Judgment hurts: The psychological consequences of experiencing stigma in multiple sclerosis

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ABSTRACT

Rationale: People living with MS often report feeling stigmatized, but little research has examined the psychological impact of this, which is important considering the high prevalence of depression in this population.
Objectives: The aim of this study was to assess, concurrently and prospectively, the association between stigma and depression in people living with MS.
Methods: Data were available from 5369 participants enrolled in the semi-annual survey conducted by the North American Research Committee on Multiple Sclerosis (NARCOMS). Participants reported their MS stigma and depression in the spring 2013 update survey (T1) and their depression again one year later (T2). Demographic and health-related covariates were also assessed.
Results: People experiencing higher levels of stigma reported more depression symptoms and were more likely to meet the threshold for clinical depression at both times, even controlling for covariates. Higher levels of stigma also predicted T2 depression, controlling for T1 depression (and covariates), suggesting a possible causal association. Greater psychosocial reserve, a composite of measures assessing participants' feelings of belonging, social support, and sense of control, attenuated the association between stigma and depression.
Conclusions: Stigma is an important but understudied predictor of depression in people living with MS, but greater psychosocial reserve provides a buffer.

1. Introduction

Multiple sclerosis (MS) is an autoimmune disorder marked by chronic inflammation of the central nervous system (CNS). People diagnosed with MS face a lifetime of progressive disability, including pain, fatigue, muscle weakness, and cognitive dysfunction, as well as incontinence, sexual dysfunction, and depression (Arnett et al., 2008; Frank and Elliott, 2000). MS impacts more than two and half million individuals world-wide; there is no cure for MS (Browne et al., 2014). From the moment people are diagnosed, they are burdened with the knowledge that they have a chronic illness that will, in some ways, influence how others see them and make them a potential target of stigma (Cook et al., 2016). Yet, there is relatively little research about how stigma affects people with MS. Stigma occurs when one is viewed as lower in status and separate from others due to a given characteristic. Stigma undermines health (Link and Phelan, 2006), but its role in the mental health of people living with MS is unclear. Given the high co-morbidity of MS and depression, research is needed to examine the potential impact of stigma on mental health in this population (Patten et al., 2003). The goal of the current study was to clarify the role of stigma in depression symptoms both concurrently and longitudinally among a large national sample of people living with MS.

The lifetime prevalence rate for depression in people living with MS is around 50%, much higher than the 17% lifetime prevalence in the general population (American Psychiatric Association, 2013; Patten and Metz, 1997; Sadovnick et al., 1996). Although many constructs covary with depression in MS (e.g., social support, coping style), much of the variance in depression is left unexplained (Cadden et al., 2017; Mohr et al., 1997). The cause of depression in MS is undoubtedly multi-faceted and includes direct physiological changes in the brain. However, we posit that stigma may account for some of the unexplained variance (Hatzenbuehler et al., 2013).

Stigma has been posited as a social determinant of health (Hatzenbuehler et al., 2013). Members of stigmatized groups disproportionately experience discrimination and loss of status, which can limit access to important resources (e.g., employment, housing, medical care) that affect health (Link and Phelan, 2006). Furthermore, exposure to stigma can lead members of stigmatized groups to experience stress

and social isolation, and pursue maladaptive coping strategies (e.g., substance abuse), all of which have been linked to poorer physical and mental health outcomes (Hatzenbuehler et al., 2013; Mak et al., 2007). Individuals with chronic health problems, physical disabilities, cognitive disabilities, and depression have all reported feeling stigmatized (De Boer et al., 2008; Pyne et al., 2004; Rao et al., 2009; Susman, 1994; Swaffer, 2014). Given that MS is a chronic health disorder that often comes with both cognitive and mood disruptions in addition to physical disabilities, it makes sense that individuals with MS could feel stigmatized. In one recent study, most individuals with MS reported at least some degree of anticipated stigma (i.e., experiences and/or concerns about biased treatment) and isolation stigma (a sense of being socially isolated due to MS stigma), and anticipated stigma predicted efforts at concealing MS (Cook et al., 2016). Although based on a small convenience sample, this study joins earlier qualitative research in showing that social stigma is a primary concern among individuals living with MS (Rivera-Navarro et al., 2007). Very little research has examined potential outcomes of experiencing stigma in MS. However, in one recent study, individuals who reported feeling stigmatized due to their MS reported a lower overall quality of life, were more likely to incur productivity losses at work, and needed greater informal care (Hategeka et al., 2017). That the majority of individuals living with MS report anticipating or experiencing stigma begets the natural question—what is the psychological consequence of this?

