.58)	0.67
- 11–20	0.93	(0.58, 1.18)	0.83	0.92	(0.65, 1.30)	0.63
- ≥21	1.0			1.0		

[a] Among anxiety cohort, 31.9% (364/1140) reported clinically meaningful decline in MCS-12 score (decrease in MCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Model adjusted for all variables listed above in table (missing n=46).

[c] Model adjusted for variables listed above in table, apart from baseline MCS-12 score (missing n=46).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps.

Table D4.C Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in MCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, assessed with logistic regression vs. modified Poisson regression.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in MCS-12 Score[a] (2011 to 2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.02	(0.76, 1.39)	0.88	1.00	(0.92, 1.05)	0.89
Age in 2011 (years)						
- <45	0.78	(0.54, 1.12)	0.17	0.96	(0.91, 1.01)	0.16
- 45–64	1.0			1.0		
- ≥65	1.06	(0.67, 1.69)	0.79	1.01	(0.94, 1.09)	0.79
Sex						
- Female	1.0			1.0		
- Male	1.23	(0.83, 1.83)	0.30	1.03	(0.97, 1.10)	0.30
Race						
- White	1.0			1.0		
- People of Colour	1.35	(0.88, 2.06)	0.17	1.05	(0.98, 1.12)	0.17
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.93	(0.67, 1.28)	0.65	0.99	(0.94, 1.04)	0.67
Education						
- Secondary School/GED	1.33	(0.90, 1.97)	0.15	1.04	(0.99, 1.11)	0.14
- Associate/Technical Degree	1.24	(0.81, 1.89)	0.33	1.03	(0.97, 1.10)	0.34
- Bachelor's Degree	1.03	(0.70, 1.50)	0.89	1.00	(0.96, 1.06)	0.88
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.04	(0.61, 1.77)	0.90	1.01	(0.93, 1.09)	0.90
- $30,000–$50,000	1.10	(0.66, 1.84)	0.72	1.02	(0.94, 1.10)	0.71
- $50,001–$100,000	1.08	(0.69, 1.71)	0.73	1.01	(0.94, 1.09)	0.71
- > $100,000	1.0			1.0		
- Unanswered/missing	0.79	(0.47, 1.31)	0.35	0.97	(0.89, 1.04)	0.37
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.21	(0.87, 1.69)	0.25	1.03	(0.98, 1.08)	0.27
Disability (PDDS)						
- Minimal	1.0			1.0		
- Moderate	0.88	(0.64, 1.22)	0.46	0.98	(0.94, 1.03)	0.46
- Severe	1.36	(0.94, 1.96)	**0.099**	1.05	(0.99, 1.11)	**0.095**
Baseline MCS-12 score	1.05	(1.04, 1.06)	**<0.0001**	1.01	(1.01, 1.01)	**<0.0001**
Disease duration (years)						
- ≤10	1.02	(0.69, 1.50)	0.93	1.00	(0.95, 1.06)	0.91
- 11–20	0.93	(0.58, 1.18)	0.83	0.97	(0.92, 1.03)	0.30
- ≥21	1.0			1.0		

[a] In 2012, 31.9% (364/1140) of respondents with anxiety reported a clinically meaningful decline in MCS-12 score (vs. 68.1%, 776/1140 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=46.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; MCS – Mental Component Score; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PDDS – Patient Determined Disease Steps; RR – relative risk.

Table D5.A Adjusted associations between baseline depression treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors.

