

Disability, Depression and Suicide Ideation in People with Multiple Sclerosis

Lewis, Vicky; Katherine, Williams; Koko, Chit ; Woolmore, John ; Jones, Christopher; Powell, Theresa

DOI:

[10.1016/j.jad.2016.08.038](https://doi.org/10.1016/j.jad.2016.08.038)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Lewis, V, Katherine, W, Koko, C, Woolmore, J, Jones, C & Powell, T 2016, 'Disability, Depression and Suicide Ideation in People with Multiple Sclerosis', *Journal of Affective Disorders*.
<https://doi.org/10.1016/j.jad.2016.08.038>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

Checked for eligibility: 07/10/2016

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Manuscript prepared for publication in Journal of Affective Disorders

Conflicts of interest: none.

Contributors: Dr Chit Koko and Dr Theresa Powell conceived the project. Dr Vicky Lewis, Katherine Williams, Dr Chit KoKo and Dr Theresa Powell designed and wrote the protocol. Dr Theresa Powell supervised the research. Dr Vicky Lewis and Katherine Williams conducted the literature search and review. Dr Chit KoKo and Dr John Woolmore oversaw recruitment. Dr Vicky Lewis and Katherine Williams collected the data. Dr Chris Jones, Dr Vicky Lewis and Dr Theresa Powell conducted the statistical analysis. Dr Vicky Lewis wrote the first draft of the manuscript and all authors have approved the final manuscript.

Role of funding sources: this research was carried out as part of the Doctorate in Clinical Psychology at the University of Birmingham. The role of the funding source was education and research. Financial support for the conduct of the research was provided by the University of Birmingham, Department of Clinical Psychology. There was no sponsor and this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Title

Disability, Depression and Suicide Ideation in People with Multiple Sclerosis

V.M. Lewis^a, K. Williams^a, C. KoKo^b, J. Woolmore^c, C. Jones^a, T. Powell^{ab1},

a Department of Clinical Psychology, University of Birmingham, Birmingham, UK

b West Midlands Rehabilitation Service, Birmingham, UK

c Queen Elizabeth Hospital, Birmingham, UK

¹ Dr Theresa Powell, Programme Director, Doctorate in Clinical Psychology, School of Psychology, University of Birmingham, Frankland Building, Edgbaston, Birmingham, B15 2TT. Tel: 0121 414 7124. Email: t.powell@bham.ac.uk.

Abstract

Introduction: Depressive symptoms occur frequently in people with Multiple Sclerosis (MS) and rates of suicide ideation are higher than the general population. There is evidence for a direct association between disability and depression, disability and suicide ideation, and depression and suicide ideation in MS. However, the relationship between all three, i.e. the mediating role of depression between disability and suicidal ideation, has not been investigated. Exploring this relationship could highlight risk factors, alerting clinicians to the need for timely intervention.

Method: Seventy five people with progressive MS attending two out-patient clinics took part in this cross-sectional study. Participants completed the Beck Suicide Scale, Beck Depression Inventory, Multiple Sclerosis Impact Scale and Guy's Neurological Disability Scale.

Results: Depressive symptoms mediated the relationship between perceived and actual disability and suicide ideation. Different types of disability were associated with suicidality, including: 'tremors' and 'taking longer to do things'. A small sub-group of participants were identified who reported suicide ideation in the presence of only mild levels of depression.

Limitations: There may be a sample bias in this study as all participants were attending out-patient clinics and receiving support which may not be available to everyone with MS.

Conclusion: It is important for clinicians to screen regularly for both depression and suicide ideation, to be alert to specific types of disability for which a higher level of suicide ideation might be present and to consider the possibility of suicidal thoughts being present in people who show minimal or no depressive symptoms.

Key words: Multiple Sclerosis, disability, depression, suicide ideation, 'rational' suicide.

Background

MS is a progressive, neurodegenerative, immune-mediated disorder, characterised by deterioration of the myelin sheath (Pugliatti et al., 2006). The disease course is most often categorised into three different types referred to as: relapsing remitting MS (RRMS), primary progressive MS (PPMS) and secondary progressive MS (SPMS); irrespective of type, symptoms can vary considerably. Primary progressive MS (PPMS) encompasses increasing disability from onset with plateaus and possible minor improvements (Pugliatti et al., 2006). Secondary progressive MS (SPMS) is diagnosed if a progressive disease course follows a period of symptomatic relapses originally referred to as relapsing remitting MS (RRMS) (Tutuncu et al., 2012). Two thirds (approximately) of those diagnosed with RRMS will transition to SPMS, usually 10-15 years after diagnosis (Hooper, 2013). The rate of disease progression in both PPMS and SPMS has been found to be comparable (Kuhlman, 2013; Soldán et al., 2015). In progressive MS types, where there is a higher level of increasing disability compared to RRMS, this has been associated with higher levels of depression and suicide ideation (Chwastiak et al., 2002; Dennis et al., 2009; Sarısoy, Terzi, Gümüş, & Pazvantoğlu, 2013; Turner et al., 2006). For this reason, progressive MS types will be the focus of investigation in this research study.

Depressive symptoms occur frequently in people with Multiple Sclerosis (MS) (Dalgas et al., 2014) and are considered to be a significant problem in this condition (Gay, Vrignaud, Garitte & Meunier, 2010). The risk of depressive symptoms in MS has been found to be as high as 50% (Chwastiak et al., 2002). This is four times higher than the risk of depression reported in the general population (Ayuso-Mateos et al., 2001). Suicide rates in the MS population have been found to be twice the rate of the general population (Bronnum-Hansen, Stenager, Stenager & Kock-Henriksen, 2005) and it has been reported that over a quarter of people with MS experience suicide ideation (Feinstein, 2002).

Depression in MS has been shown to be highly correlated with suicidality (Carson, Best, Warlow & Sharpe, 2000) but depressive symptoms are often undetected and untreated (Feinstein, 2004; Patten, Beck, Williams, Barbui & Metz, 2003). This may be due to a difficulty in distinguishing depression from the common symptoms of MS, for example, fatigue and cognitive dysfunction, both of which can be observed in MS without the presence of depressive symptoms (Siegert & Abernethy, 2005). Alternatively, Caine and Schwid (2002) suggest that suicide ideation in MS may not be identified because patients tend to minimise these thoughts during assessment in order to provide superficial reassurance to their clinicians that they will not harm themselves.

Suicide ideation in people with disabilities is a complex and imperative health concern (Giannini et al., 2010). Not only is depression a key predictor of suicide risk in MS (Paparrigopoulos, Ferentinos, Kouzoupis, Koutsis & Papadimitriou, 2010) but the presence of depression is known to have a significant impact upon quality of life, general health (Feinstein, 2007; Lester, Stepleman & Hughes, 2007) and adherence to treatment (Mohr, Goodkin, Gatto & Van Der Wende, 1997). Attending to depression and suicidality in MS is therefore, a medical priority, to the extent that suicide may be an avoidable tragedy (Faber, 2003).

