

# Adverse health behaviours are associated with depression and anxiety in multiple sclerosis: A prospective multisite study

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## Abstract

**Background:** Depression and anxiety are common among people with multiple sclerosis (MS), as are adverse health behaviours, but the associations between these factors are unclear.

**Objective:** To evaluate the associations between cigarette smoking, alcohol use, and depression and anxiety in MS in a cross-Canada prospective study.

**Methods:** From July 2010 to March 2011 we recruited consecutive MS patients from four MS clinics. At three visits over two years, clinical and demographic information was collected, and participants completed questionnaires regarding health behaviours and mental health.

**Results:** Of 949 participants, 75.2% were women, with a mean age of 48.6 years; most had a relapsing–remitting course (72.4%). Alcohol dependence was associated with increased odds of anxiety (OR: 1.84; 95% CI: 1.32–2.58) and depression (OR: 1.53; 95% CI: 1.05–2.23) adjusting for age, sex, Expanded Disability Status Scale (EDSS), and smoking status. Smoking was associated with increased odds of anxiety (OR: 1.29; 95% CI: 1.02–1.63) and depression (OR: 1.37; 95% CI: 1.04–1.78) adjusting for age, sex, EDSS, and alcohol dependence. Alcohol dependence was associated with an increased incidence of depression but not anxiety. Depression was associated with an increased incidence of alcohol dependence.

**Conclusion:** Alcohol dependence and smoking were associated with anxiety and depression. Awareness of the effects of adverse health behaviours on mental health in MS might help target counselling and support for those ‘at risk’.

**Keywords:** Multiple sclerosis, health behaviour, anxiety, depression, cohort

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## Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS) associated with physical, cognitive, and emotional challenges. Depression and anxiety occur at elevated frequencies in the MS population.<sup>1,2</sup> Adverse health behaviours, such as cigarette smoking and alcohol use, have received less attention, but are common among people with MS as well.<sup>3</sup> Both health behaviours have consistently been associated with depression and anxiety in the general population,<sup>4</sup> but this relationship is less clear in MS.<sup>5–8</sup>

An understanding of these associations is especially important in MS because both alcohol and tobacco

can lead to damage of the CNS<sup>9,10</sup> which is already compromised in people with MS. Cigarette smoking and alcohol have specifically been linked to increased MS susceptibility, as well as accelerated disease progression.<sup>11,12</sup> Further, depression and anxiety have each been associated with numerous negative consequences in MS, including increased risk of suicide, impaired cognition, and a worse quality of life.<sup>1</sup>

We aimed to evaluate the association between adverse health behaviours and mental health among people with MS in a prospective multisite longitudinal study. We hypothesized that adverse health behaviours

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would be associated with higher rates of depression and anxiety in this population.

## Methods

### *Study population*

From July 2010 to March 2011 we recruited consecutive patients attending a routine visit at one of four participating MS clinics in British Columbia, Alberta, Manitoba and Nova Scotia. Participants were approached by a trained research coordinator using a standardized script and invited to participate in a study involving completion of specific questionnaires at three time-points over two years. The three time-points (baseline, year one, and year two) coincided with the typical annual visits to the respective MS clinic. For individuals unable to attend their annual clinic visit, follow-up questionnaires were offered via telephone, mail or email to minimize loss to follow-up. Inclusion criteria were: a confirmed diagnosis of definite MS or clinically isolated syndrome (CIS) according to the prevailing diagnostic criteria at the time the participant had been diagnosed;<sup>13–15</sup> age  $\geq 18$  years; resident in the province where data collection was occurring; ability and willingness to provide informed consent and to complete the study questionnaires in English.

### *Clinical and demographic information*

Demographic and clinical information was captured from each individual's medical record using a standardized data abstraction form including sex, date of birth, race (white, non-white), highest education level achieved, date of MS symptom onset, disease duration, clinical course (relapsing–remitting [RR], secondary progressive [SP], primary progressive [PP], CIS),<sup>16</sup> per the treating neurologist, and Expanded Disability Status Score (EDSS) as recorded the day of recruitment and at each follow-up visit.