Perceived stigma has been found to predict depression in lung cancer patients (Cataldo et al., 2012), people living with HIV/AIDS (Charles et al., 2012), and individuals suffering from mental-illness (Pyne et al., 2004). To our knowledge, only one study has examined whether stigma predicts depression in people living with MS. In this study, those with the highest levels of stigma were more likely to be depressed (Viner et al., 2014). However, this study was limited by a cross-sectional design and absence of potentially confounding demographic and health-related variables that may co-vary with depression. Therefore, a more rigorous longitudinal examination of stigma's association with depression in MS is needed.

Identifying the role of stigma in depression is important for considering potential intervention strategies. Hatzenbuehler et al. (2013) posited that stigma diminishes individuals' psychological resources and leaves them vulnerable to physical and mental health decline. If so, then individuals living with MS who have more psychological resources, hereafter "psychosocial reserve," may better be able to endure stigma with less risk to physical and mental health. This suggests that psychosocial reserve may moderate any association between stigma and depression. To our knowledge, this has not been investigated empirically. Interventions to bolster psychosocial reserve may be effective if their absence is a contributing factor to depression in people with MS who experience stigma.

To capture the concept of psychosocial reserve, we turned to the literature on fundamental psychological needs. Unlike physical needs (e.g., air, water, food), which are required for survival, psychological needs are thought to be required for thriving, and when thwarted, can lead to deterioration of physical and mental health (Pittman and Zeigler, 2007). We assessed two needs that consistently appear in core needs models (e.g., Fiske, 2004; Maslow, 1943; Murray, 1938; Ryan and Deci, 2000): the need to belong and the need for basic autonomy or control. Relevant to the focus of the current study, research has found that higher levels of belonging can buffer against the deleterious effects of stress on depression (Choenarom et al., 2005), and that social support, a related concept, can buffer against depression in the general population (Lin and Dean, 1984) and among those with MS (Cadden et al., 2017). Previous research has also found beneficial effects of a personal control intervention on people's well-being (Langer and Rodin, 1976). The present study examined whether belonging, perceptions of social support, and perceived autonomy collectively moderated any association between stigma and depression.

Our ultimate goal was to clarify the association between stigma and depression, both concurrently and longitudinally, with a large national sample of people living with MS. To eliminate potential confounds, we control for relevant demographic and health-related variables and test psychosocial reserve as a moderator of the association between stigma and depression.

2. Methods

Data were collected as part of the semi-annual, volunteer survey of people living with MS, administered by the North American Research Committee on Multiple Sclerosis (NARCOMS) and approved by the Institutional Review Board of the University of Alabama at Birmingham. Participants in the NARCOMS registry initially complete an enrollment form and subsequently are prompted to update their information twice a year. Informed consent was obtained in writing at the enrollment and update surveys. Details on the NARCOMS registry are available elsewhere (Bebo et al., 2017; Marrie et al., 2008b). In the spring 2013 update survey (T1), we included several psychological items assessing stigma and psychosocial reserve (described below). T1 data were linked to participants' enrollment survey, and to their spring 2014 update survey (T2), when disease status and depression were assessed again. We limited eligibility to participants who reported their stigma level at T1 and their depression at T1 and T2. This resulted in a sample of 5413 individuals. Another 44 were excluded because of missing data on covariates (see below) resulting in a final sample of 5369.

The final sample was primarily female (78.4%) and White, non-Hispanic (90.4%) with the rest either Black/African American (2.1%), Hispanic/Latino (0.9%) or another/mixed-race/ethnicity (6.6%). Participants' T1 age ranged from 23 to 93 ($M = 58.27$, $SD = 10.19$). Most had obtained a technical, associate, or bachelor's degree (45.5%), while 31.5% had a high school diploma or less, and 23.0% had completed post-graduate education. Most were unemployed (68.5%). Participants had been diagnosed with MS for 19.82 years on average ($SD = 9.69$), with a range from 1 to 67 years. The majority of participants (55.7%) reported a disease course (i.e., the clinical pattern of symptoms used to describe MS) that was relapsing-remitting (including benign, clinically isolated, and unconfirmed diagnoses). Relapsing-remitting MS generally involves repeated cycles of acute symptom onset followed by resolution of most symptoms within weeks to months. An additional 32.2% reported a progressive disease course (including primary progressive, secondary progressive, and progressive relapsing diagnoses). Progressive MS involves gradual symptoms onset without resolution over time (i.e., progressively worsening disability). The remaining 12.1% were unsure or did not answer. The vast majority had health insurance (97.1%) and were non-smokers (89.1%). Approximately half reported exercising during the past month (58.2%) and nearly the same number (56.1%) reported taking a disease modifying therapy (DMT). Approximately 17.8% reported having a relapse in the past 6 months.