Disability (impairments in body structure or function and activity limitation, with one study measuring participation level, as defined by the World Health Organisation, 2002) in MS has been found to have an impact upon both depression and suicide ideation when explored separately. No existing research has investigated the interrelationship between all three variables. Therefore, the present study will explore whether depression mediates the relationship between disability and suicidal ideation.

The direct relationship between depressive symptoms and disability was considered in a systematic review by Arnett, Barwick and Beeney (2008) and resulted in equivocal

findings. For the majority of studies included in the review, the measure of disability was the Expanded Disability Status Scale (EDSS) developed by Kurtzke (1983) which measures impairments in the following functional systems: pyramidal (ability to walk), cerebellar (coordination), brain stem (speech and swallowing), sensory (touch and pain), bladder and bowel, visual, mental and any other neurological symptoms caused by MS. Other measures utilised were the Sickness Impact Profile (SIP), physical summary subscale (Bergner, Bobbitt, Carter, and Gilson, 1981) which measures somatic autonomy and mobility control; and the London Handicap Scale (LHS) (Harwood and Ebrahim, 1995) which measures mobility, physical independence, occupation, social integration, orientation and economic self-sufficiency. All measures provide a total score and the higher the score the higher the level of disability.

Null findings were reported in eleven studies but five of these had a small sample size (ranging from $n = 10 - 50$). Five studies had a reasonable sample size (ranging from $n = 83 - 98$) using standard measures of disability and depression. One other study used a non-standardised measure of disability. Conversely, eleven studies reported statistically significant findings, all suggesting a positive correlation between disability and depression, with effect sizes in the moderate range, suggesting increased disability is related to increased depression. All except one used standardised measures, and sample sizes ranged from $n = 76 - 1374$ except for two ($n = 18$ and $n = 45$). Since this review, several other studies have confirmed this association (Anhoque, Domingues, Carvalho, Teixeira & Domingues, 2011; Arnett et al., 2008; Beal et al., 2007; da Silva et al., 2011; Gay et al., 2010; Sarisoy et al., 2013; Smith & Arnett, 2013).

With regards to the direct relationship between depressive symptoms and suicide ideation in people with MS, this has been explored in three studies (Feinstein, 2002; Viner et al. 2014; Turner et al., 2006); one did not find a significant association between level of

depression and suicide ideation (Feinstein, 2002) and there are methodological weaknesses in the two which did find a significant association due to low to moderate response rates: 39.5% (Viner et al. 2014) and 43.7% (Turner et al. 2006) and the use of non-standardised measures. Feinstein (2002) measured suicide ideation by using just three self-report questions derived from the Beck Suicide Scale (Beck and Steer, 1993) and thus the psychometric properties of these three questions are unknown. Similarly, Viner et al. (2014) used a self-designed measure of disability rather than a standardised and validated measure and both Turner et al. (2006) and Viner et al. (2014) assessed suicide ideation by selecting a single item from the Patient Health Questionnaire (PHQ-9) (Kroenke and Spitzer, 2002), and although the measure itself is said to have good psychometric properties (Manea, Gilbody, McMillan, 2015), these are unknown for a single item.

Looking at the direct relationship between disability and suicide ideation, Feinstein (2002) did not find a significant association. However, two more recent studies reported that self-reported bladder or bowel difficulties, and communication and swallowing difficulties were risk factors for suicide ideation (Viner et al., 2014, Turner et al., 2006) and in addition, Turner et al. (2006) found that mobility problems and a higher level of perceived disability was associated with suicide ideation. Assessing a person's own perspective of disability is important (Turk, Okifuji & Scharff, 1995) and there are an increasing number of studies incorporating these measures (Freeman et al., 2001). For example, it has been found in a study exploring obesity related disability, that level of perceived disability can be different from actual physical limitation (Larsson & Mattsson, 2001). Therefore, the present study will explore both self-reported disability and the degree to which this is seen as a problem for the person.

Finally, two studies have explored the direct relationship between disability and completed suicide in MS during a study of risk factors. One found that those with a moderate

level of disability were most at risk (Stenager et al., 1996) and one found that those who were more severely disabled were more at risk (Berman & Samuel, 1993).

As mentioned earlier, the interrelationship disability, depression and suicide ideation has not been investigated in the MS population although, Meltzer et al. (2012) found depression to mediate the relationship between disability and suicide ideation in the general population. If increasing levels of disability are found to be important, or any specific type of disability, found to be a 'red flag' for depression and hence suicide, it emphasises the importance of screening for both in the future. Findings could also alert clinicians to the need for more timely interventions in order to ameliorate distress.

A related concept termed 'rational' suicide would also benefit from consideration within the interrelationship of these three variables. Although it is well recognised that suicide ideation is a core symptom of major depression (Pompili et al., 2012), it has been found that in the MS population, not all suicides have occurred in the context of depressive symptoms (Sadovnick et al., 1991). It has been suggested that people can freely desire suicide or a hastened death based upon a logical, carefully contemplated decision in the absence of depression or psychiatric difficulties (Onkay-Ho, 2014).

Criteria for 'rational' suicide have been defined as: "(i) the presence of an unremittingly hopeless condition, (ii) a suicidal decision made as a free choice and (iii) the presence of an informed decision-making process" (Werth & Cobia, 1995, p. 1). In a MS specific study by Gaskill, Foley, Kolzet and Picone (2011) a perceived loss of control was found to be associated with suicide ideation suggesting that the ideation could provide a fall back means of still feeling in control for people faced with the burden of an unpredictable disease. There is no research to date exploring whether there is a sub-group of people with suicide ideation with only a minimal or mild level of depression in MS, therefore this will be examined in the present study.

The term disability in this study refers to disability as measured by Guys Neurological Disability Scale (GNDS) (Sharrack & Hughes, 1999) (which asks questions about: memory and concentration, mood and emotions, vision, speech and communication, swallowing, use of the arms and hands, mobility, bladder and bowel function, sexual function and fatigue) or perceived disability as measured by the Multiple Sclerosis Impact Scale (MSIS-29) (Hobart, Lamping, Fitzpatrick, Riazi & Thompson, 2001) which assesses the physical and psychological impact of MS.

Aims of the current study

Do depressive symptoms mediate the relationship between perceived disability and suicide ideation?

Do depressive symptoms mediate the relationship between actual disability and suicide ideation?

Based on the work of Turner et al. (2006) and Viner et al. (2014) is any specific type of disability related to suicide ideation?

Based upon the work of Onkay-Ho (2014) is there a sub-group of individuals who report suicide ideation with only a minimal or mild level of depressive symptoms?

Methods

A cross-sectional study design was utilised. Ethics approval was received from the West Midlands branch of National Research Ethics Committee.

Participants

Participants were recruited from two MS clinics in Birmingham. The first was an interdisciplinary specialist rehabilitation clinic for people with MS who have complex needs

in terms of disability management. The second clinic was a specialist MS clinic in an acute hospital which monitored all patients in the local area with MS.

