Abstract

Objective: To review the evidence for the effectiveness of telephone-psychotherapy on psychological outcomes in people with Multiple Sclerosis (MS).

Methods: We conducted a systematic search of EMBASE, PsycINFO, PsycARTICLES, MEDLINE, CINAHL, Web of Science, and hand-searched relevant journals to identify randomised controlled trials (RCTs) that evaluated the effectiveness of telephone-psychotherapy on psychological outcomes in people with MS (last search completed on 1st October 2015). The methodological quality of each included trial was assessed, based on a standardised list of methodological criteria. Where available, data were extracted and combined in meta-analysis to compute effect size estimates.

Results: Eleven RCTs and 1104 participants were identified. Meta-analysis found a moderate effect of the intervention on depression (SMD of 0.47 (95% CI of 0.21 to 0.73)). Meta-analysis also found small to moderate short-term effects of the intervention on fatigue, quality of life (QOL), MS-symptoms, physical activity, and medication adherence, compared to controls and other interventions. RCT designs were heterogeneous. All studies had at least one high or unclear risk of bias.

Conclusion: Telephone-psychotherapy provides small and moderate benefits in depression, fatigue, QOL, MS-symptoms, physical activity and medication adherence in the short-term. Few gains were sustained in the long term. Studies of better quality are needed.

Key Words: Multiple Sclerosis, teletherapy, psychotherapy.
Impact and Implications Statement

- There is some evidence that providing telephone-psychotherapy for people with MS has small-to-moderate benefits on depression, fatigue, physical activity, medication adherence, and MS symptoms in the short-term.

- Telephone-psychotherapy may be an effective and feasible method for clinicians to support people with MS.
Telephone-psychotherapy in Multiple Sclerosis: A systematic review and meta-analysis.

Introduction

Multiple Sclerosis (MS) is a progressive neurological condition with no cure that affects two and half million people worldwide (MS Trust, 2015). The majority of those with MS have a relapsing-remitting form, whereby symptoms develop during a relapse, typically lasting two to six weeks, before remitting. Eventually, symptoms become permanent and the condition becomes worse over time, which is called secondary progressive MS. MS can have diverse and unpredictable effects on physical and psychological functioning (Wilkinson & das Nair, 2013), so there is a need for accessible and effective psychotherapeutic support. Psychological and psychosocial problems frequently arise in areas such as physical functioning, fatigue, pain, cognition, and problems with the support they receive from people around them (Khan, Turner-Stokes, Ng, & Kilpatrick, 2007). These types of problems are thought to be highly prevalent in the MS population. The lifetime prevalence of depression in MS, for instance, is estimated at 50% (NICE, 2003), compared to 17% in a non-clinical population (Blazer & Kessler, 1994). Psychosocial distress may arise through various interacting pathways, making the precise aetiology of psychological distress difficult to discern.

Many people with MS already take multiple medications for their condition and physical sequelae, and the pharmacological management of mood problems adds to their medical regimen. Psychotherapy, which has the potential to be effective in this population (Thomas, Thomas, Hillier, Galvin, & Baker, 2006), may provide an
alternative treatment of choice for many. However, those with MS may not be able to access face-to-face psychological therapies due to fatigue, reduced mobility and other condition-related limitations. Furthermore, clinical experience suggests that psychological interventions may be perceived as costly and therefore not always funded by healthcare providers. Therefore, research into other ways of making such care available is warranted.