2.1. Measures

Stigma was measured at T1 with 9 self-report items used by Cook et al. (2016) rated on scale from 1 (not at all true) to 5 (very true), with higher scores indicating greater stigma perception. Four items assessed participants' anticipation or experience of MS stigma (Cronbach's $\alpha = 0.78$) (e.g., "People are uncomfortable around someone with MS"). Five items assessed isolation due to MS stigma ($\alpha = 0.86$) (e.g., "Because of my MS, I feel left out of things"). Because these subscales were highly correlated ($r = 0.58$), and analysis of them individually led to a consistent pattern of results, we averaged the subscales to form a composite stigma measure.

Depression was measured at T1 and T2 using the NARCOMS Depression Scale, a validated single-item self-report scale of depression symptoms (Marrie et al., 2008a). Respondents are asked to check a

Table 1

Descriptive statistics and bivariate correlations between stigma and depression at time 1 (T1) and 2 (T2).

Variable	Mean	SD	r T1 Depression	r T2 Depression
T1 Depression	1.17	1.16	–	–
T2 Depression	1.16	1.16	.744	–
Stigma	2.09	0.81	.464	.432

Note. All correlations are significant at $p < .001$. $N = 5369$.

single category from a list that most accurately describes their symptoms of depression in the past month. Six categories are presented on a scale from 0 to 5 with anchors of Normal, Minimal Depression, Mild Depression, Moderate Depression, Severe Depression, and Total Depression. Each category has a description associated with its anchor. For instance the category, Normal, is described as, "I have not noticed any problems with depression," whereas the category, Total Depression, is described as "Every day, depression problems force me to modify my daily activities." Consistent with previous research, individuals with scores ≥2 were categorized as clinically depressed (i.e., equivalent to Major Depressive Disorder) (Marrie et al., 2008a). In the final sample analyzed here, 31.8% and 32.2% were clinically depressed at T1 and T2, respectively (see Table 1).

Following Cook et al. (2017), psychosocial reserve was calculated by averaging participant responses on three measures at T1, selected as brief face-valid assessments of belonging and agency (Cohen and Hoberman, 1983; Fiske, 2004; Ryan and Deci, 2000). For belonging, we included a general item ("I feel like I belong," adapted from Walton and Cohen, 2007), and an author-generated item measuring perceived social support ("There are people I can count on to support me"). Another author-generated item assessed agency ("I am able to advocate for my needs"). All three items were rated on scales from 1 (not at all true) to 5 (very true) ($\alpha = 0.76$).

Demographic and health-related variables from enrollment included sex, race/ethnicity, year of birth, year of MS diagnosis, and education level. The T1 update survey assessed participants' current employment, smoking, and health-insurance status; their MS type; whether they used a DMT medication; whether they had had a relapse in the past 6 months; and whether they had engaged recently in physical exercise. Participants' level of disability at T1 and T2 was measured with the Patient Determined Disease Steps (PDDS), which assesses overall disability from 0 to 8 (Learmonth et al., 2013). Scores of 0–2 indicate mild to moderate disability that does not impair ambulation while scores of 3–5 indicate gait disruption and use of canes or other assistive devices. A score of 6 indicates the need for bilateral supportive assistive devices. A score of 7 indicates wheelchair use and a score of 8 indicates being bedbound. The final sample had an average T1 PDDS score of 3.6 ($SD = 2.4$).

2.2. Data analysis strategy

Missing data. A total of 44 cases were excluded due to missing data on the PDDS ($n = 29$) and psychosocial reserve ($n = 16$) (one person had missing data on both). Data were also missing from 40 people on their year of diagnosis. Given a moderately high correlation between age and years with MS ($r = 0.53$), and in order to avoid removing additional cases, we formed a composite "Years" variable by averaging age and years with MS after first standardizing each (Cook et al., 2017). There were no differences between the final sample of 5369 and the 44 excluded cases in reported stigma or depression at T1 or T2 ($ps \geq 0.39$). To avoid listwise deletion, a missing-data category was added to categorical covariates with missing data (see Table 2).

Analyses below follow a set of ordered steps to maximally illuminate the association of stigma with depression. In Step 1, we conducted bivariate correlations between stigma (T1) and depression at T1 and T2.