Baseline Characteristics (2011)	**Depression Cohort** Clinically Meaningful Decline in PCS-12 Score (2011 to 2012)					
	Full Cohort (n=2784) Adjusted[b]			**Restricted Cohort**[a] (n=2594) Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.88	(0.70, 1.12)	0.31	0.94	(0.70, 1.28)	0.70
Age in 2011 (years)						
- <45	0.76	(0.59, 0.98)	**0.033**	0.74	(0.57, 1.28)	**0.027**
- 45–64	1.0			1.0		
- ≥65	1.03	(0.78, 1.36)	0.84	0.97	(0.73, 1.28)	0.81
Sex						
- Female	1.0			1.0		
- Male	1.01	(0.81, 1.27)	0.92	1.04	(0.83, 1.32)	0.74
Race						
- White	1.0			1.0		
- People of Colour/Other	1.20	(0.90, 1.60)	0.21	1.20	(0.89, 1.61)	0.23
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.77, 1.16)	0.59	0.95	(0.77, 1.18)	0.65
Education						
- Secondary School/GED	0.85	(0.66, 1.08)	0.17	0.85	(0.66, 1.10)	0.21
- Associate/Technical Degree	0.95	(0.73, 1.25)	0.72	1.00	(0.76, 1.32)	1.00
- Bachelor's Degree	0.84	(0.67, 1.06)	0.15	0.81	(0.63, 1.03)	**0.087**
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.63	(1.15, 2.31)	**0.0059**	1.57	(1.10, 2.25)	**0.014**
- $30,000–$50,000	1.44	(1.04, 2.01)	**0.031**	1.40	(0.99, 1.97)	**0.055**
- $50,001–$100,000	1.37	(1.02, 1.84)	**0.038**	1.37	(1.01, 1.86)	**0.046**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.50	(1.08, 2.07)	**0.015**	1.48	(1.06, 2.07)	**0.021**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.76	(1.42, 2.18)	**<0.0001**	1.70	(1.36, 2.12)	**<0.0001**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.32	(1.10, 1.57)	**0.0024**	1.29	(1.08, 1.55)	**0.0064**
Baseline PCS-12 score	1.04	(1.04, 1.05)	**<0.0001**	1.06	(1.05, 1.07)	**<0.0001**
Disease duration (years)						
- ≤10	1.13	(0.88, 1.44)	0.35	1.11	(0.86, 1.43)	0.44
- 11–20	1.06	(0.86, 1.31)	0.60	1.07	(0.86, 1.33)	0.57
- ≥21	1.0			1.0		

[a] Among full depression cohort, 32.9% (915/2784) reported clinically meaningful decline in PCS-12 score (decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Excludes respondents whose only reported treatment barrier at baseline was "not having symptoms now" (190/432).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=101; [d] missing, n=91).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table D5.B Adjusted associations between baseline depression treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, adjusting vs. not adjusting for Spring 2011 PCS-12 score.

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)					
	Including Baseline Score Adjusted[b]			**Excluding Baseline Score** Adjusted[c]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.88	(0.70, 1.12)	0.31	0.97	(0.77, 1.23)	0.82
Age in 2011 (years)						
- <45	0.76	(0.59, 0.98)	**0.033**	0.98	(0.77, 1.25)	0.89
- 45–64	1.0			1.0		
- ≥65	1.03	(0.78, 1.36)	0.84	0.96	(0.74 , 1.26)	0.77
Sex						
- Female	1.0			1.0		
- Male	1.01	(0.81, 1.27)	0.92	0.91	(0.73, 1.13)	0.39
Race						
- White	1.0			1.0		
- People of Colour/Other	1.20	(0.90, 1.60)	0.21	1.20	(0.91, 1.58)	0.20
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.77, 1.16)	0.59	1.00	(0.82, 1.21)	0.98
Education						
- Secondary School/GED	0.85	(0.66, 1.08)	0.17	0.82	(0.65, 1.04)	**0.097**
- Associate/Technical Degree	0.95	(0.73, 1.25)	0.72	0.94	(0.72, 1.21)	0.62
- Bachelor's Degree	0.84	(0.67, 1.06)	0.15	0.84	(0.67, 1.05)	0.13
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.63	(1.15, 2.31)	**0.0059**	1.25	(0.90, 1.75)	0.18
- $30,000–$50,000	1.44	(1.04, 2.01)	**0.031**	1.24	(0.90, 1.70)	0.19
- $50,001–$100,000	1.37	(1.02, 1.84)	**0.038**	1.24	(0.94, 1.65)	0.13
- > $100,000	1.0			1.0		
- Unanswered/missing	1.50	(1.08, 2.07)	**0.015**	1.35	(0.99, 1.84)	**0.062**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.76	(1.42, 2.18)	**<0.0001**	1.05	(0.87, 1.27)	0.64
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.32	(1.10, 1.57)	**0.0024**	1.19	(1.00, 1.41)	**0.047**
Baseline PCS-12 score	1.06	(1.05, 1.07)	**<0.0001**			
Disease duration (years)						
- ≤10	1.13	(0.88, 1.44)	0.35	1.14	(0.90, 1.44)	0.29
- 11–20	1.06	(0.86, 1.31)	0.60	1.07	(0.87, 1.31)	0.55
- ≥21	1.0			1.0		

[a] Among depression cohort, 32.9% (915/2784) reported clinically meaningful decline in PCS-12 score (decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Model adjusted for all variables listed above in table (missing n=101).