### *Self-reported measures*

Each participant completed several questionnaires at the three time-points (baseline, year one, and year two). The Hospital Anxiety and Depression Scale (HADS) was the primary measure of current mental health status. It is a 14-item questionnaire that assesses symptoms of anxiety and depression separately, and was created for use in the setting of hospital medical outpatient clinics.<sup>17</sup> Validated cut-off scores of  $\geq 8$  on the HADS scale were used to define depression and anxiety.<sup>18</sup> To screen for alcohol dependence, we used the CAGE (Cutting down, Annoyance by criticism,

Guilty feeling, Eye-openers) questionnaire. A score of  $\geq 2$  out of a possible 4 suggests alcohol dependence.<sup>19</sup> Smoking was captured as 'current', 'past', or 'never' (less than 100 cigarettes smoked over a lifetime).<sup>20</sup>

### *Statistical analysis*

The presence of depression, anxiety, smoking, and alcohol dependence was described as frequencies (percentages). The baseline clinical and demographic characteristics (sex, race, age, EDSS, education level, and site) of patients were compared to the two mental health issues (anxiety, depression) and two health behaviours (alcohol dependence, smoking) of interest; initially using the Pearson  $\chi^2$  test or Fisher's exact test, then by logistic regression.

We aimed to explore the association between health behaviours and mental health. Given the uncertainties regarding the direction of this relationship, and to maximally use the available data, we initially conducted prevalence analyses, followed by more targeted incidence analyses. We explored the relationship between prevalent health behaviours and prevalent depression and anxiety using logistic generalized estimating (GEE) equations with an unstructured correlation matrix. This method allows for the simultaneous analysis of data from all time-points while accounting for correlations between the repeated measures for individuals. Analyses of the odds of having depression or anxiety were measured based on the presence of alcohol dependence or current smoking status, the latter defined as non-smoker or current smoker. Second, to evaluate the incidence of anxiety or depression during the course of the study, we excluded all participants who met criteria for either condition at baseline and then evaluated the risk of developing either condition at year one or two based on baseline health behaviours using logistic regression. Given that the literature in the general population has reported an increased risk of adverse health behaviours secondary to mental health conditions we also evaluated the risk of incident alcohol dependence and smoking.<sup>4</sup> Covariates in the models included current age, sex, concurrent disability status measured by the EDSS (categorized as mild [0–2.5], moderate [3.0–5.5], or severe [6.0+]), and baseline education level (categorized as high school or less, any post-secondary or more, and other). Covariates were included either for clinical relevance (e.g. age) or on the basis of their association with the outcome from the baseline analysis ( $p < 0.1$ ). Findings from all regression analyses were expressed as odds ratios with corresponding 95% confidence intervals (CI).

All analyses were performed using SAS Statistical Software Package 9.4 (SAS Institute Inc., Cary, NC).

## Results

Of 1632 patients who visited one of the four MS clinics between July 2010 and March 2011, 1144 met the inclusion criteria. Of these, 949 (82.6%) consented to participate. Over the course of the two follow-up assessments, 58 patients missed their year one assessment (and could not be contacted by phone, mail or email), and 64 missed the year two assessment, for a total of 93.2% (885/949) with complete follow-up. In total, 65 patients had a follow-up assessment by telephone interview. The mean age at baseline was 48.6 years, 75.2% were women and most had a relapsing–remitting course (72.4%). Most participants were white (94.6%), and had achieved a post-secondary education or higher (67.0%) (Table 1).

The occurrence of mental health disorders (anxiety and depression) and adverse health behaviours (alcohol and smoking) over the study period are summarized in Table 2. The median HADS-Anxiety score was 6 (25<sup>th</sup>–75<sup>th</sup> percentile: 3–9) and the median HADS-Depression score was 4 (25<sup>th</sup>–75<sup>th</sup> percentile: 2–7) across all three assessments. Over the entire study, 53.8% of participants met the HADS-Anxiety criterion and 35.1% met the HADS-Depression criterion at some point (baseline, year one, or year two) (Table 3). The percentage of patients who met the criteria for alcohol dependence, as measured by a score of  $\geq 2$  on the CAGE questionnaire, ranged from 6.0% to 6.6% over the three assessments (Table 3). At baseline, 56.7% of respondents had ever smoked ( $\geq 100$  cigarettes in a lifetime), of whom 63.7% no longer smoked. Of the total cohort, 20.6% self-identified as current smokers. Of the past smokers, 52.6% quit after their MS onset and only 4.7% of ever smokers began smoking after their MS onset.