This was important to establish the unadjusted association between stigma and depression. In Step 2, we analyzed the prospective association between stigma and T2 depression, while controlling for T1 depression. If stigma in part causes depression, any effects of stigma on depression were likely already being exerted prior to T1. Thus, by controlling for T1 depression, Step 2 takes a more conservative approach, testing whether stigma predicts *change* in depression over a one-year period. In Step 3, we identified demographic and health-related variables associated with depression, and in Step 4, we controlled for these while analyzing again the concurrent and prospective associations between stigma and depression. We also modeled the dichotomous indicator of clinical depression diagnosis at T2 as an outcome. In Step 5, we tested whether psychosocial reserve moderated any observed association between stigma and T2 depression.

3. Results

3.1. Steps 1 and 2: bivariate correlations between stigma and depression

Stigma explained 21.5% of the variance in T1 depression, r (5367) = 0.46, $p < .001$, and 18.7% of the variance in T2 depression, r (5367) = 0.43, $p < .001$ (see Table 1). After controlling for T1 depression, stigma explained 2.2% of the variance in T2 depression, r (5366) = 0.15, $p < .001$. Thus, there was a moderate bivariate correlation between stigma and depression measured concurrently and one-year later, and a small prospective association between stigma and worsening depression.

3.2. Step 3: identification of relevant covariates

Regression analyses revealed that all tested demographic and health-related variables were associated with depression (see Table 2), and thus, all were retained. Greater depression was associated with being female, with having more severe MS-related symptoms (e.g., higher PDDS, progressive disease course, and a recent relapse), and with having fewer social and economic resources (e.g., lower education, being unemployed, no health insurance, lower psychosocial reserve). Positive health-related factors such as taking DMTs, engaging in physical activity, and not smoking were associated with lower depression.

3.3. Step 4: covariate-adjusted association of stigma with depression

Multiple linear and logistic regression analyses tested whether stigma predicted depression beyond the covariates identified in Step 3.

Continuous depression symptoms. The final model including all covariates and stigma explained 28.2% of the variance in *concurrent* (T1) depression, $F(24, 5344) = 87.55$, $p < .001$ (see Table 3). Of note, stigma alone accounted for approximately 10% of the variance, whereas all the other covariates combined explained 18%. Put another way, stigma accounted for 35% of the explained variance in depression, $t(5344) = 27.00$, $p < .001$.

With respect to *prospective* (T2) depression, the final model explained 24.8% of the variance, $F(24, 5344) = 73.42$, $p < .001$ (see Table 3), with approximately 8% explained by stigma, $t(5344) = 24.16$, $p < .001$, and 17% explained by the remaining covariates. After additionally controlling for T1 depression, stigma continued to explain approximately 0.5% of the variance in T2 depression, $t(5343) = 8.05$, $p < .001$. Thus, higher levels of stigma prospectively predicted worsening depression over a one-year period. This effect remained significant after including T2 PDDS, suggesting that stigma's posited role in depression change is not explained by worsening disability over the same year.

Clinical depression. Controlling for demographic and health-related covariates, stigma also predicted the likelihood of being clinically depressed at T2 (OR = 2.27, $p < .001$), with each one-unit increase in stigma increasing by 69% the chance that a person would be clinically

Table 2
Association between covariates at time 1 (T1) and depression at times 1 and 2 (T2).

Covariate	T1 Depression				T2 Depression			
	B	SE	95% CI		B	SE	95% CI	
Continuous Covariates								
Age/Years Composite	− 0.05*	0.02	− 0.09,	− 0.02	− 0.04*	0.02	− 0.08,	− 0.01
PDDS	0.08**	0.01	0.07,	0.10	0.08**	0.01	0.07,	0.10
Psychosocial Reserve	− 0.36**	0.02	− 0.38,	− 0.33	− 0.33**	0.02	− 0.36,	− 0.30
Categorical Covariates								
Sex	− 0.08*	0.04	− 0.16,	− 0.01	− 0.08*	0.04	− 0.16,	− 0.01
Race/Ethnicity 1	0.05	0.11	− 0.17,	0.27	0.03	0.11	− 0.19,	0.25
Race/Ethnicity 2	− 0.08	0.17	− 0.41,	0.24	− 0.10	0.17	− 0.42,	0.23
Race/Ethnicity 3	0.14*	0.06	0.01,	0.26	0.10	0.06	− 0.03,	0.22
Education 1	0.15**	0.04	0.08,	0.22	0.20**	0.04	0.13,	0.27
Education 2	− 0.19**	0.04	− 0.27,	− 0.11	− 0.18**	0.04	− 0.26,	− 0.10
Education 3	0.27	0.14	− 0.01,	0.55	0.08	0.14	− 0.20,	0.35
Employment Status 1	− 0.46**	0.03	− 0.53,	− 0.39	− 0.42**	0.03	− 0.48,	− 0.35
Employment Status 2	0.03	0.17	− 0.30,	0.36	− 0.16	0.17	− 0.49,	0.17
Smoking Status 1	0.46**	0.05	0.36,	0.56	0.47**	0.05	0.37,	0.57
Smoking Status 2	0.20	0.13	− 0.07,	0.46	0.12	0.13	− 0.15,	0.38
Physical activity 1	− 0.25**	0.03	− 0.32,	− 0.19	− 0.28**	0.03	− 0.34,	− 0.22
Physical activity 2	0.01	0.12	− 0.23,	0.24	− 0.14	0.12	− 0.37,	0.10
Recent Relapse 1	0.64**	0.04	0.56,	0.72	0.59**	0.04	0.51,	0.67
Recent Relapse 2	0.46**	0.05	0.36,	0.56	0.44**	0.05	0.34,	0.55
Insurance 1	0.63**	0.11	0.41,	0.85	0.50**	0.11	0.28,	0.73
Insurance 2	0.04	0.17	− 0.28,	0.37	− 0.13	0.17	− 0.46,	0.19
DMT	− 0.07*	0.03	− 0.13,	− 0.00	− 0.07*	0.03	− 0.13,	− 0.01
MS Type 1	0.18**	0.04	0.12,	0.25	0.20**	0.04	0.13,	0.27
MS Type 2	0.02	0.05	− 0.08,	0.11	0.03	0.05	− 0.07,	0.13