Telephone-psychotherapy is an intervention that offers the opportunity to deliver psychological therapies to people in their own homes who otherwise might find it difficult to travel to a healthcare location to receive face-to-face therapy, or where there are limited resources to allow therapists to conduct home-visits. Previous systematic reviews have demonstrated the potential effectiveness of telephone-based interventions across a broad range of physical (Hailey, Roine, Ohinmaa, & Dennett, 2011) and mental health domains (Leach & Christensen, 2006), including stroke (Johansson & Wild, 2011; Paré, Jaana, & Sicotte, 2007) and spinal cord injury (Dorstyn, Mathias, & Denson, 2013; Hailey, Roine, Ohinmaa, & Dennett, 2013). Telephone-psychotherapy is thought to work in a similar way to face-to-face delivered psychotherapy, but may provide lower attrition rates (Mohr, Vella, Hart, Heckman, & Simon, 2008). Client satisfaction and acceptance of telephone psychotherapy has also found to be high (Bee et al., 2008). While there are studies which have explored the usefulness of telephone-psychotherapy, there is no consensus as to whether it can provide a similar quality of care compared to face-to-face interventions at a reduced cost (Mistry, 2012).
To our knowledge, there is no systematic review that evaluates the clinical effectiveness of telephone psychotherapies on psychological outcomes in MS. Results from this review will direct future research and practice on the potential applicability of this type of intervention with people with MS.

This systematic literature review aims to determine the effectiveness of telephone-based psychotherapies for people with MS, compared to those receiving no treatment, standard care or other control, on psychological and physical outcomes.

**Methods**

We searched the following electronic databases (from inception to 1st October 2015) to identify potential studies: EMBASE, PsycINFO, PsycARTICLES, MEDLINE, CINHAL, and Web of Science. The search strategy was based around the subjects: MS, telephone-based psychotherapies, and RCTs. An example of the search strategy is presented in Appendix 1. Manual citation tracking of all primary studies, forward citation tracking, and scanning references lists from review articles were conducted as another search strategy. The WHO International Clinical Trials Registry Platform (ICTRP) and [www.clinicaltrials.com](http://www.clinicaltrials.com) were searched to identify registered trials that met the inclusion criteria but with no data published. If any trials appeared to meet the inclusion criteria, the authors were contacted to request their data.

Trials including people with MS in which a telephone-delivered psychological therapy was compared to a control, were sought for inclusion in the review. RCTs and the pre-crossover component of randomised crossover trials were considered for
inclusion if they met other criteria. Papers reporting secondary analysis of studies were included if they included between-group comparisons of outcomes of interest not reported in the original paper. Studies from conference presentations, dissertations or other grey literature were excluded.

We included trials with patients with all sub-types of MS. Trials with mixed diagnosis populations where MS data were not separable were excluded. Trials in which there was a comparison between a treatment group that received a telephone-based psychological therapy and a control group that either received no intervention or another type of intervention were included. To be considered a ‘psychological therapy’ the interventions should have been described as wholly or partially based on established psychological theories, models or principles. Therapy was considered to consist of a minimum of four sessions, so as to eliminate evaluations of telephone hotlines or crisis counselling services. Studies that delivered therapy via video-conference (including web/internet) technologies without adjunct teletherapy were excluded. Therapies could be delivered by any trained clinician (e.g. doctors, nurses, therapists).

The primary outcome of interest was depression. If there was more than one outcome measure measuring this construct, we used the following hierarchy of commonly used tests:

a) Beck Depression Inventory (BDI) (Beck, Steer, & Carbin, 1988).

b) Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960).

c) Any other depression outcomes.
Secondary outcomes were anxiety, fatigue, quality of life (QOL), MS symptoms, medication adherence, and level of physical activity.

All outcomes were either defined as short-term or long-term. Short-term outcomes were assessed immediately post-intervention. Long-term outcomes were defined as the outcome assessed nearest to 12 months post-randomisation, within a range of 6 to 18 months. Separate analyses were conducted for each of these time-points where possible. Total scores were taken over domain scores (subtest sections) if both were available. If subscale scores were reported without total scale scores, then first individual effect sizes were calculated for each subscale, then combined using the Rosenthal and Rubin (Rosenthal & Rubin, 1986) method for computing accurate combination of effect sizes incorporating the estimated inter-correlation between the subscales. Self-report scores were taken over clinician-rated scores if both were available.