Inclusion criteria:

1. A diagnosis of progressive MS following neurological examination, cerebrospinal fluid (CSF) examination or magnetic resonance imaging (MRI) and determined by the McDonald criteria (Polman et al., 2011).
2. Ability to provide informed consent to participate in the study.
3. Sufficient command of English language to complete the study measures with the researcher.
4. Age at least 16 years.

Exclusion criteria:

1. A current diagnosis of psychosis or any other degenerative neurological condition, for example dementia or Parkinson's disease.

Seventy-five participants with progressive MS participated in the study. Information about the number of participants approached by the clinicians was unavailable but four additional participants registered an interest but then decided not to participate in the study. Participants were recruited between March 2013 and March 2015 from the MS specialist rehabilitation clinic ($n = 70$) and between August 2014 and March 2015 ($n = 5$) from the MS clinic in the acute hospital.

MS clinic staff identified those who met the inclusion criteria from a clinic database and invited them to participate in the research. Prospective participants were given an information sheet about the study and all participants were given at least 48 hours to consider their participation. The participant information sheet informed participants that they were being invited to take part in a study investigating negative thoughts, feelings and disability in MS. It explained that they would be asked questions about depression and thoughts of

harming themselves which might be upsetting. It was also explained that if the researcher had concerns that the participant was at risk of harming themselves then clinic staff and their general practitioner would be informed. The opportunity to discuss the study in further detail with a researcher before providing consent was also offered.

Measures

The Beck Suicide Scale (BSS) (Beck & Steer, 1993) was used to measure suicide ideation. The highest total possible score is 42 and the higher the score the higher the level of suicide ideation.

Beck Depression Inventory (BDI-II) (Beck, Steer & Brown, 1996) was used to measure depressive symptoms. The highest total possible score is 63 and the higher the score the higher the level of depressive symptoms. There are clinical cut off points to categorise the level of depression: mild = 14-19, moderate = 20-28. Severe = 29-63 (Beck, Steer & Brown, 1996).

Multiple Sclerosis Impact Scale (MSIS-29) (Hobart, Lamping, Fitzpatrick, Riazi & Thompson, 2001) was used to measure perceived disability assessing how much the respondent is 'bothered' by specific types of disability. The highest total possible score is 145, the higher the score the higher the level of disability. Perceived physical impact is assessed in 20 questions (highest possible score: 100) and perceived psychological impact is assessed in 9 questions (highest possible score: 45).

Guys Neurological Disability Scale (GNDS) (Sharrack & Hughes, 1999) was used to measure actual disability, the highest total possible score is 60.

All measures have been used previously in MS research. Each measure was chosen based upon its clinical relevance, applicability and robust psychometric properties.

Procedure

Data collection was carried out either at the MS clinic or at the participant's own home. Demographic data was collected followed by a set of questions asking about type of MS, any history of depression and/or suicidality, wheelchair and catheter use, medication use, alcohol use and any comorbid conditions. Four measures were then utilised assessing: suicide ideation, depression, perceived disability and actual disability, in that order. Many participants had visual difficulties and so each question was read out by the researcher. One participant with a hearing impairment required the use of an interpreter. All other participants completed the measures independently in the presence of the researcher.

Following completion of the suicide ideation measure, if any suicidal thoughts were disclosed a thorough risk assessment was completed by the researcher, including clinical questions used to determine the level of suicide ideation and whether the participant had formulated a plan to take their own life. When there was an immediate concern, the participant was not left alone and a duty psychiatrist was contacted via the participant's general practitioner (GP) and requested to visit the participant. When there was concern but not of such an immediate level, the respective clinic was informed on the same day and a decision was made as to whether to contact the participant's GP and/or make a referral for talking therapy. A referral for the latter was offered to 13 participants. One participant was already receiving therapeutic support.

Data analysis

The main analysis was a mediation model (Preacher & Hayes, 2008; Preacher & Hayes, 2004). Data from the BSS and BDI-II were not normally distributed and scores from the MSIS-29 and GNDS were normally distributed.

In order to explore the relationship between disability, depressive symptoms and suicide ideation, mediation analysis procedures were used to examine the potential mediating

effects of depressive symptoms (Preacher & Hayes, 2008; Preacher & Hayes, 2004). This particular strategy reports bias corrected bootstrap confidence intervals which are robust to violation of parametric inference assumptions and therefore overcomes the problem of non-normality as described above and provides robust confidence intervals in smaller sample situations (Hardle & Marron, 1991; Moore & McCabe, 2005). Furthermore, given this is a clinical population, it cannot be assumed that the reference population itself has a normal distribution of scores so the decision was taken that it would be inappropriate to correct the sample distributions for normality.

Prior to the analysis, in order to standardise the regression parameters and to enable direct comparison between parameter coefficients within the mediation model, all of the variables were transformed into z scores ($M = 0$, $SD = 1$).

Results

The sample consisted of 31 males and 44 females, with an average age of 55 years ($SD = 10.08$, range: 38-79). The average age of onset was 33 years ($SD = 11.62$, range: 13-68) and the average time since onset was 23 years ($SD = 12.48$, range: 5-55).

There were 52 participants living with a spouse/partner/or other relative and 11 were in full or part time paid work. Twenty six participants had a diagnosis of primary progressive MS (PPMS) and 49 had a diagnosis of secondary progressive MS (SPMS). Sixty two reported using a wheelchair either continuously or for community access and 35 used either a permanent or temporary catheter. One participant was taking disease modifying medication. There were 15 participants with co-morbid physical health conditions (for example asthma, high blood pressure, underactive thyroid) including three who had experienced a mild stroke more than six months ago.

Fifteen participants reported using prescribed anti-depressant medication with 47 disclosing a history of depression and five describing a history of other mental health

problems. Eight participants reported current or past alcohol misuse. Eleven participants disclosed previous suicide ideation and, when asked if suicide had ever been attempted in the past, seven participants reported at least one or more attempt. One participant disclosed 11 previous attempts, the first of which followed the diagnosis of MS.

Following the same procedure described by Crane, Shah, Barnhofer and Holmes (2012), participants were split into two groups according to their BSS score: 49 participants reported no suicide ideation as defined by a BSS score of zero and 26 reported some level of suicide ideation defined as a BSS score greater than or equal to one. The mean score for depressive symptoms for all participants fell in the clinical category of ‘mild’ according to Beck, Steer & Brown (1996). The numbers of participants in each clinical category were: minimal n= 37, mild n= 21, moderate n= 11 and severe n= 6. Table I shows descriptive statistics for each measure including the Cronbach’s alpha calculated from the study data.