[c] Model adjusted for variables listed above in table, apart from baseline PCS-12 score (missing n=101).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table D5.C Adjusted associations between baseline depression treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with depression, assessed with logistic regression vs. modified Poisson regression.

Baseline Characteristics (2011)	**Depression Cohort** (n=2784) Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline depression treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	0.88	(0.70, 1.12)	0.31	0.98	(0.95, 1.02)	0.32
Age in 2011 (years)						
- <45	0.76	(0.59, 0.98)	**0.033**	0.96	(0.92, 1.00)	**0.034**
- 45–64	1.0			1.0		
- ≥65	1.03	(0.78, 1.36)	0.84	1.00	(0.96, 1.05)	0.84
Sex						
- Female	1.0			1.0		
- Male	1.01	(0.81, 1.27)	0.92	1.00	(0.97, 1.04)	0.93
Race						
- White	1.0			1.0		
- People of Colour	1.20	(0.90, 1.60)	0.21	1.03	(0.98, 1.07)	0.20
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.95	(0.77, 1.16)	0.59	0.99	(0.96, 1.02)	0.59
Education						
- Secondary School/GED	0.85	(0.66, 1.08)	0.17	0.97	(0.94, 1.01)	0.16
- Associate/Technical Degree	0.95	(0.73, 1.25)	0.72	0.99	(0.95, 1.03)	0.70
- Bachelor's Degree	0.84	(0.67, 1.06)	0.15	0.97	(0.94, 1.01)	0.14
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	1.63	(1.15, 2.31)	**0.0059**	1.08	(1.02, 1.13)	**0.0066**
- $30,000–$50,000	1.44	(1.04, 2.01)	**0.031**	1.06	(1.00, 1.11)	**0.032**
- $50,001–$100,000	1.37	(1.02, 1.84)	**0.038**	1.05	(1.00, 1.09)	**0.043**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.50	(1.08, 2.07)	**0.015**	1.06	(1.01, 1.11)	**0.017**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.76	(1.42, 2.18)	**<0.0001**	1.09	(1.05, 1.13)	**<0.0001**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.32	(1.10, 1.57)	**0.0024**	1.04	(1.01, 1.07)	**0.0027**
Baseline PCS-12 score	1.06	(1.05, 1.07)	**<0.0001**	1.01	(1.01, 1.01)	**<0.0001**
Disease duration (years)						
- ≤10	1.13	(0.88, 1.44)	0.35	1.02	(0.98, 1.06)	0.33
- 11–20	1.06	(0.86, 1.31)	0.60	1.01	(0.98, 1.04)	0.57
- ≥21	1.0			1.0		

[a] In 2012, 32.9% (915/2784) of respondents with depression reported a clinically meaningful decline in PCS-12 score (vs 67.1%, 1869/2784 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n= 101.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score; RR – relative risk.

Table D6.A Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, including vs. excluding untreated respondents whose only reported treatment barrier at baseline was need factors.