At baseline, anxiety was associated with female sex (OR: 1.55; 95% CI: 1.13–2.13), and reduced odds of severe disability (OR: 0.64; 95% CI: 0.45–0.91), while depression was associated with increased odds of severe disability (OR: 2.71; 95% CI: 1.85–3.99) when compared to mild disability. Both alcohol dependence (OR: 1.83; 95% CI: 1.06–3.16) and smoking every day (OR: 1.73; 95% CI: 1.20–2.50) were reported more frequently by men (Table 3). Alcohol dependence also was reported more frequently among non-white patients (OR: 3.19; 95% CI: 1.35–7.55) and those with moderate disability (compared to mild, OR: 2.48; 95% CI: 1.39–4.44). Patients who achieved a

post-secondary education or higher were less likely to smoke (OR: 0.50; 95% CI: 0.35–0.73). Age was not associated with any of the mental health or health behaviours of interest ( $p > 0.06$ ). All baseline associations are outlined in Table 3.

In the prevalence analyses, alcohol dependence was associated with increased odds of anxiety (OR: 1.88; 95% CI: 1.37–2.57). The association persisted after adjusting for age, sex, EDSS, and smoking status (OR: 1.84; 95% CI: 1.32–2.58, see Table 4). Alcohol dependence was also associated with increased odds of depression (OR: 1.51; 95% CI: 1.07–2.15), which remained statistically significant after adjusting for age, sex, EDSS, and smoking status (OR: 1.53; 95% CI: 1.05–2.23).

Smoking was assessed in a similar manner to alcohol, with current smokers compared to non-smokers across the study period. Smoking was associated with increased odds of anxiety (unadjusted OR: 1.32; 95% CI: 1.05–1.65). When adjusted for age, sex, EDSS, and alcohol dependence, the relationship persisted (OR: 1.29; 95% CI: 1.02–1.63). There was also an association between smoking and depression (unadjusted OR: 1.42; 95% CI: 1.10–1.83), which was tempered slightly after adjusting for age, sex, EDSS, and alcohol dependence, but remained statistically significant (OR: 1.37; 95% CI: 1.04–1.78) (see Table 4).

For the incidence analysis, those with baseline depression ( $n=200$ ) and anxiety ( $n=366$ ) were excluded. By study end there were 138 cases of incident anxiety and 128 cases of incident depression (Table 1). There was no increased risk of developing anxiety at year one or two related to alcohol dependence at baseline (OR: 0.46; 95% CI: 0.14–1.59). However, there was an increased risk of depression (OR: 3.19; 95% CI: 1.65–6.17). This relationship remained after adjusting for age, sex, EDSS, and smoking status (see Table 5). Smoking at baseline was not associated with an altered risk of subsequent anxiety (OR: 1.22; 95% CI: 0.73–2.05) or depression (OR: 1.01; 95% CI: 0.60–1.72) during the follow-up period (see Table 5).

Because none of the participants began smoking during the study period, we could not examine the risk of smoking. However, 42 patients developed alcohol dependence during the study period. When adjusted for covariates, we found that baseline depression increased the risk of developing alcohol dependence during follow-up (OR: 2.12; 95% CI: 1.04–4.30). Anxiety was not associated with an increased risk of alcohol dependence (Table 5).

**Table 1.** Demographic and clinical characteristics of study participants at baseline. Examples of 'other' education level include nursing school, film school, and police academy.