Table I. Measures of central tendency and internal reliability for all measures

Measure	M	SD	Mdn	Mode	Range	Cronbach’s alpha
BSS (<i>max score 42</i>)	2.44	5.67	0.00	0.00	0.00-35.00	0.93
BDI-II (<i>max score 63</i>)	13.8	8.88	13.00	9.00	0.00-39.00	0.88
MSIS-29 (<i>max score 145</i>)	86.75	25.36	88.00	71.00	14.00-22.00	0.93
MSIS (physical subscale) (<i>max score 100</i>)	64.71	19.27	65.00	46.00	0.00-96.00	0.91
MSIS (psychological subscale) (<i>max score 45</i>)	21.91	8.32	20.00	19.00	9.00-41.00	0.85
GNDS (<i>max score 60</i>)	24.73	8.92	24.00	23.00	1.00-49.00	0.71

As can be seen from table 1, good internal reliability was found for all measures.

Do depressive symptoms mediate the relationship between perceived disability and suicide ideation?

Table II below displays the outcomes of the mediation analysis for perceived disability and Figure 1 below displays the mediation model.

Table II. Mediated relationship between depression, perceived disability and suicide ideation

	Path Estimate β	Standard Error SE	p value	Lower 95% Bootstrap Confidence Interval	Upper 95% Bootstrap Confidence Interval
Correlation between perceived disability and suicide ideation in the unmediated model	0.42	0.16	0.014	0.09	0.74
Correlation between perceived disability and suicide ideation in the mediated model	0.10	0.11	0.399	-0.13	0.33
Depression as mediator	0.32	0.15	NA	0.12	0.73
Path from perceived disability to depression	0.66	0.10	0.001	0.46	0.87
Path from depression to suicidal ideation	0.48	0.22	0.029	0.05	0.91

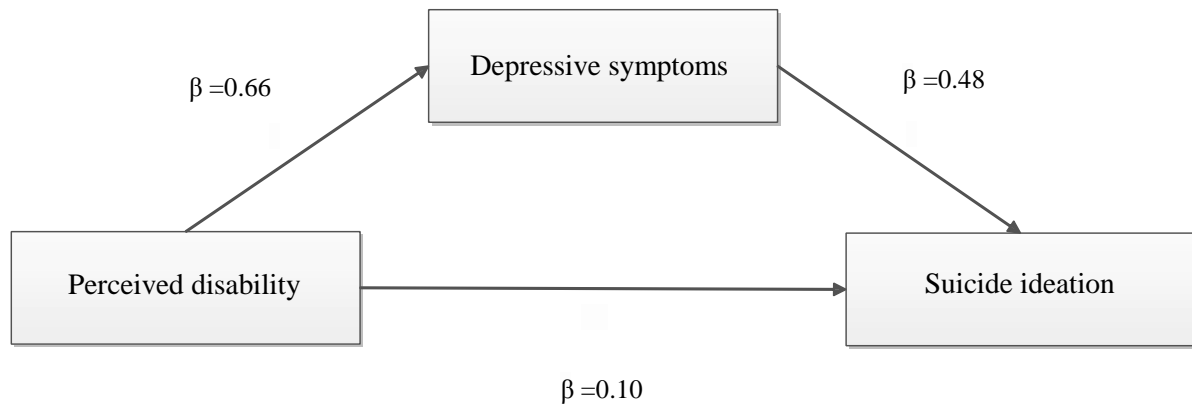


Figure 1. The mediating effect of depressive symptoms upon perceived disability and suicide ideation

In the unmediated model, the effect of perceived disability on suicide ideation was positive and significant ($\beta = 0.42$, $SE = 0.16$, $p=0.014$). This was reduced when the mediating effect of depressive symptoms was included in the analysis ($\beta = 0.10$, $SE = 0.11$, $p = 0.399$), accounting for approximately 32% of the original relationship between perceived disability and suicide ideation. Significant path coefficients were reported for both the path to the mediator variable ($\beta = 0.66$, $SE = 0.10$, $p = 0.001$) and from the mediator variable to suicide ideation ($\beta = 0.48$, $SE = 0.22$, $p = 0.029$). Accordingly, a complete mediation effect was observed.

Do depressive symptoms mediate the relationship between actual disability and suicide ideation?

Table III below displays the outcomes of the mediation analysis for disability and Figure 2 displays the hypothesised model.

Table III. Mediated relationship between depression, perceived disability and suicide ideation

	Path Estimate β	Standard Error SE	p value	Lower 95% Bootstrap Confidence Interval	Upper 95% Bootstrap Confidence Interval
Correlation between perceived disability and suicide ideation in the unmediated model	0.36	0.18	0.047	0.04	0.72
Correlation between perceived disability and suicide ideation in the mediated model	0.05	0.11	0.631	-0.13	0.28
Depression as mediator	0.31	0.12	NA	0.13	0.61
Path from perceived disability to depression	0.60	0.10	0.001	0.41	0.80
Path from depression to suicidal ideation	0.51	0.19	0.008	0.14	0.89

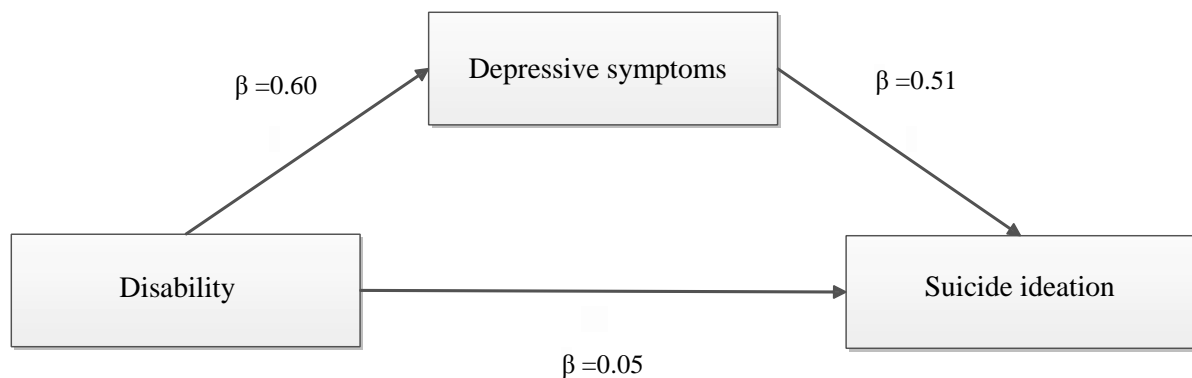


Figure 2. The mediating effect of depressive symptoms upon disability and suicide ideation

In the unmediated model, the effect of perceived disability on suicide ideation was positive and significant ($\beta = 0.36$, $SE = 0.18$, $p=0.047$). This was reduced when the mediating effect of depressive symptoms was included in the analysis ($\beta = 0.05$, $SE = 0.11$, $p = 0.631$), accounting for approximately 31% of the original relationship between perceived disability and suicide ideation. Significant path coefficients were reported for both the path

to the mediator variable ($\beta = 0.60$, $SE = 0.10$, $p = 0.001$) and from the mediator variable to suicide ideation ($\beta = 0.51$, $SE = 0.19$, $p = 0.008$). Accordingly, a complete mediation effect was observed.