Baseline Characteristics (2011)	**Anxiety Cohort** Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)					
	Full Cohort (n=1140) Adjusted[c]			**Restricted Cohort**[b] (n=987) Adjusted[d]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.17	(0.86, 1.60)	0.31	1.30	(0.87, 1.95)	0.20
Age in 2011 (years)						
- <45	0.80	(0.56, 1.14)	0.22	0.78	(0.53, 1.14)	0.20
- 45–64	1.0			1.0		
- ≥65	0.96	(0.59, 1.57)	0.87	0.78	(0.45, 1.35)	0.32
Sex						
- Female	1.0			1.0		
- Male	0.92	(0.60, 1.39)	0.68	1.00	(0.64, 1.56)	0.99
Race						
- White	1.0			1.0		
- People of Colour/Other	1.14	(0.74, 1.75)	0.55	1.28	(0.81, 2.04)	0.29
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.97	(0.70, 1.33)	0.83	0.88	(0.63, 1.25)	0.48
Education						
- Secondary School/GED	0.74	(0.50, 1.09)	0.13	0.80	(0.52, 1.21)	0.29
- Associate/Technical Degree	0.78	(0.51, 1.20)	0.26	0.77	(0.48, 1.23)	0.27
- Bachelor’s Degree	0.88	(0.61, 1.29)	0.52	0.96	(0.65, 1.45)	0.85
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	2.14	(1.22, 3.77)	**0.0084**	1.96	(1.07, 3.62)	**0.031**
- $30,000–$50,000	2.15	(1.26, 3.68)	**0.0053**	1.88	(1.04, 3.37)	**0.035**
- $50,001–$100,000	1.65	(1.02, 2.69)	**0.043**	1.51	(0.89, 2.57)	0.13
- > $100,000	1.0			1.0		
- Unanswered/missing	1.89	(1.12, 3.19)	**0.018**	1.61	(0.94, 2.95)	**0.082**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.85	(1.30, 2.63)	**<0.0001**	1.61	(1.10, 2.36)	**0.014**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.10	(0.83, 1.47)	0.50	1.07	(0.78, 1.46)	0.67
Baseline PCS-12 score	1.07	(1.05, 1.08)	**<0.0001**	1.07	(1.05, 1.09)	**<0.0001**
Disease duration (years)						
- ≤10	0.90	(0.61. 1.33)	0.60	0.87	(0.57, 1.32)	0.52
- 11–20	0.77	(0.53, 1.11)	0.16	0.76	(0.51, 1.12)	0.17
- ≥21	1.0			1.0		

[a] Among full anxiety cohort, 31.0% (354/1140) reported clinically meaningful decline in PCS-12 score (decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Excludes respondents whose only reported treatment barrier at baseline was “not having symptoms now” (153/300).

[c,d] Both models adjusted for all variables listed above in table ([c] missing, n=46; [d] missing, n=36).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table D6.B Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, adjusting vs. not adjusting for Spring 2011 PCS-12 score.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in PCS-12 Score (2011 to 2012)					
	Including Baseline Score Adjusted[a]			**Excluding Baseline Score** Adjusted[b]		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.17	(0.86, 1.60)	0.31	1.18	(0.88, 1.59)	0.27
Age in 2011 (years)						
- <45	0.80	(0.56, 1.14)	0.22	1.01	(0.72, 1.41)	0.97
- 45–64	1.0			1.0		
- ≥65	0.96	(0.59, 1.57)	0.87	0.88	(0.55, 1.41)	0.58
Sex						
- Female	1.0			1.0		
- Male	0.92	(0.60, 1.39)	0.68	0.82	(0.55, 1.23)	0.34
Race						
- White	1.0			1.0		
- People of Colour/Other	1.14	(0.74, 1.75)	0.55	1.16	(0.77, 1.76)	0.48
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.97	(0.70, 1.33)	0.83	0.99	(0.72, 1.35)	0.94
Education						
- Secondary School/GED	0.74	(0.50, 1.09)	0.13	0.73	(0.50, 1.07)	0.11
- Associate/Technical Degree	0.78	(0.51, 1.20)	0.26	0.78	(0.51, 1.18)	0.24
- Bachelor’s Degree	0.88	(0.61, 1.29)	0.52	0.89	(0.62, 1.28)	0.53
- Post Bachelor’s Degree	1.0			1.0		
Income						
- <$30,000	2.14	(1.22, 3.77)	**0.0084**	1.49	(0.87, 2.56)	0.15
- $30,000–$50,000	2.15	(1.26, 3.68)	**0.0053**	1.81	(1.08, 3.03)	**0.025**
- $50,001–$100,000	1.65	(1.02, 2.69)	**0.043**	1.38	(0.87, 2.20)	0.17
- > $100,000	1.0			1.0		
- Unanswered/missing	1.89	(1.12, 3.19)	**0.018**	1.68	(1.02, 2.79)	**0.043**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.85	(1.30, 2.63)	**<0.0001**	0.98	(0.72, 1.34)	0.92
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.10	(0.83, 1.47)	0.50	0.95	(0.72, 1.25)	0.71
Baseline PCS-12 score	1.07	(1.05, 1.08)	**<0.0001**			
Disease duration (years)						
- ≤10	0.90	(0.61. 1.33)	0.60	0.85	(0.59, 1.24)	0.41
- 11–20	0.77	(0.53, 1.11)	0.16	0.77	(0.54, 1.09)	0.14
- ≥21	1.0			1.0		

[a] Among anxiety cohort, 31.0% (354/1140) reported clinically meaningful decline in PCS-12 score (decrease in PCS-12 score by ≥3 points between NARCOMS Spring 2011 and 2012 surveys).