Included trials were assessed for methodological quality, and rated using the "Risk of Bias Table" from the Cochrane Handbook for Systematic Reviews of Interventions, guidelines 5.1.0 (Higgins & Green, 2008). Potential sources of bias were judged to be low risk, high risk, or unclear risk by one researcher (BP) and checked by another researcher (WV). RdN and NM arbitrated if there were any discrepancies. An overall evaluation of the risk for all included studies was completed.

The review was conducted using the Cochrane Review Manager software, RevMan 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Standardised Mean Difference (SMD) was used as a summary statistic.
Only data that were deemed to be similar or comparable enough to meaningfully pool, on the basis of the outcome measures, were entered into the meta-analysis. Depending on the heterogeneity of the data, fixed-effect or random-effects models were considered. Where continuous data were available, means and standard deviations (SD) were entered into RevMan (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014), and the effect estimate (with 95% confidence intervals) was calculated using inverse variance method to apply a weighting to each analysis and displayed as a SMD. Where data were dichotomous, Mantel-Haenszel analysis was completed to produce an Odds Ratio effect estimate, with 95% confidence intervals.

Where medians with upper and lower quartiles were reported, medians were treated as means and interquartile ranges were used to estimate the SD, according to the formula: SD= interquartile range / 1.35.

The data were estimated to be of a roughly normal distribution, if, by subtracting the lowest value on each scale from the estimated median and dividing this by the estimated SD, the value produced was higher than one. The I² statistic (Higgins & Green, 2008) was used to assess heterogeneity in meta-analysis.

Results

A description of the included studies can be seen in Table 1. A total of 125 studies were identified after removing duplicates. Based on our inclusion criteria, 11 studies, comprising 1104 participants were included in the review, with 1032 participants from 10 studies included in the meta-analysis (Berger, Liang, & Hudmon, 2004; Bombardier et al., 2008, 2013; Cosio, Jin, Siddique, & Mohr, 2011; Egner, Phillips,
Vora, & Wiggers, 2003; Finlayson, Preissner, Cho, & Plow, 2011; Mohr et al., 2000, 2005; Mohr, Hart, & Vella, 2007; Turner, Sloan, Kivlahan, & Haselkorn, 2014). The PRISMA (Liberati et al., 2009) diagram in Figure 1 details the flow of the search strategy and reasons for exclusion.

Overall the risk of bias was mixed across the 11 included studies, detailed in Table 2 and summarised in Figures 2 and 3.

Comparisons were split into two categories: comparisons of telephone-psychotherapy to waiting lists or no intervention controls and comparisons of telephone cognitive-behaviour therapy (T-CBT) to Telephone Support Emotion Focused Therapy (T-SEFT).

Of the included studies, one was not considered for the meta-analysis: The Baron study (Baron, Corden, Jin, & Mohr, 2011) was not included because it did not present sufficient data on between-group differences. It reported no significant difference between the T-CBT and T-SEFT groups on insomnia, measured using the three insomnia sub-items of the HDRS (Hamilton, 1960).
Where applicable, visual inspections of funnel plots revealed symmetrical distributions.

**Comparisons of interventions to waiting list or no intervention controls**

**Depression**

Three studies (Bombardier et al., 2013; Egner et al., 2003; Mohr et al., 2000) included short-term measures of depression using HDRS (Hamilton, 1960), Centre for Epidemiologic Studies Depression Scale (CES-D) (Orme, Reis, & Herz, 1986) and the BDI (Beck et al., 1988). A moderate effect on depression was found (SMD of 0.47 (95% CI of 0.21 to 0.73)), as seen in figure 4 below. Statistical heterogeneity assessed using I² was 0%. The Egner study (Egner et al., 2003) included long-term measurement of depression using the CES-D (Orme et al., 1986). A small non-significant treatment effect was found on depression favouring the control group (SMD of -0.33, (95% CI of -1.22 to 0.56)).