Note. N = 5369. *$p < .05$. **$p < .001$. B = unstandardized coefficient. SE = standard error of the coefficient. All categorical variables were dummy coded (reference group = 0, comparison group = 1). For sex, the reference group is female, compared to male. For race/ethnicity, the reference group is non-Hispanic Whites, compared to Blacks/African Americans (Race/Ethnicity 1), Hispanics/Latinos (Race/Ethnicity 2), and all others (Race/Ethnicity 3). For education, the reference group is those with a technical, associate's, or bachelor's degree, compared to those with a high school diploma or less (Education 1), those with post-graduate education (Education 2), and those with missing data (Education 3). For employment status, the reference group is those unemployed, compared to those with part- or full-time employment (Employment Status 1), and those with missing data (Employment Status 2). For smoking status, the reference group is non-smokers, compared to smokers (Smoking Status 1), and those with missing data (Smoking Status 2). For physical activity, the reference group is those who had not engaged in recent physical activity, compared to those who had (Physical Activity 1), and those with missing data (Physical Activity 2). For recent relapse, the reference group is those without a relapse in the last 6 months, compared to those who had a relapse (Recent Relapse 1), and those who were unsure or had missing data (Recent Relapse 2). For insurance, the reference group is those with insurance, compared to those without insurance (Insurance 1), and those with missing data (Insurance 2). For DMT, the reference group is those not taking a DMT (or did not answer), compared to those taking a DMT. For MS Type, the reference group is those with relapse-remitting MS, compared to those with progressive MS (MS Type 1), and those who were unsure or did not answer (MS Type 2).

depressed. Adding T1 depression to the model, stigma continued to predict T2 depression status (OR = 1.36, $p < .001$), with each one-unit increase in stigma increasing the chance of clinical depression by 58%. These analyses suggest that stigma contributes to clinically meaningful levels of depression and not simply to sub-clinical reports of low mood or distress.

3.4. Step 5: moderating effect of psychosocial reserve

Continuous depression symptoms. Controlling for the demographic and health-related covariates, psychosocial reserve moderated the association between stigma and T2 depression, $t(5343) = −6.46$, $p < .001$, $R^2 = 0.01$ (see Fig. 1). Stigma predicted T2 depression at low and high levels of psychosocial reserve (i.e., ± 1 SD from the mean). However, stigma predicted depression more strongly at low levels of psychosocial reserve, B = 0.55, $R^2 = 0.08$, than at higher levels, B = 0.34, $R^2 = 0.02$. This suggests that stigma has less impact on depression among individuals with higher levels of psychosocial reserve.

Adding T1 depression to the model led the moderating effect of psychosocial reserve to become non-significant ($p = .10$), indicating that psychosocial reserve had little effect on change in depression from stigma over a one-year period.

Clinical depression. Controlling for the demographic and health-related covariates, psychosocial reserve also moderated the association between stigma and T2 clinical depression status, OR = 0.85, $p < .001$. Stigma predicted T2 depression status at low and high levels of psychosocial reserve (i.e., ± 1 SD from the mean), but its effects were stronger at low, OR = 2.54, $p < .001$, than high, OR = 1.81,

$p < .001$, levels.

Adding T1 depression status to the model led the moderating effect of psychosocial reserve to become non-significant ($p = .19$). Thus, within the constraints of change in depression status over a one-year period, psychosocial reserve did not reliably moderate the effect of stigma.