	Total cohort	Cases of incident anxiety	Cases of incident depression	Cases of incident alcohol dependence
<b>Variable</b>	<b>n =949</b>	<b>n =138</b>	<b>n=128</b>	<b>n=42</b>
<b>Sex, N (%)</b>				
Female	714 (75.2)	99 (71.7)	96 (75.0)	25 (59.5)
Male	235 (24.8)	39 (28.3)	32 (25.0)	17 (40.5)
<b>Race, N (%)</b>				
White	810 (94.6)	121 (94.5)	101 (91.0)	33 (97.1)
Non-white	46 (5.4)	7 (5.5)	10 (9.0)	1 (2.9)
<b>Age, mean (SD)</b>	48.6 (11.4)	48.5 (11.2)	48.8 (11.3)	47.0 (11.5)
<b>Age (categorized), N (%)</b>				
18–29	58 (6.1)	11 (8.0)	9 (7.0)	4 (9.5)
30–39	149 (15.7)	20 (14.5)	17 (13.3)	7 (16.7)
40–49	305 (32.2)	42 (30.4)	47 (36.7)	13 (31.0)
50+	436 (46.0)	65 (47.1)	55 (43.0)	18 (42.9)
<b>Age of onset, mean (SD)</b>	33.2 (10.0)	33.5 (10.6)	32.2 (9.9)	32.7 (9.0)
<b>Disease duration, mean (SD)</b>	15.4 (10.2)	14.9 (9.9)	16.1 (10.0)	14.3 (8.0)
<b>EDSS, median (IQR)*</b>	2.5 (1.5–5.0)	3.0 (2.0 – 6.0)	3.0 (2.0 – 5.0)	2.5 (1.5 – 4.0)
<b>Clinical course, N (%)</b>				
RRMS	687 (72.4)	91 (65.9)	92 (71.9)	34 (81.0)
SPMS	193 (20.3)	37 (26.8)	29 (22.7)	7 (16.7)
PPMS	60 (6.3)	8 (5.8)	7 (5.5)	1 (2.4)
CIS	5 (0.5)	2 (1.5)	0 (0.0)	0 (0.0)
Unknown	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Current disease modifying therapy use</b>				
Yes	477 (50.4)	64 (45.7)	75 (58.6)	21 (50.0)
No	470 (49.6)	76 (54.3)	53 (41.4)	21 (50.0)
<b>Education</b>				
High school or less	258 (30.1)	36 (28.1)	36 (32.4)	7 (20.6)
Any post-secondary or more	574 (67.1)	91 (71.1)	72 (64.9)	26 (76.5)
Other	24 (2.8)	1 (0.8)	3 (2.7)	1 (2.9)

EDSS = Expanded Disability Status Scale; IQR = interquartile range; RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; PPMS = primary progressive MS; CIS = clinically isolated syndrome.  
\*47 patients from the total cohort were missing an EDSS score at baseline.

## Discussion

We found that alcohol dependence and smoking were associated with both anxiety and depression in this large, representative cohort of clinic-attending MS patients. Smoking at study entry had no measurable influence on the risk of developing subsequent incident mental health symptoms. However, alcohol dependence at study entry increased the risk for incident depression, and depression at baseline increased the risk for incident alcohol dependence during two years of follow-up.

Surprisingly few studies have examined the relationships of health behaviours and mental health symptoms in MS despite a general recognition of the importance of these issues and extensive study in the general population.<sup>4</sup> Similar to our own findings, the lone prior longitudinal study that examined the association between cigarette smoking and mental health in MS patients also found an increased prevalence of anxiety and depression in smokers, a link that is well established in the general population.<sup>4</sup> We found three cross-sectional studies examining the relationship

**Table 2.** Occurrence of mental health (anxiety and depression) and adverse health behaviours (alcohol and smoking) over the study period.

	Baseline	Year one	Year two	Ever met criteria (at baseline or year 1 or 2)	Met criteria at all three time-points (at baseline and year 1 and 2)
<b>Mental health</b>					
<b>Anxiety, N (%)</b>	366/932 (39.3)	320/907 (35.3)	309/882 (35.0)	511/949 (53.8)	170/868 (19.6)
<b>Depression, N (%)</b>	200/930 (21.5)	207/907(22.8)	197/882 (22.3)	333/949 (35.1)	89/868 (10.3)
<b>Adverse health behaviours</b>					
<b>Alcohol dependence, N (%)</b>	60/946 (6.3)	60/906 (6.6)	53/882 (6.0)	102/949 (10.7)	18/868 (2.1)
<b>Never smoker, N (%)</b>	411/947 (43.4)	398/911 (43.7)	382/885 (43.2)	384/949 (40.5)	358/732 (48.9)
<b>Past smoker, N (%)</b>	341/947 (36.0)	330/911 (36.2)	336/885 (37.9)	333/949 (35.1)	272/732 (37.2)
<b>Current smoker, N (%)</b>	195/947 (20.6)	180/911 (19.8)	165/885 (18.7)	232/949 (24.4)	102/732 (13.9)