[b] Model adjusted for all variables listed above in table (missing n=45).

[c] Model adjusted for variables listed above in table, apart from baseline PCS-12 score (missing n=45).

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score.

Table D6.C Adjusted associations between baseline anxiety treatment status and clinically meaningful decline in PCS-12 score (2011 to 2012) among NARCOMS Spring 2011 respondents diagnosed with anxiety, assessed with logistic regression vs. modified Poisson regression.

Baseline Characteristics (2011)	**Anxiety Cohort** (n=1140) Clinically Meaningful Decline in PCS-12 Score[a] (2011 to 2012)					
	Logistic Regression[b] (Odds Ratios)			**Modified Poisson Regression[b] (Relative Risk)**		
	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Baseline anxiety treatment status						
- Receiving treatment	1.0			1.0		
- Not receiving treatment	1.17	(0.86, 1.60)	0.31	1.02	(0.98, 1.07)	0.31
Age in 2011 (years)						
- <45	0.80	(0.56, 1.14)	0.22	0.97	(0.92, 1.02)	0.21
- 45–64	1.0			1.0		
- ≥65	0.96	(0.59, 1.57)	0.87	0.99	(0.92, 1.07)	0.84
Sex						
- Female	1.0			1.0		
- Male	0.92	(0.60, 1.39)	0.68	0.99	(0.93, 1.05)	0.69
Race						
- White	1.0			1.0		
- People of Colour	1.14	(0.74, 1.75)	0.55	1.02	(0.96, 1.09)	0.57
Marital status						
- Married/cohabitating	1.0			1.0		
- Single/living alone	0.97	(0.70, 1.33)	0.83	0.99	(0.95, 1.04)	0.81
Education						
- Secondary School/GED	0.74	(0.50, 1.09)	0.13	0.95	(0.90, 1.01)	0.12
- Associate/Technical Degree	0.78	(0.51, 1.20)	0.26	0.96	(0.90, 1.03)	0.24
- Bachelor's Degree	0.88	(0.61, 1.29)	0.52	0.98	(0.93, 1.04)	0.53
- Post Bachelor's Degree	1.0			1.0		
Income						
- <$30,000	2.14	(1.22, 3.77)	**0.0084**	1.12	(1.03, 1.21)	**0.0093**
- $30,000–$50,000	2.15	(1.26, 3.68)	**0.0053**	1.12	(1.03, 1.21)	**0.0057**
- $50,001–$100,000	1.65	(1.02, 2.69)	**0.043**	1.07	(1.00, 1.15)	**0.049**
- > $100,000	1.0			1.0		
- Unanswered/missing	1.89	(1.12, 3.19)	**0.018**	1.10	(1.01, 1.18)	**0.020**
Employment						
- Employed	1.0			1.0		
- Unemployed/missing	1.85	(1.30, 2.63)	**<0.0001**	1.09	(1.04, 1.15)	**0.0009**
Baseline NARCOMS Depression score						
- <2	1.0			1.0		
- ≥2	1.10	(0.83, 1.47)	0.50	1.01	(0.97, 1.06)	0.56
Baseline PCS-12 score	1.07	(1.05, 1.08)	**<0.0001**	1.01	(1.01, 1.01)	**<0.0001**
Disease duration (years)						
- ≤10	0.90	(0.61. 1.33)	0.60	0.98	(0.93, 1.05)	0.62
- 11–20	0.77	(0.53, 1.11)	0.16	0.96	(0.91, 1.02)	0.18
- ≥21	1.0			1.0		

[a] In 2012, 31.1% (354/1140) of respondents with anxiety reported a clinically meaningful decline in PCS-12 score (vs. 69.0%, 786/1140 for improved/no decline).

[b] Adjusted for all variables listed in above table; missing n=45.

Bolded estimates indicate p<0.10.

Abbreviations: CI – Confidence interval; GED – General Educational Development; NARCOMS – North American Research Committee on Multiple Sclerosis; OR – odds ratio; PCS – Physical Component Score; RR – relative risk.