4. Discussion

Results from a national study of people living with MS revealed that individuals experiencing greater levels of stigma reported more symptoms of depression and were more likely to be clinically depressed. This was true even after controlling for relevant demographic and health-related variables and whether using the individual stigma subscales or their composite. In fact, stigma's large effect size – comparable to all the covariates combined – suggests its importance as a clinically relevant predictor of depression. Perhaps most importantly, we found higher levels of stigma to predict later depression even controlling for earlier levels of depression. This suggests that for people living with MS, stigma may partly cause depression. Although the effect size of stigma was expectedly smaller in this prospective analysis, it is notable that study participants had been diagnosed with MS for nearly 20 years on average, such that stigma had been part of their lives for many years. That stigma continued to predict change in depression over a relatively short one-year period speaks to how a small yearly effect over a lifetime can accumulate to be an important overall contributor. Reports of depression among people with higher levels of psychosocial reserve, a composite of belonging, social support, and sense of control, were less

Table 3
Results of linear regression models predicting depression at time 1 (T1) and 2 (T2).

	B	SE	95% CI		p	F	R^2
Overall Model of T1 Depression	–	–	–	–	< .001	87.55	.282
Constant	0.882	0.088	0.710,	1.053	< .001		
Age/Years Composite	−0.071	0.019	−0.108,	−0.033	< .001		
PDDS	−0.014	0.008	−0.031,	0.002	.081		
Psychosocial Reserve	−0.181	0.014	−0.209,	−0.154	< .001		
Sex	−0.062	0.033	−0.127,	0.004	.065		
Race/Ethnicity 1	−0.048	0.096	−0.236,	0.140	.620		
Race/Ethnicity 2	−0.324	0.141	−0.600,	−0.048	.021		
Race/Ethnicity 3	0.023	0.055	−0.084,	0.131	.671		
Education 1	0.056	0.032	−0.007,	0.119	.079		
Education 2	−0.069	0.035	−0.138,	0.000	.051		
Education 3	0.263	0.121	0.026,	0.500	.030		
Employment Status 1	−0.256	0.034	−0.323,	−0.189	< .001		
Employment Status 2	0.102	0.204	−0.298,	0.501	.618		
Smoking Status 1	0.253	0.045	0.166,	0.340	< .001		
Smoking Status 2	0.110	0.217	−0.315,	0.536	.612		
Physical Activity 1	−0.053	0.031	−0.113,	0.007	.084		
Physical Activity 2	−0.083	0.193	−0.460,	0.295	.668		
Recent Relapse 1	0.347	0.037	0.275,	0.419	< .001		
Recent Relapse 2	0.173	0.046	0.083,	0.263	< .001		
Insurance 1	0.281	0.098	0.089,	0.474	.004		
Insurance 2	−0.162	0.199	−0.552,	0.227	.414		
DMT	−0.048	0.029	−0.106,	0.010	.104		
MS Type 1	−0.045	0.037	−0.118,	0.028	.226		
MS Type 2	−0.104	0.046	−0.194,	−0.013	.025		
Stigma	0.534	0.020	0.495,	0.573	< .001		

	B	SE	95% CI		p	F	R^2
Overall Model of T2 Depression	–	–	–	–	< .001	73.416	0.248
Constant	0.882	0.089	0.706,	1.057	< .001		
Age/Years Composite	−0.066	0.019	−0.104,	−0.028	.001		
PDDS	−0.009	0.008	−0.025,	0.008	.309		
Psychosocial Reserve	−0.170	0.014	−0.198,	−0.142	< .001		
Sex	−0.070	0.034	−0.137,	−0.003	.040		
Race/Ethnicity 1	−0.068	0.098	−0.260,	0.124	.487		
Race/Ethnicity 2	−0.320	0.144	−0.602,	−0.039	.026		
Race/Ethnicity 3	0.002	0.056	−0.108,	0.112	.972		
Education 1	0.109	0.033	0.045,	0.173	.001		
Education 2	−0.068	0.036	−0.138,	0.002	.058		
Education 3	0.069	0.123	−0.173,	0.311	.576		
Employment Status 1	−0.198	0.035	−0.266,	−0.129	< .001		
Employment Status 2	−0.024	0.208	−0.432,	0.383	.906		
Smoking Status 1	0.278	0.045	0.189,	0.367	< .001		
Smoking Status 2	0.268	0.221	−0.166,	0.701	.227		
Physical Activity 1	−0.077	0.031	−0.139,	−0.016	.014		
Physical Activity 2	−0.300	0.196	−0.685,	0.085	.127		
Recent Relapse 1	0.318	0.037	0.245,	0.391	< .001		
Recent Relapse 2	0.173	0.047	0.081,	0.265	< .001		
Insurance 1	0.180	0.100	−0.016,	0.376	.072		
Insurance 2	−0.228	0.203	−0.625,	0.169	.261		
DMT	−0.042	0.030	−0.100,	0.017	.166		
MS Type 1	−0.019	0.038	−0.093,	0.056	.623		
MS Type 2	−0.088	0.047	−0.180,	0.005	.063		
Stigma	0.487	0.020	0.447,	0.526	< .001		