between alcohol use and mental health in MS, with mixed findings.<sup>5-7</sup> A study of 140 clinic patients in the province of Ontario, Canada reported an association between anxiety, but not depression, and problem drinking as measured using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition or weekly consumption of alcohol (14 drinks or more for males, 9 for females).<sup>5</sup> A USA-based study of MS clinic-attending patients (n=157) reported no associations between alcohol dependence (measured using the Alcohol Use Disorders Identification Test Consumption and CAGE) and depression or anxiety.<sup>6</sup> Last, a study of a community sample from the USA (n=739) that utilized a mail-out survey suggested that depression and possible problem drinking were associated (anxiety was not examined).<sup>7</sup> The lack of consistency amongst the findings of these studies and our own may be due to the varied assessments of both mental health symptoms and alcohol dependence, as each study employed different scales. The relatively small sample sizes of previous clinic-based studies may also explain at least some of the disparity in results, especially given that the rates of problem drinking were generally low. However, our finding that the odds of anxiety were nearly two-fold in those with alcohol dependence is in concordance with two large general population-based surveys, which reported odds ratios between 1.5 and 4.0.<sup>21</sup>

We were unable to find any other prior studies that had evaluated the risk of incident mental health disorders associated with alcohol dependence in people with MS. While we found no altered risk of anxiety associated with alcohol dependence this may have been related to the small number of individuals with alcohol dependence who were at risk for incident anxiety. Studies from the general population that have attempted to elucidate the direction of the relationship between anxiety

and alcohol dependence, have had inconsistent results, suggesting that the relationship may be cyclical.<sup>21</sup> We found that the risk for incident depression at follow-up was increased among MS patients who met criteria for alcohol dependence at baseline. Moreover, the risk for alcohol dependence was also increased in those who were depressed at baseline, suggesting a bidirectional relationship.<sup>22</sup> Given the consequences of depression and alcohol dependence,<sup>1,9</sup> this finding is particularly concerning and points to the importance of close monitoring of health behaviours and mental health as an integral part of MS care.

We found that smoking at baseline did not alter the risk of developing incident anxiety or depression at follow-up. For some, smoking may be a means of coping with mental health disorders, and therefore would not predict the onset of these disorders. There is evidence from the general population that smoking can lead to both anxiety and depression, but is more likely an indicator of risk than a true causal factor.<sup>23</sup> None of the participants enrolled in this study began smoking during the study period, and more than one-third identified as past smokers. The increased prevalence of depression seen among smokers could be related to an inability to quit, due to nicotine dependence, social habituation, or possibly depression itself.<sup>24</sup> Despite the belief among many smokers that quitting will lead to worsened mental health, smoking cessation is associated with reduced anxiety and depression.<sup>25</sup> Smoking cessation should be a major focus in treating people with MS as it is the only modifiable lifestyle factor that has consistently been associated with worsened long-term disease progression.<sup>11</sup>

Our rates of smoking, alcohol dependence, anxiety, and depression were as expected, based on previous studies in MS. In our cohort, approximately one out of five were current smokers and most of those who had ever been

**Table 3.** Frequencies of baseline clinical and demographic variables associated with the four variables of interest: anxiety, depression, alcohol dependence, and current smoking status.

