# Psychological interventions for depression in people with multiple sclerosis

## Abstract

A systematic review was conducted to investigate the effectiveness of published trials that used psychological interventions to decrease depression in people with multiple sclerosis. A search of electronic databases (PsycARTICLES, Medline, CINAHL and Science Direct) was conducted as well as hand searching the reference sections of relevant literature and reviews. A final total of 11 studies were included, using a range of methods e.g. cognitive behaviour therapy (n = 7), mindfulness based stress reduction (n = 1), a general chronic illness group (n = 1), motivational interviewing (n = 1) and relaxation (n = 1). Psychological interventions such as cognitive behaviour therapy, mindfulness-based stress reduction and motivational interviewing can have a beneficial effect on the symptoms of depression in people with MS; however more rigorous research needs to be conducted in this area.  The results highlight the need for further research into the less common types of psychological intervention, and in particular randomised controlled trials which employ an active comparison group.

## Background

Multiple sclerosis (MS) is a neurological condition which affects the central nervous system. It can lead to a large variety of distressing symptoms, such as fatigue, tremor, cognitive impairment, vision and balance problems, bladder issues and weakness (World Health Organisation, 2008).

Depression is the most common type of psychological distress present in people with MS (Sa, 2008). Estimates of the prevalence of depression can vary, however it appears to be

around 50% (Benito-León, Manuel Morales, Rivera-Navarro, & Mitchell, 2003). Such high

figures have been attributed to a wide variety of issues; regarding the illness itself, the

unpredictable nature of the disease progression, the lack of a known cure, as well as the wide

range of often unpleasant symptoms often present in the illness (Rigby, Thornton, & Young,

2008).

Because medication for depression is not always appropriate (Forman & Lincoln,

2010), a sizeable proportion of the research dedicated to depression in people with MS has

had a psychological emphasis. A Cochrane review (Thomas, Thomas, Hillier, Galvin, &

Baker, 2006) looked at the efficacy of psychological interventions for depression and found

that CBT could be beneficial in treating depression in this population, however were unable

to draw definite conclusions. In another review, Hind et al. (2014) found CBT to provide

modest benefits for depression in people with MS.  However, CBT does not always work for

everyone, and thus other psychological interventions should be compared to assess which of

these various options appear to be the most effective for people with MS (Mohr et al., 2001).

The aim of this current review therefore is to build on recent appraisal of the

literature, but to also include other types of psychological intervention.

## Method

### Inclusion and exclusion criteria

The following inclusion criteria were identified: the report was published in English

and published in a peer-reviewed journal. The study had to be quantitative in design and

analysis, and had to have a significant psychological element. Participants had to be 18 years

old or over. Only randomised controlled trials (RCTs) were considered for review. Papers

were excluded if participants in the study were family members or carers reporting on the experience of the person living with MS, or if the intervention did not measure depression.

**Search strategy**

Relevant papers were identified by searching Medline, PsycArticles, CINAHL, Web of Science and Science Direct databases in April 2014. The databases were searched from 2004-2014, giving a date range of just over 10 years. The lead author can be contacted for a comprehensive list of search terms used as well as the full search strategy employed. The search returned a total of 2687 studies from all databases. The journal article titles were then read as well as abstracts unless it was immediately clear that the article was irrelevant to the review. This left a possible 51 articles for inclusion. The remaining articles were then read in more depth, applying the inclusion and exclusion criteria, to leave a final 11 studies.

## Results

After applying the inclusion and exclusion criteria, a total of 11 studies were deemed suitable for inclusion in the review (Table 1).