Note. N = 5369. B = unstandardized coefficient. SE = standard error of the coefficient. β = standardized coefficient. All categorical variables were dummy coded (reference group = 0, comparison group = 1). For sex, the reference group is female, compared to male. For race/ethnicity, the reference group is non-Hispanic Whites, compared to Blacks/African Americans (Race/Ethnicity 1), Hispanics/Latinos (Race/Ethnicity 2), and all others (Race/Ethnicity 3). For education, the reference group is those with a technical, associate's, or bachelor's degree, compared to those with a high school diploma or less (Education 1), those with post-graduate education (Education 2), and those with missing data (Education 3). For employment status, the reference group is those unemployed, compared to those with part- or full-time employment (Employment Status 1), and those with missing data (Employment Status 2). For smoking status, the reference group is non-smokers, compared to smokers (Smoking Status 1), and those with missing data (Smoking Status 2). For physical activity, the reference group is those who had not engaged in recent physical activity, compared to those who had (Physical Activity 1), and those with missing data (Physical Activity 2). For recent relapse, the reference group is those without a relapse in the last 6 months, compared to those who had a relapse (Recent Relapse 1), and those who were unsure or had missing data (Recent Relapse 2). For insurance, the reference group is those with insurance, compared to those without insurance (Insurance 1), and those with missing data (Insurance 2). For DMT, the reference group is those not taking a DMT (or did not answer), compared to those taking a DMT. For MS Type, the reference group is those with relapse-remitting MS, compared to those with progressive MS (MS Type 1), and those who were unsure or did not answer (MS Type 2).

affected by stigma.

Results of the current study contribute to the MS literature by highlighting the role of stigma in explaining the high prevalence of depression among people living with MS (Patten and Metz, 1997). Given the ongoing search to explain the association of MS with

depression (Siegert and Abernethy, 2005), results suggest that stigma may be an important but understudied predictor. People's sense that they will be set apart from others and treated negatively because of their MS may contribute to depression in addition to any direct physical effects of the illness. Moreover, as results here suggest, the association
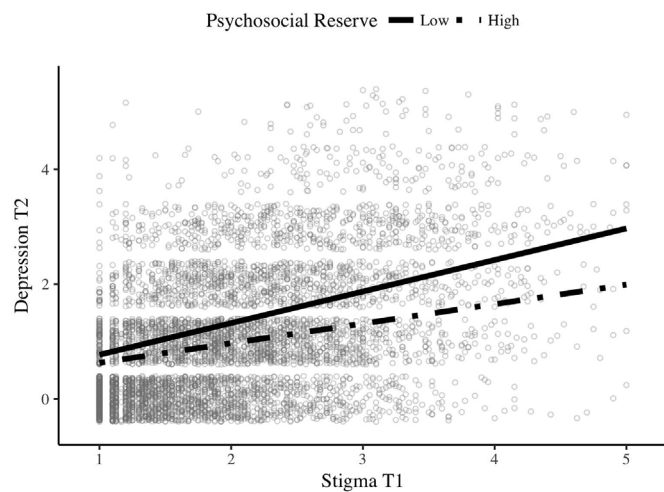
Fig. 1. Association of Stigma with T2 Depression as a Function of Psychosocial Reserve. Lines represent the linear slope of stigma with T2 depression at 1 standard deviation above (high) and below (low) the mean of psychosocial reserve, controlling for demographic and health-related covariates. Scatterplot represents the unadjusted association of stigma with T2 depression. Plotted data points are slightly jittered to reduce overlap.

of stigma with MS go beyond subclinical mood changes, as higher levels of stigma predicted a greater likelihood of being clinically depressed.

Results also contribute to the stigma literature. Most research on the association of stigma with depression has tended to rely on cross-sectional designs (e.g., Chaudoir et al., 2012; Grov et al., 2010). The releatively few longitudinal studies examining the effects of stigma on depression generally use relatively small samples (e.g., Link et al., 1997) and/or samples from a specific service setting (e.g., Link et al., 1997; Markowitz, 1998). The data presented here highlight the prospective association of stigma with depression using a large and diverse national sample. Our results confirm and add confidence to previous research findings that stigma predicts depression over time.