Predictor variable	Anxiety (n=366)	p-value	Depression (n=200)	p-value	Alcohol dependence (n=60)	p-value	Current smoker (n=195)	p-value
<b>SEX</b>								
Females	294/704 (41.8%)	<b>0.006<sup>a</sup></b>	151/702 (21.5%)	0.995 <sup>a</sup>	38/711 (5.3%)	<b>0.029<sup>a</sup></b>	131/714 (18.4%)	<b>0.003<sup>a</sup></b>
Males	72/228 (31.6%)		49/228 (21.5%)		22/235 (9.4%)		64/235 (27.2%)	
<b>RACE</b>								
White	305/793 (38.5%)	0.331 <sup>a</sup>	165/791 (20.9%)	0.621 <sup>a</sup>	43/807 (5.3%)	<b>0.014<sup>b</sup></b>	170/810 (21.0%)	0.559 <sup>a</sup>
Non-white	21/46 (45.6%)		11/46 (23.9%)		7/46 (15.2%)		8/46 (17.4%)	
<b>AGE</b>								
18–29	20/56 (35.7%)	0.314 <sup>a</sup>	4/54 (7.4%)	0.061 <sup>a</sup>	7/58 (12.1%)	0.310 <sup>a</sup>	13/58 (22.4%)	0.314 <sup>a</sup>
30–39	65/144 (45.1%)		29/145 (20.0%)		10/149 (6.7%)		34/149 (15.7%)	
40–49	123/304 (40.5%)		68/303 (22.4%)		18/305 (5.9%)		70/305 (23.0%)	
50+	158/428 (36.9%)		99/428 (23.1%)		25/434 (5.8%)		78/436 (17.9%)	
<b>EDSS</b>								
Mild [0–2.5]	199/475 (41.9%)	<b>0.043<sup>a</sup></b>	73/472 (15.5%)	<b>&lt; 0.0001<sup>a</sup></b>	25/487 (5.1%)	<b>0.0006<sup>a</sup></b>	99/487 (20.3%)	0.558 <sup>a</sup>
Moderate [3.0–5.5]	84/210 (40.0%)		51/210 (24.3%)		25/211 (11.9%)		49/211 (23.2%)	
Severe [6.0+]	64/202 (31.7%)		67/202 (33.2%)		7/202 (3.5%)		39/204 (19.1%)	
<b>EDUCATION LEVEL</b>								
High school or Less	94/254 (37.0%)	0.805 <sup>a</sup>	61/253 (24.1%)	0.382 <sup>a</sup>	16/256 (6.3%)	0.813 <sup>a</sup>	73/258 (28.3%)	<b>0.0009<sup>a</sup></b>
Any post-secondary or more	221/561 (39.4%)		111/560 (19.8%)		32/573 (5.6%)		98/573 (17.1%)	
Other	9/24 (37.5%)		5/24 (20.8%)		2/24 (8.3%)		6/24 (25.0%)	
<b>SITE</b>								
Nova Scotia	156/392 (39.8%)	0.745 <sup>a</sup>	83/392 (21.2%)	0.441 <sup>a</sup>	13/400 (3.3%)	<b>0.0012<sup>a</sup></b>	93/401 (23.2%)	0.260 <sup>a</sup>
Manitoba	42/121 (34.7%)		26/119 (21.9%)		10/121 (8.3%)		26/121 (21.5%)	
Alberta	32/81 (39.5%)		23/81 (28.4%)		3/84 (3.6%)		17/86 (19.8%)	
British Columbia	136/338 (40.2%)		68/338 (20.1%)		34/341 (10.0%)		59/341 (17.3%)	
<sup>a</sup> By Pearson's chi-squared test. <sup>b</sup> By Fisher's Exact test.								

**Table 4.** Association between health behaviours and: (i) anxiety; (ii) depression across all three visits using GEE analysis with an unstructured correlation matrix.

Association between anxiety and:	Crude OR (95% CI)	Adjusted OR* (95%CI)
<b>No alcohol dependence (reference)</b>	1	1
<b>Alcohol dependence</b>	1.88 (1.37–2.57)	1.84 (1.32–2.58)
<b>Non-smoker (reference)</b>	1	1
<b>Current smoker</b>	1.32 (1.05–1.65)	1.29 (1.02–1.63)
Association between depression and:	Crude OR (95% CI)	Adjusted OR* (95%CI)
<b>No alcohol dependence (reference)</b>	1	1
<b>Alcohol dependence</b>	1.51 (1.07–2.15)	1.53 (1.05–2.23)
<b>Non-smoker (reference)</b>	1	1
<b>Current smoker</b>	1.42 (1.10–1.83)	1.37 (1.04–1.78)
*Adjusted for age, sex, EDSS, and smoking status or alcohol dependence.		