Table 1
Study Characteristics

| Authors, (year), country | N Gender % (Male: M; Female:F) | Mean Age (years) Range | Intervention | Mean Disease Duration (years) EDSS | Study Design Comparator | Outcome measures (all outcomes) |
|---|---|---|---|---|---|---|
| Artemiadis et al. (2012) Greece | 61 M: 20 F: 80 | 39.7 Not reported | RB and PMR exercises to be practiced at home every day 8 weeks | 7 <4 | RCT TAU with weekly phone calls | Depression: BDI; Stress: PSS; HLC: HLC; Anxiety: STAI; Symptoms of MS: Diary. |
| Barlow et al. (2009) UK | 216 M: 27 F: 73 | 51.1 Not reported | Six, weekly, 2hr sessions of Chronic Disease Self-Management Course taught by lay persons | 11.95 Not reported | RCT Wait-list control plus comparison group | Self-efficacy: LS-ES, SMSE. Impact of MS:MSIS-29. Pain and fatigue: VAS. Anxiety and Depression: HADS. Self-management: scales designed for CDSMC. |
| Bombardier et al. (2013) USA | 92 M:27 F:73 | 48.4 29-64 | Initial in-person MI based counseling session to increase physical activity, 7x phone sessions, final in-person session. | 10.6 <5.5 | RCT Wait-list control | Depression: HAM-D, SCID, SCL-20. Affect: PANAS. Side-effects: MS-related checklist |
| Cooper et al. (2011) UK | 24 M: 25 F: 75 | 45 31-57 | 8, weekly, 50m computerised CBT sessions | Not reported 4.2 | Pilot RCT TAU | Depression: BDI, PHQ. Anxiety: GAD-7, PHQ. QOL: MSIS-29, SF-36, |
| Forman & Lincoln (2010) UK | 40 M: 26.5 F: 73.5 | 47.7 25-68 | 6 x 2.5h sessions over 12 weeks- group cognitive behavioural and psycho education | 9.7 Not reported | Pilot RCT Wait-list control | Depression & Anxiety: HADS. General health: GHQ, SF-36. MS: MSIS, MSSES,. |

| Authors, (year), country | N Gender % (Male: M; Female:F) | Mean Age (years) Range | Intervention | Mean Disease Duration (years) EDSS | Study Design Comparator | Outcome measures (Primary, secondary) |
|---|---|---|---|---|---|---|
| Graziano et al. (2014) Italy | 82 M: 36 F: 64 | 40.5 Not reported | 4 x 2h sessions of group-based CBT over 2 months then 5th follow-up at 6m. | 7.9 1-5.5 | RCT Information | MS: MSQOL-54. Affect: PANAS. Depression: CES-D. Identity: IMS |
| Grossman et al. (2010) Switzerland | 150 M: 21 F: 79 | 47.9 | 5, weekly, 2.5h classes following MBSR | 8.7 | RCT TAU | HRQOL: PQOLC, HAQUAMS. Depression: CES-D. Fatigue: MFIS. Anxiety: STAI. |
| Lincoln et al. (2011) UK | 151 M/ F: Not recorded | 46 | 6 x 2.5h sessions over 12 weeks- group cognitive behavioural and psycho education | 9.9 Not reported | RCT Wait-list control | Depression: BDI, GHQ-012. QOL: MSIS, EuroQol. Adjustment: MSSE. Impairment: GNDS. |
| Mohr et al. (2005) USA | 172 M:23 F: 77 | 47.9 Not reported | 16, weekly, 50m sessions of telephone CBT course. | 11.2 Not reported | RCT Telephone SEFT | Depression: SCID, HAM-D, BDI-II. Affect: PANAS |
| Moss-Morris et al. (2012) UK/ New Zealand | 40 M:20 F:80 | 40.8 Not reported | 8, weekly, 25-50m sessions of MS specific computerised CBT plus 3 phone support sessions | 18.8 | Pilot RCT Wait-list control | Fatigue: FS; MFIS. Anxiety & depression: HADS. QOL: EuroQOL. |
| Rigby et al. (2008) UK | 147 M: 37 F: 63 | Not reported Not reported | 3, 90m cognitive behavioural group sessions plus info book | 9 6 (median) | RCT 1 group social discussions. 1 group info only | MS: MSSE. Anxiety & depression: HADS. Hardiness: DRI |