The present research also contributes to the stigma literature by examining a type of stigma that is less counfounded by perceptions of personal responsibility than others commonly studied. Much of the research on stigma, and particularly on the association of stigma with depression, focuses on stigma from HIV or from mental health and substance use disorders. Perceptions among the general public that such conditions may be controllable can exacerbate stigma (Jones et al., 1984), leaving ambiguity as to whether previous findings would apply to sources of stigma like MS, a chronic illness whose cause is thought to be beyond individual control (Grytten and Måseide, 2005). Our results suggest the generalizability of stigma in predicting depression across stigmatizing conditions. That stigma predicts depression in MS speaks to how powerfully social factors related to chronic illness can affect mental health.

The finding of a moderating effect of psychosocial reserve is another contribution of this research. The association of stigma with depression varied based on people's level of psychosocial reserve (though psychosocial reserve did not moderate change in depression over time). This suggests the multilevel nature of stigma, in that its effects depend, in part, on people's interpretation of themselves in their social environments. In the current research, this was represented by people's sense of belonging, perceptions of social support, and perceived autonomy, key elements of core psychological needs theories (Pittman and Zeigler, 2007). That psychosocial reserve moderated associations of stigma with depression supports the idea that the effect of stigma on individual outcomes like health are determined in part by people's interactions with their social systems over time. This is consistent with multilevel perspectives on the causes and consequences of stigma (Cook et al., 2014; Hatzenbuehler et al., 2013). People with greater resources – i.e., higher levels of psychosocial reserve – may be relatively more

protected from stigma compared to those with fewer resources. The moderation result also suggests that effects of stigma are not uniform and may be mitigated by interventions that help people cope more effectively with stigma (Chaudoir et al., 2012; Moskowitz et al., 2009).

Beyond its contribution to theory, results of the current research also have clinical implications. For instance, healthcare professionals may want to more routinely assess patients' perceived stigma to identify those most at risk for depression and advise them on appropriate treatment. As depression has been shown to worsen MS disease progression (Brown et al., 2009), and be associated with less consistent adherence to DMTs (Bruce et al., 2010), identifying those at risk is important for physical and mental health. That people with lower levels of psychosocial reserve were more vulnerable to the effect of stigma on depression suggests a potential point of intervention. A variety of potential intervention strategies could be considered, including brief psychological interventions designed to bolster elements of psychosocial reserve, educational interventions for healthcare workers, and psychotherapy and support groups that address stigma (see Cook et al., 2014).

4.1. Limitations

Our use of self-report measures introduces some shared method confound. However, as fear about being a target of stigma can be psychologically influential even in the absence of observable bias, self-report is an appropriate method of assessment. Future research may benefit from using a more comprehensive set of stigma items. The use of a single-item depression measure is a potential limitation, but this measure has been shown to have adequate criterion, construct, and divergent validity. For instance, it is highly correlated with the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), and based on a score ≥ 2, has high sensitivity and specificity for depression diagnoses (Marrie et al., 2008a). Future researchers may consider using additional measures of depression that rely less on self-report, such as diagnostic interviews. Future research is also needed to verify findings regarding psychosocial reserve, ideally using a measure with more items and established psychometric properties. Of course, many of these limitations are a necessary compromise for accessing a large longitudinal sample, which is a strength of the current research.

Our study provides insight into the longitudinal contribution of stigma to depression. However, the assessment of stigma and potential explanatory variables concurrently at T1 precludes the ability to satisfactorily test causal pathways by which stigma may increase depression. Future studies should strive to uncover such mechanisms, using longitudinal designs that allow repeated assessment of possible explanatory variables along with health outcomes. Stigma may diminish people's psychological resources, which can increase their vulnerability to physical and mental health risks (Hatzenbuehler et al., 2013), like depression. Potential variables to assess could include participants' access to resources, sense of status, and stress, as well as items assessing belonging, perceptions of social support, and perceived autonomy. Understanding the mechanisms by which stigma leads to depression would be helpful in informing future interventions that seek to mitigate the adverse impact of stigma on health.

5. Conclusions

Despite limitations, our study is the first to demonstrate the association between stigma and depression in MS using a large, demographically diverse sample. Given the 50% lifetime prevalence of depression in MS, identifying potential factors associated with depression is important. As treatment for depression is effective in only about 50% of people living with MS, it may be useful to consider interventions to help reduce stigma and help bolster psychosocial reserve.

Declaration of conflicting interests

Conflicts of interest: none.

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