Is any specific type of disability related to suicide ideation?

As distributions for disability measures were consistent with parametric assumptions, a series of independent-sample t-tests were carried out to identify whether high or low suicide ideation groups are associated with specific disability. As explained earlier, participants were categorised as either: no suicide ideation (a score of 0 on the BSS, $n = 49$); or suicide ideation (a score ≥ 1 on the BSS, $n = 26$).

When comparing differences between groups on the physical subscales of the MSIS-29 which measured *perceived* disability, significant differences were found for: ‘moving about indoors’, $t(73) = -1.90$, $p < .05$, no suicide ideation group ($M = 0.98$, $SD = 1.66$), suicide ideation group ($M = 3.69$, $SD = 1.29$); tremors, $t(73) = -1.74$, $p < .05$, no suicide ideation group ($M = 2.33$, $SD = 1.30$) suicide ideation group ($M = 2.92$, $SD = 1.62$); ‘taking longer to do things’ $t(73) = -1.80$, $p \leq .01$, no suicide ideation group ($M = 3.10$, $SD = 1.57$) and suicide ideation group ($M = 3.73$, $SD = 1.15$).

On the psychological subscales of the MSIS-29 significant differences were found between groups on: ‘problems sleeping’, $t(73) = -1.52$, $p < .05$, no suicide ideation group ($M = 2.00$, $SD = 1.24$) suicide ideation group ($M = 2.50$, $SD = 1.56$); ‘anxiety and tension’, $t(73) = -1.70$, $p \leq .01$, no suicide ideation group ($M = 2.16$, $SD = 1.26$), suicide ideation group ($M = 2.73$, $SD = 1.56$), and ‘feeling depressed’, $t(73) = -2.99$, $p < .01$, no suicide ideation group ($M = 1.69$, $SD = 2.54$), suicide ideation group ($M = 2.54$, $SD = 1.48$).

No significant differences were found between the no suicide ideation and suicide ideation groups when comparing types of actual disability based upon the GNDS.

Is there a sub-group of individuals who report suicide ideation with only a minimal or mild level of depressive symptoms?

Participants were split into those with a BSS score of zero versus above zero as described above, and a BDI score either above or below 19, below 19 indicating minimal or mild depressive symptoms (Beck, Steer & Brown, 1996). Twelve participants reported suicidal ideation in the presence of moderate or more marked depression, 14 reported suicidal ideation but were not depressed or had very mild symptoms, four reported no ideation in the presence of moderate or more marked depression and 45 were neither depressed or reported suicidal ideation. This suggests an absolute risk of suicidal ideation in none or mildly depressed participants of 0.24 (95% CI 0.13 to 0.35), which rises to 0.75 (95% CI 0.54 to 0.96) in their depressed counterparts. Thus just fewer than 25% of participants who were not depressed experienced some suicidal ideation. The relative risk ratio of suicidal ideation in those who were depressed was 3.16 (95% CI 1.85 to 5.41), suggesting that depressed participants were a little over three times more likely to experience suicidal ideation than those who had no or minimal depression.

Discussion

The present study investigated the relationship between three variables: disability, depression and suicide ideation in progressive MS. The main aim of the study was to explore the relationship between all three variables using a mediation model, including a measure of perceived and actual disability. The study also aimed to find out whether different types of disability were associated with suicide ideation and if there were a sub-group of participants who disclosed suicide ideation with only a minimal or mild level of depressive symptoms. Very little previous research has examined depression, suicide or the relationship between the two in progressive MS. Therefore the findings of this research provide a novel contribution to the literature.

The prevalence of suicidality was 35% which is slightly higher than the findings of Feinstein (2002) and Turner et al. (2006) who did not use a standardised suicide ideation measure. The overall mean total BDI-II score was found to be similar to that of participants in other MS studies for example Pujol et al. (2000). The observed scores on the MSIS-29 physical and psychological subscales were also found to be similar to previous studies on similar populations, for example Motl, Suh, and Weikert (2010); as were the GNDS scores for example Nicholl, Lincoln, Francis, and Stephan (2001).

Depressive symptoms were found to mediate the relationship between perceived disability and suicide ideation. This is a new finding and it is the first time it has been investigated in MS. It is consistent with the findings of Meltzer et al. (2012) who found that the relationship between limitations of daily living activities in adults from the general population and suicidality were mediated by depression. In the present study we have extended this to show that in MS, a direct relationship exists between actual disability and depressive symptoms, as well as perceived disability and suicide ideation. The latter finding is similar to the study by Turner et al. (2006) who also found a direct relationship between perceived disability and suicide ideation in a sample of veterans who had received services for MS in the United States of America. It seems that there is still a lack of research investigating the impact of perceived disability in MS despite Turk et al. (1995) advocating for its use in disability research generally. In the present study at least 30% of the direct relationship between perceived disability and suicide ideation was accounted for by depressive symptoms, highlighting the need to have an open discussion with patients about the degree to which they are distressed by their symptoms, as well as the actual impact of symptoms and the need to target interventions to alleviate distress and hence reduce the risk of suicide. For example, in a systematic review and meta-analysis of seven studies exploring the use of cognitive behavioural therapy (CBT) for depression in MS, Hind, Cotter, Thake,

Bradburn, Cooper, Isaac and House, (2014) found a medium size treatment effect for CBT when compared mainly with those who received 'standard care', were waiting list controls or received other supportive therapy.

Depressive symptoms were also found to mediate the relationship between actual disability and suicide ideation. Again, this is a new finding which has not been investigated in MS before. Consistent with the findings of Meltzer et al. (2012) depressive symptoms had an indirect effect upon the direct relationship between actual disability and suicide ideation in MS. In the present study, depressive symptoms accounted for at least 30% of the relationship. They are a modifiable contributory factor to suicide ideation and therefore need to be addressed. Finding a significant direct relationship between actual disability and depressive symptoms has mirrored the findings of several other studies in this population, most recently the study by Smith and Arnett (2013). The finding of a significant relationship between depressive symptoms and suicide ideation has added to the few studies in this area that have reported similar findings (Turner et al., 2006; Viner et al., 2014).

Based on the commonly used measure, the GNDS, no differences were found between individuals with and without suicide ideation in terms of types of actual disability. However, there were several differences for perceived disability based upon the MSIS-29 namely: 'moving about indoors', 'tremors', 'taking longer to do things' and 'difficulty doing things spontaneously' for the physical subscale; 'problems sleeping', 'anxiety and tension' and 'feeling depressed' for the psychological subscale. Whilst the psychological symptoms are clearly linked to suicide ideation through the mediating effect of depression, the physical symptoms may require greater attention from clinicians as potential risk factors. Tremors have been referred to as one of the most physically disabling manifestations of MS (Thompson et al., 2001) and our findings confirm that they are a source of particular distress that may be associated with suicide ideation. Previous studies addressing this issue have used

non-validated measures of disability and found that problems with mobility (Turner et al., 2006), bladder and bowel functioning (Turner et al., 2006; Viner et al., 2014) and communication and swallowing difficulties (Viner et al., 2014) were associated with suicide ideation. As there are few studies investigating the perceived impact of symptoms as risk factors for suicide ideation, further investigation is required in this area.