BDI: Beck Depression Inventory; BDI-II: Beck Depression Inventory Second Edition; CBT: Cognitive Behaviour Therapy; CDSMC : Chronic Disease Self-Management Course; CES-D: Centre for Epidemiologic Studies Depression Scale; DRI: Dispositional Resilience Index; EDSS: Expanded Disability Status Scale; FS: Fatigue Scale; GAD: Generalised Anxiety Disorder; GHQ-12: General Health Questionnaire (12 point scale); HADS: Hospital Anxiety and

Depression Scale; GNDS: Guy's Neurological Disability Scale; HAM-D: Hamilton Depression Rating Scale; HAQUAMS: Hamburg Quality of Life Questionnaire in Multiple Sclerosis; HLC: Health Locus of Control; HRQOL: Health Related Quality of Life; IMS: Identity Motives Scale; LS-ES: Liverpool Self-Efficacy Scale; MBSR: Mindfulness-based Stress Reduction; MFIS: Modified Fatigue Impact Scale; MI: Motivational Interviewing; MSIS-29: Multiple Sclerosis Impact Scale; MSQOL-59- Multiple Sclerosis Quality of Life; MSSES: Multiple Sclerosis Self-efficacy Scale; PANAS: Positive and Negative Affect Scale; PHQ-9: Patient Health Questionnaire; PMR: Progressive Muscle Relaxation; PQOLC: Profile of Health Related Quality of Life; PSS: Perceived Stress Scale; QOL: Quality of Life; RB: Relaxation breathing; SCID: Structured Clinical Interview for DSM Disorders; SCL-20: The Hopkins Symptoms Checklist; SEFT: Supportive Emotion-focused therapy; SESA: Scale for the Evaluation of Self-Acceptance; SMSE: SF-36: SF-36; Medical Outcome Study Short Form 36; SPSI-R: Social Problem Solving Inventory Revised; STAI: Spielberger Trait Anxiety Inventory; TAU: Treatment as Usual; VAS: Visual Analogue Scales.

**Study characteristics**

The studies were conducted in the UK ($n$ = 6), USA ($n$ = 2), Greece ($n$ = 1), Italy ($n$ = 1), Switzerland ($n$ = 1). Of the 11 RCTs included in this review, three were pilot RCTs. Only three studies reported using diagnostic criteria for MS during recruitment. The participant numbers ranged from 24 (Cooper et al., 2011) to 216 (Barlow, Turner, Edwards, & Gilchrist, 2009).

**Participant characteristics**

1175 participants took part in the 11 studies; the mean age of participants, where reported, was 46.81 years ($N$ = 1072). The mean time that participants had lived with MS was 10.47 years, with a range of seven years (Artemiadis et al, 2012) to 18.8 years (Mohr et al., 2005).

**Intervention characteristics**

The studies used a variety of psychological interventions: telephone based CBT (Mohr et al., 2005), group CBT (Forman & Lincoln, 2010; Graziano et al., 2014; Lincoln et al., Rigby et al., 2008) online CBT (Cooper et al., 2011; Moss-Morris et al., 2012), Mindfulness Based Stress Reduction (Grossman et al., 2010), a support and psycho education group for people with chronic illness (Barlow et al., 2009), motivational interviewing (Bombardier et al., 2013) and relaxation (Artemiadis et al., 2012). Only four of the trials had MS specific components in the interventions that were delivered (Forman & Lincoln, 2010; Graziano et al., 2014; Lincoln et al., 2011; Moss-Morris et al., 2012). One study had group members who were comprised of people with a range of other chronic illnesses (Barlow et al., 2009).

**Quality Appraisal**

Using the QATQSD (Effective Public Health Practice Project 1998), only three of the 11 studies were given a global rating of 'Strong' (Grossman et al., 2010; Lincoln et al., 2011; Mohr et al. 2005), two were 'Moderate' (Bombardier et al., 2013; Rigby et al., 2008), and the remaining six were classed as 'Weak' study design. None of the studies adequately reported both whether the participants were fully aware of the research question, and whether outcome assessors were blinded to what arm the participants were assigned to. This meant that none of the studies reviewed here could be given a 'Strong' rating in the 'blinding' category of the tool.