**Table 5.** Association between baseline health behaviours and incident mental health at year one and two.

<i>Association between incident anxiety at year one or two and baseline:</i>	Crude OR (95% CI)	Adjusted OR* (95%CI)
<b>No alcohol dependence (reference)</b>	1	1
<b>Alcohol dependence</b>	0.46 (0.14–1.59)	0.43 (0.13–1.50)
<b>Never smoker (reference)</b>	1	1
<b>Current smoker</b>	1.22 (0.73–2.05)	1.20 (0.71–2.04)
<i>Association between incident depression at year one or two and baseline:</i>	Crude OR (95% CI)	Adjusted OR* (95%CI)
<b>No alcohol dependence (reference)</b>	1	1
<b>Alcohol dependence</b>	3.19 (1.65–6.17)	2.97 (1.48–5.96)
<b>Non-smoker (reference)</b>	1	1
<b>Current smoker</b>	1.01 (0.60–1.72)	0.94 (0.54–1.64)
<i>Association between incident alcohol dependence at year one or two and baseline:</i>	Crude OR (95% CI)	Adjusted OR* (95%CI)
<b>No anxiety (reference)</b>	1	1
<b>Anxiety</b>	1.06 (0.56–2.02)	1.18 (0.60–2.33)
<b>No depression (reference)</b>	1	1
<b>Depression</b>	1.82 (0.92–3.59)	2.12 (1.04–4.30)

\*Adjusted for age, sex, EDSS, and smoking status or alcohol dependence.

smokers were past smokers, similar to what has been shown in other MS cohorts.<sup>26</sup> Men and participants with less time spent in formal education were more likely to identify themselves as smokers, similar to findings in the general population.<sup>27</sup> Few participants began smoking after their MS onset, and most of those who identified as past smokers quit after disease onset, suggesting that a diagnosis of MS may influence smoking patterns. Alcohol dependence was reported in a minority of participants – approximately 6%, which is in accordance with previous studies of alcohol dependence in MS that also employed the CAGE questionnaire.<sup>6,7</sup> Since a large Canadian general population-based survey reported similar results (5.8%),<sup>28</sup> people with MS do not appear at an increased risk of alcohol dependence overall. Importantly, however, the rates of alcohol dependence in our sample were influenced by level of disability; those with moderate disability appeared to be at the highest risk of alcohol dependence relative to mild or severe disability. Patients with severe disability have a greater probability of experiencing bladder dysfunction,<sup>29</sup> which may compel them to abstain. Mobility limitations or the need for full-time care may also reduce their access to alcohol. A recent systematic review reported a summary estimate of 23.7% (95% CI: 17.4–30.0) for the prevalence of depression in people with MS, though rates ranged widely between studies, likely due to varied follow-up times and measures of depression.<sup>30</sup> Anxiety has been studied less frequently, but prevalence estimates range from 1.2–44.6%.<sup>30</sup> It is not clear whether these

mental health disorders are caused by an endogenous mechanism related to the pathology of MS,<sup>31</sup> or a psychosocial response to a chronic illness,<sup>32</sup> or, most likely, a combination of both.

Strengths of this study included the large multisite cohort, longitudinal design, high completion rate (>90%) over the three assessments and the use of validated questionnaires that have previously been employed in an MS population. The consecutive nature of recruitment and high proportion of individuals who agreed to participate suggests that our cohort is representative of individuals attending an MS clinic. Further, two of the clinics deliver the only MS care in their province (Manitoba and Nova Scotia) which also suggests these findings are generalizable to the wider MS population. A limitation of this study was the reliance on self-reported adverse health behaviours, which are susceptible to reporting bias.<sup>33</sup> Although this is the most common approach used to assess such behaviours and we used validated instruments, it remains possible that people have varied perspectives on what constitutes problem drinking, and some people may have been misclassified for this reason. It would be of value in the future to consider the influence of cognition on these relationships.

We examined the burden of comorbidity between adverse health behaviours and mental health, and the risk for developing mental health symptoms, and

alcohol dependence. Alcohol dependence and smoking were associated with both anxiety and depression. Alcohol dependence was also associated with an increased risk of developing subsequent depression, and depression was associated with incident alcohol dependence. Prevention or reduction of the severity of these mental health problems is of considerable importance in MS care. Aside from the general benefits associated with the promotion of healthy behaviours, our findings suggest that promoting cessation of smoking and alcohol use will specifically contribute to improving mental health in MS. Physician advice to reduce alcohol use is effective,<sup>34</sup> as are pharmacological treatments aimed at smoking cessation.<sup>35</sup> Increased awareness of the effects of adverse health behaviours on mental health in MS might help target appropriate counselling and support for those 'at risk'.

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### Conflicts of interest

Kyla McKay, Lindsay Berrigan, and Kirsten Fiest report no disclosures.

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