Finally, the present study identified that there was a sub-group of individuals who reported suicide ideation with only a minimal or mild level of depressive symptoms. As the inclusion of the mediated variable between disability and suicide ideation meant that the path estimate reduced to not quite zero, for both perceived and actual disability, it could be suggested that the residual amount accounted for the sub-group of participants who reported suicide ideation but only a minimal or mild level of depression. With some cautiousness, this finding could support the notion of 'rational' suicide, wherein, as suggested by Onkay-Ho (2014), suicide might be seen as a way of managing the condition, possibly to gain a sense of mastery (Siegel & Meyer, 1999). Findings of the present study could also be in agreement with Gaskill et al. (2011), who suggested that perceived loss of control is the major disease-related variable associated with suicide ideation in MS. However, it is also important to note that although participants experiencing active psychosis or any other degenerative neurological conditions were excluded from the study, people with other comorbid psychiatric disorders such as anxiety were not excluded and these conditions could be potential reasons for suicide ideation, as could other factors such as substance misuse or psychosocial stressors. Further research is therefore required in this area.

The present study has identified several important factors which require consideration in the context of clinical management of MS. The relationship found between all three variables (disability, depressive symptoms and suicide ideation) suggests that it is particularly important to screen for depression in those with more severe disability. Depression is a

modifiable factor in MS which can be treated effectively with antidepressants (Arciniegas & Anderson, 2002) or psychological therapy and if not ameliorated can lead to suicidality (Paparrigopoulos et al., 2010; Raskind, 2008). Additionally, the findings of this study have highlighted that individuals with suicide ideation may not be detected via depression screening, an important implication for clinicians when screening in the future. It is notable that suicidal behaviour in the general population has been conceptualised as existing on a continuum from suicide ideation, to formulation of a plan, to attempted or completed suicide (Kessler, Berglund, Borges, Nock & Wang, 2005). Thus clinicians need to feel confident to ask patients whether they are experiencing any thoughts about harming themselves and also remain aware of the types of perceived disabilities associated with suicide ideation.

Limitations

All participants in the present study were attending MS outpatient clinics for review appointments and/or rehabilitation support. There may thus be a sample bias as those attending clinics could be either suffering more symptoms/distress or in receipt of services that are reducing symptoms/distress. Also, previous research has suggested that higher levels of suicide ideation are present within the first year after diagnosis (Fredrikson et al., 2002), possibly continuing into the following four years (Bronnum-Hansen et al., 2005), whereas no participants in the present study had been diagnosed for less than five years. Information was not obtained about the number of potential participants approached, declined or ineligible. Rates of depressive symptoms and suicide ideation in this sample group could therefore be under representative of the whole MS population. Furthermore, some participants ($n = 15$) were taking antidepressants which could have reduced depressive symptoms and suicide ideation. Finally, the MSIS-29 and GNDS did not measure equivalent items and thus the differences in perceived and actual disability could reflect the range of items, although items such as tremors and taking longer to do things could be considered to be implicit in GNDS

items measuring problems using arms and hands. Unfortunately there is no available validated measure that includes both viewpoints.

Conclusion

Suicide ideation in MS is potentially a treatable cause of both morbidity and mortality (Feinstein, 1997; 2002). Given that suicide ideation is associated with an increased risk for making plans, attempting suicide and completing suicide (Kessler et al., 2005; Nock et al., 2008), regular screening in clinical practice alongside further research in this area is imperative, especially taking into consideration the impact of perceived disability and the concept of 'rational' suicide. For those who disclose minimal or mild levels of depression it cannot be assumed that there is no suicide risk.

Acknowledgements

Special thanks to those who participated in this research and the staff team from the West Midlands Rehabilitation Service who recruited participants.

References

- Anhoque, C.F., Domingues, S.C.A., Carvalho, T., Teixeira, A.L., & Domingues, R.B., 2011. Anxiety and depressive symptoms in clinically isolated syndrome and multiple sclerosis. *Arquivos de neuro-psiquiatria*. 69(6), 882-886. doi: 10.1590/S0004-282X2011000700006
- Arciniegas, D.B., & Anderson, C.A., 2002. Suicide in neurologic illness. Current treatment options in neurology. 4(6), 457-468.
- Arnett, P.A., Barwick, F.H., & Beeney, J.E., 2008. Depression in multiple sclerosis: review and theoretical proposal. *Journal of the International Neuropsychological Society*. 14(05), 691-724. doi: 10.1017/S1355617708081174
- Ayuso-Mateos, Jose Luis, Vázquez-Barquero, Jose Luis, Dowrick, Christopher, Lehtinen, Ville, Dalgard, Odd Steffen, Casey, Patricia, . . . Dunn, Graham., 2001. Depressive disorders in Europe: prevalence figures from the ODIN study. *The British Journal of Psychiatry*. 179(4), 308-316.
- Beal, C.C., Stuifbergen, A.K., & Brown, A., 2007. Depression in multiple sclerosis: a longitudinal analysis. *Archives of psychiatric nursing*. 21(4), 181-191. doi: 10.1016/j.apnu.2007.02.008
- Beck, A.T., & Steer, R.A., 1993. Beck Scale for Suicide Ideation. United States of America: Pearson.
- Beck, A.T., Steer, R.A., & Brown, G.K., 1996. Beck Depression Inventory-II (2nd ed.). United States of America: Pearson.
- Bergner, M., Bobbitt, R. A., Carter, W.B., Gilson, B.S. 1981. The Sickness Impact Profile: development and final revision of a health status measure. *Medical care* 19(8): 787-805.
- Berman, A.L., & Samuel, L., 1993. Suicide among people with multiple sclerosis. *Neurorehabilitation and Neural Repair*. 7(2), 53-62. doi: 10.1177/136140969300700202
- Bronnum-Hansen, H., Stenager, E., Stenager, E.N., & Kock-Henriksen, N., 2005. Suicide among Danes with multiple sclerosis. *Journal of Neurology, Neuropsychiatry and Psychiatry*. 76, 1457-1459. doi: 10.1136/jnnp.2004.056747
- Caine, E. D., & Schwid, S. R., 2002. Multiple sclerosis, depression, and the risk of suicide. *Neurology*. 59(5), 662-663. doi: 10.1212/WNL.59.5.662
- Carson, A.J., Best, S., Warlow, C., & Sharpe, M., 2000. Suicidal ideation among outpatients at general neurology clinics: prospective study. *BMJ*, 320(7245), 1311-1312. doi: 10.1136/bmj.320.7245.1311
- Chwastiak, L., Ehde, D.M. , Gibbons, L.E., Sullivan, M., Bowen, J.D., & Kraft, G.H., 2002. Depressive symptoms and severity of illness in multiple sclerosis: Epidemiological study of a large community sample. *American Journal of Psychiatry*. 159, 1862-1868. doi: 10.1176/appi.ajp.159.11.1862
- Crane, C., Shah, D., Barnhofer, T., & Holmes, E.A., 2012. Suicidal imagery in a previously depressed community sample. *Clinical Psychology & Psychotherapy*. 19(1), 57-69. doi: 10.1002/cpp.741
- da Silva, A.M., Vilhena, E., Lopes, A., Santos, E., Gonçalves, M.A., Pinto, C., . . . Cavaco, S., 2011. Depression and anxiety in a Portuguese MS population: associations with physical disability and severity of disease. *Journal of the neurological sciences*. 306(1), 66-70. doi: 10.1016/j.jns.2011.03.042
- Dalgas, U., Stenager, E., & Sloth, M., 2014. The effect of exercise on depressive symptoms in multiple sclerosis based on a meta-analysis and critical review of the literature. *European Journal of Neurology*. doi: 10.1111/ene.12576