**Outcomes**

One study did not provide detailed inferential statistics (Cooper et al., 2011) however reported a drop in depression score on the BDI to 18 for the active arm compared to 24.1 for the treatment as usual (TAU) control group, which is still above clinical significance. Four studies did not report statistically significant differences in reduction of depression between intervention and control groups (Artemiadis et al., 2012; Barlow et al., 2009; Graziano et al., 2014; Rigby et al., 2008) with the remaining six reporting statistically significant results. Of the different types of intervention, the general chronic illness support group, relaxation CDs, and three of the eight CBT interventions did not provide significant reductions in depressive symptoms. Four of the eight CBT interventions reported statistically significant results (Forman & Lincoln, 2010; Lincoln et al., 2011; Moss-Morris et al., 2012), as did three of the six group therapy interventions (Forman & Lincoln, 2010; Grossman et al., 2010; Lincoln et al., 2011). Of those studies which reported effect sizes, one reported a large effect size regarding change in scores on the depression measures used from baseline to post treatment in the treatment group (Bombardier et al., 2013), two reported a medium effect size (Artemiadis et al., 2012; Grossman et al., 2010) and one a small effect size (Barlow et al,

2009). The medium effect size was reduced to a small effect size at follow up in one study (Grossman et al. 2010).

## Discussion

This review indicates that seven of the 11 studies reported significant reductions in depression in the treatment arm compared to the control. In the most commonly used intervention (CBT), 62.5% of the studies reported reductions. Of the six studies that reported effect sizes, 67% reported a medium effect size in reduction of depression scores compared to the control group. The most commonly used active treatment was CBT, which was used in seven of the 11 studies. Of these studies, five reported significant reductions in depression post treatment.

### Methodological issues

Many limitations in the studies were evident. In the majority of studies, the comparison group was treatment as usual, or a wait-list control group and so the specificity of the treatment arm was not being tested. This runs the risk of performance bias as there may be many effects of attending a group or completing a programme such as those reviewed here. A comparison intervention in which the control group is also receiving a similar amount of attention or social support from other group members would be far more advantageous.

### Limitations of the study

Only 11 suitable studies were retrieved during the search which indicates that there is a lack of research internationally on depression in people with MS. This is concerning particularly given the inconsistent findings regarding the effectiveness of CBT interventions, and also that there is such a wide range of other treatment options that need to be tested in controlled studies.

**Need for further research.**

Future research regarding the use of online CBT courses for the reduction of depressive symptoms should take into account the difficulties reported here, as all the studies reported low compliance rates and issues with participants completing the intervention due to lack of flexibility.

Current UK National Institute for Health and Care Excellence (NICE, 2009) guidelines for people with mild to moderate depression and a chronic physical illness recommend group based peer support such as that conducted by Barlow et al (2009), structured physical activity, computerised CBT (Cooper et al., 2011) or guided CBT based self-help. For those with moderate depression, group CBT, individual CBT or behavioural couples therapy are recommended if the individual has a partner and if their physical and psychological difficulties are affecting the relationship. It is interesting to note that of this latter recommendation that no such study was identified during this review. Some of the study designs reported here such as MBSR (Grossman et al., 2010), and telephone CBT (Mohr et al., 2005) yielded promising results regarding reducing depression, however are not currently included in these guidelines. Further research is therefore needed in these areas to strengthen the evidence base regarding these interventions as they may prove to be useful methods for treating depression in those with MS.

## Conclusion

Treating depression in people with MS by using psychological interventions can in some circumstances significantly reduce symptoms when compared to control groups, however there are several methodological limitations in the studies reviewed here. More research needs to be done to clarify the conflicting results. In particular, there is a need for more RCTs that have an active control, as well as studies with participants that are selected

from a more representative population in order to make the results of the study more easily generalisable to the wider population who are living with MS. Specifically, interventions using CBT, MBSR-based treatment components, and increased physical activity through Motivational Interviewing techniques appear to significantly reduce depression in this population, however more research needs to be conducted and by using more rigorous methodological study designs and by selecting participants by using more representative methods.

## References

**\* Denotes study included in review**

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