- Dennis, M., Baillon, S., Brugha, T., Lindesay, J., Stewart, R., & Meltzer, H. 2009. The influence of limitation in activity of daily living and physical health on suicidal ideation: results from a population survey of Great Britain. *Social Psychiatry and Psychiatric Epidemiology*. 44(8), 608-613.
- Faber, R.A., 2003. Suicide in neurological disorders. *Neuroepidemiology*. 22(2), 103-105. doi: 10.1159/000068751
- Feinstein, A., 1997. Multiple sclerosis, depression, and suicide. Clinicians should pay more attention to psychopathology. *British Medical Journal*. 315(7110), 691-692.
- Feinstein, A., 2002. An examination of suicidal intent in patients with multiple sclerosis. *Neurology*. 59(5), 674-678. doi: 10.1212/WNL.59.5.674
- Feinstein, A., 2004. The neuropsychiatry of multiple sclerosis. *Canadian Journal of Psychiatry*. 49, 157-163.
- Feinstein, A., 2007. *The Clinical Neuropsychiatry of Multiple Sclerosis*. Cambridge: Cambridge University Press.
- Fredrikson, S., Cheng, Q., Jiang, G.X., & Wasserman, D. 2002. Elevated suicide risk among patients with multiple sclerosis in Sweden. *Neuroepidemiology*. 22(2), 146-152. doi: 10.1159/000068746
- Freeman, J.A., Thompson, A.J., Fitzpatrick, R., Hutchinson, M., Miltenburger, C., Beckmann, K., . . . Pozzilli, C., 2001. Interferon- β 1b in the treatment of secondary progressive MS Impact on quality of life. *Neurology*, 57(10), 1870-1875.
- Gaskill, A., Foley, F.W., Kolzet, J., & Picone, M.A., 2011. Suicidal thinking in multiple sclerosis. *Disability and Rehabilitation*. 33(17-18), 1528-1536. doi: 10.3109/09638288.2010.533813
- Gay, M.C., Vrignaud, P., Garitte, C., & Meunier, C., 2010. Predictors of depression in multiple sclerosis patients. *Acta Neurologica Scandinavica*. 121(3), 161-170. doi: 10.1111/j.1600-0404.2009.01232.x
- Giannini, M. J., Bergmark, B., Kreshover, S., Elias, E., Plummer, C., & O'Keefe, E., 2010. Understanding suicide and disability through three major disabling conditions: Intellectual disability, spinal cord injury, and multiple sclerosis. *Disability and Health Journal*. 3(2), 74-78. doi: 10.1016/j.dhjo.2009.09.001
- Hardle, W., & Marron, J.S., 1991. Bootstrap simultaneous error bars for nonparametric regression. *The Annals of Statistics*. 778-796. doi: 10.1214/aos/1176348120
- Harwood, R.H. & Ebrahim, S., 1995. *Manual of the London Handicap Scale*. Nottingham: University of Nottingham.
- Hind, D., Cotter, J., Thake, A., Bradburn, M., Cooper, C., Isaac, C., & House, A., 2014. Cognitive behavioural therapy for the treatment of depression in people with multiple sclerosis: a systematic review and meta-analysis. *BMC Psychiatry*. 14:5. doi: 10.1186/1471-244X-14-5
- Hobart, J., Lamping, D., Fitzpatrick, R., Riazi, A., & Thompson, A., 2001. The multiple sclerosis impact scale (MSIS-29). A new patient-based outcome measure. *Brain*. 124, 962-973.
- Hooper, K. 2013. *Managing Progressive Multiple Sclerosis*. New York: National Multiple Sclerosis Society.
- Kessler, R.C., Berglund, P., Borges, G., Nock, M., & Wang, P.S. 2005. Trends in suicide ideation, plans, gestures, and attempts in the United States, 1990-1992 to 2001-2003. *Jama*. 293(20), 2487-2495. doi: 10.1001/jama.293.20.2487.
- Kroenke, K., & Spitzer, R.L., 2002. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatric Annals*. 32(9), 1-7.

- Kuhlman, T. 2013. Relapsing–remitting and primary progressive MS have the same cause(s): the neuropathologist’s view: 2. *Multiple Sclerosis Journal*. 19(3), 268-269. doi: 10.1177/1352458513476563
- Kurtzke, J.F. 1983. Rating neurologic impairment in multiple sclerosis an expanded disability status scale (EDSS). *Neurology*. 33(11), 1444-1444.
- Larsson, U.E., & Mattsson, E., 2001. Perceived disability and observed functional limitations in obese women. *International Journal of Obesity and Related Metabolic Disorders*, 25(11), 1705-1712. doi: 10.1038/sj.ijo.0801805
- Lester, K., Stepleman, L., & Hughes, M., 2007. The association of illness severity, self-reported cognitive impairment, and perceived illness management with depression and anxiety in a multiple sclerosis clinic population. *Journal of Behavioral Medicine*. 30(2), 177-186. doi: 10.1007/s10865-007-9095-6
- Manea, L., Gilbody, S., & McMillan, D., 2015. A diagnostic meta-analysis of the Patient Health Questionnaire-9 (PHQ-9) algorithm scoring method as a screen for depression. *General hospital psychiatry*. 37(1), 67-75.
- Meltzer, H., Brugha, T., Dennis, M.S., Hassiotis, A., Jenkins, R., McManus, S., . . . Bebbington, P., 2012. The influence of disability on suicidal behaviour. *ALTER-European Journal of Disability Research*. 6(1), 1-12. doi: 10.1016/j.alter.2011.11.004
- Mohr, D.C., Goodkin, D.E., Gatto, N., & Van Der Wende, J., 1997. Depression, coping and level of neurological impairment in multiple sclerosis. *Multiple sclerosis*. 3(4), 254-258. doi: 10.1177/13524585970030040
- Moore, D.S., & McCabe, G.P., 2005. *Introduction to the Practice of Statistics*: WH Freeman/Times Books/Henry Holt & Co.
- Motl, R.W., Suh, Y., & Weikert, M., 2010. Symptom cluster and quality of life in multiple sclerosis. *Journal of Pain and Symptom Management*. 39(6), 1025-1032. doi: 10.1016/j.jpainsymman.2009.11.312
- Nicholl, C.R., Lincoln, N.B., Francis, V.M., & Stephan, T.F., 2001. Assessment of emotional problems in people with multiple sclerosis. *Clinical Rehabilitation*. 15(6), 657-668. doi: 10.1191/0269215501cr427oa
- Nock, M.K., Borges, G., Bromet, E.J., Alonso, J., Angermeyer, M., Beautrais, A., . . . Gluzman, S., 2008. Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. *The British Journal of Psychiatry*. 192(2), 98-105. doi: 10.1192/bjp.bp.107.040113
- Onkay-Ho, A., 2014. Suicide: rationality and responsibility for life. *Canadian Journal of Psychiatry*. 59(3), 141-147
- Paparrigopoulos, T., Ferentinos, P., Kouzoupis, A., Koutsis, G., & Papadimitriou, G.N., 2010. The neuropsychiatry of multiple sclerosis: focus on disorders of mood, affect and behaviour. *International Review of Psychiatry*. 22(1), 14-21. doi: 10.3109/09540261003589323
- Patten, S.B., Beck, C.A., Williams, J.V.A., Barbui, C., & Metz, L.M., 2003. Major depression in multiple sclerosis. *Neurology*. 61, 1524-1527. doi: 10.1212/01.WNL.0000095964.34294.B4
- Polman, C.H., Reingold, S.C., Banwell, B., Clanet, M., Cohen, J.A., Filippi, M., . . . Kappos, L., 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Annals of Neurology*, 69(2), 292-302.
- Pompili, M., Forte, A., Palermo, M., Stefani, H., Lamis, D. A., Serafini, G., . . . Girardi, P., 2012. Suicide risk in multiple sclerosis: A systematic review of current literature. *Journal of Psychosomatic Research*. 73(6), 411-417. doi: 10.1016/j.psychores.2012.09.011

- Preacher, K.J., & Hayes, A.F., 2008. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behaviour Research Methods*, 40(3), 879 - 891. doi: doi:10.3758/BRM.40.3.879
- Preacher, K.J., & Hayes, A.F., 2004. SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, & Computers*. 36(4), 717-731. doi: 10.3758/BF03206553
- Pugliatti, M., Rosati, G., Carton, H., Riise, T., Drulovic, J., Vécsei, L., & Milanov, I. 2006. The epidemiology of multiple sclerosis in Europe. *European Journal of Neurology*. 13(7), 700-722. doi: 10.1111/j.1468-1331.2006.01342.x
- Pujol, J., Bello, J., Deus, J., Cardoner, N., Martí-Vilalta, J.L., & Capdevila, A., 2000. Beck Depression Inventory factors related to demyelinating lesions of the left arcuate fasciculus region. *Psychiatry Research: Neuroimaging*. 99(3), 151-159. doi: 10.1016/S0925-4927(00)00061-5
- Raskind, M.A., 2008. Diagnosis and treatment of depression comorbid with neurologic disorders. *The American Journal of Medicine*. 121(11), S28-S37. doi: 10.1016/j.amjmed.2008.09.011
- Sadovnick, A.D., Eisen, K., Ebers, G.C., & Paty, D.W., 1991. Cause of death in patients attending multiple sclerosis clinics. *Neurology*. 41(8), 1193-1193. doi: 10.1212/WNL.41.8.1193
- Sarisoy, G., Terzi, M., Gümüş, K., & Pazvantoğlu, O., 2013. Psychiatric symptoms in patients with multiple sclerosis. *General Hospital Psychiatry*. 35(2), 134-140. doi: 10.1016/j.genhosppsy.2012.10.011
- Sharrack, B., & Hughes, R.A.C., 1999. The Guy's Neurological Disability Scale (GNDS): a new disability measure for multiple sclerosis. *Multiple Sclerosis*. 5, 223-233.
- Siegel, K., & Meyer, I.H., 1999. Hope and resilience in suicide ideation and behavior of gay and bisexual men following notification of HIV infection. *AIDS Education and Prevention*. 11, 53-64.
- Siebert, R., & Abernethy, D., 2005. Depression in multiple sclerosis: A review. *Journal of Neurology, Neurosurgery & Psychiatry*. 76(4), 469-475. doi: 10.1136/jnnp.2004.054635
- Smith, M.M., & Arnett, P.A., 2013. Perfectionism and physical disability predict depression in multiple sclerosis. *Journal of Psychosomatic Research*. 75(2), 187-189. doi: 0.1016/j.jpsychores.2013.06.001
- Soldán, M.M.P., Novotna, M., Zeid, N.A., Kale, N., Tutuncu, M., Crusan, D.J., . . . Pirko, I. 2015. Relapses and disability accumulation in progressive multiple sclerosis. *Neurology*. 84(1), 81-88.
- Stenager, E.N., Koch-Henriksen, N., & Stenager, E., 1996. Risk factors for suicide in multiple sclerosis. *Psychotherapy and Psychosomatics*. 65(2), 86-90. doi: 10.1159/000289052
- Thompson, A.J., 2001. Symptomatic management and rehabilitation in multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry*. 71(supplement 2), ii22-ii27.
- Turk, D.C., Okifuji, A., & Scharff, L., 1995. Chronic pain and depression: role of perceived impact and perceived control in different age cohorts. *Pain*. 61(1), 93-101. doi: 10.1016/0304-3959(94)00167-D
- Turner, A.P., Williams, R.M., Bowen, J.D., Kivlahan, D.R., & Haselkorn, J.K., 2006. Suicidal Ideation in Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation*, 87(8), 1073-1078. doi: 10.1016/j.apmr.2006.04.021
- Tutuncu, M., Tang, J., Zeid, N.A., Kale, N., Crusan, D.J., Atkinson, E.J., . . . Keegan, B.M. 2012. Onset of progressive phase is an age-dependent clinical milestone in multiple

- sclerosis. *Multiple Sclerosis Journal*. 1352458512451510. doi: 10.1177/1352458512451510
- Viner, R., Patten, S.B., Berzins, S., Bulloch, A.G.M., & Fiest, K.M., 2014. Prevalence and risk factors for suicidal ideation in a multiple sclerosis population. *Journal of psychosomatic research*. 76(4), 312-316. doi: 10.1016/j.jpsychores.2013.12.010
- Werth, J.L., & Cobia, D.C., 1995. Empirically based criteria for rational suicide: A survey of psychotherapists. *Suicide and Life-Threatening Behavior*. 25(2), 231-240. doi: 10.1111/j.1943-278X.1995.tb00922.x
- World Health Organization., 2002. *A Common Language for Functioning, Disability and Health ICF*. Geneva.