[Figure 4]

**Fatigue**

The Finlayson study (Finlayson et al., 2011) reported short-term effect estimates and standard errors for three subscales of the Fatigue Impact Scale (FIS) (Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994). The three subscales were converted into effect sizes and averaged, taking into account the sub-scale intercorrelation of 0.87 (Fisk, Ritvo, et al., 1994). A moderate composite effect size was found in favour of the intervention (SMD of 0.49 (95% CI 0.82 to 0.17)). One of the two Bombardier studies (Bombardier et al., 2008) and the Egner study (2003) reported short-term
continuous data on fatigue using the Modified Fatigue Impact Scale (MFIS) (Fisk, Ritvo, et al., 1994) and the Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). A small non-significant effect favouring the control was found (SMD of -0.31 (95% CI of -0.63 and 0.02), as seen in figure 5 below. Statistical heterogeneity assessed using I² was 0%. The Egner study (2003) reported on the long-term effects on fatigue on the FSS (Krupp et al., 1989), with no effect found (SMD of 0.00 (95% CI of -0.95 and 0.95)).

[Figure 5]

Quality of life

Two studies (Bombardier et al., 2008; Egner et al., 2003) reported short-term data on QOL using the Short Form 36 measure (SF36) (Jenkinson, Coulter, & Wright, 1993) and the Quality of Wellbeing Scale (QWB) (McDowell, 2006). No effect was found (SMD of 0.05 (CI 95% of -0.27 to 0.38)), as shown in figure 6 below. Statistical heterogeneity assessed using I² was 0%.

[Figure 6]

The Egner study (2003) reported long-term continuous data on QOL, using the QWB (McDowell, 2006), finding no effect (SMD of 0.00 (95% CI of -0.95 and 0.95)).

Medication adherence

The Berger study (2004) study reported dichotomous data on medication adherence: the number of participants who had stopped taking their medication. A significant but negligible effect was found (SMD of 0.12 (95% CI of 0.03 and 0.54). The Turner
study (2014) reported continuous data on medication adherence, asking how often participants had missed doses in the last month. A small non-significant effect was found in favour of the intervention (SMD of 0.33 (95% CI of -0.6 and 1.27). The same study reported long-term effects of medication adherence, finding a large but non-significant effect in favour of the intervention (SMD of 0.89 (95% CI of -0.09 and 1.88)).

**Physical health**

Both Bombardier studies (2008; 2013) reported data on the short-term effects on physical health, using the Health Promotion Lifestyles Profile (HPLP-II) (Walker, Sechrist, & Pender, 1987,) and the 7 day physical activity recall measure (7-Day Par) (Sallis et al., 1985). A small effect was found favouring the intervention (SMD 0.44 (95% CI of 0.17 and 0.71)), as seen in figure 7 below. Statistical heterogeneity assessed using I^2 was 0%.

[Figure 7]

One Bombardier study (2013) included short-term measures of MS symptoms using the MS-Related Symptoms Checklist (Gulick, 1989). A moderate effect was found favouring the intervention (SMD of 0.51 (95% CI of 0.09 and 0.93)).

**Comparisons of T-CBT to T-SEFT**

One Mohr study (2005) included short-term measures of depression, using the BDI (Beck et al., 1988). A small non-significant effect was found favouring T-CBT (SMD of 0.33 (95% CI of -0.03 to 0.69)) compared to T-SEFT. The same study included
long-term measures of depression, using the BDI (Beck et al., 1988). No effect was found favouring either intervention (SMD of 0.06 (95% CI of -0.3 to 0.43)).

One Mohr study (2007) reported on short-term measures of fatigue, using the FIS (Fisk, Pontefract, et al., 1994). A small non-significant effect was found favouring T-CBT over T-SEFT (SMD of 0.18 (95% CI of -0.18 to 0.54)).

The Cosio study (2011) included short-term measures of QOL, which was a single-item question about QOL. A moderate effect favouring the T-CBT over T-SEFT was found (SMD of 0.60 (95% CI of 0.43 to 0.84)).

**Discussion**

There is some mixed and poor quality evidence that suggest that providing telephone-psychotherapy to people with MS has small-to-moderate benefits on depression, fatigue, physical activity, medication adherence and MS symptoms in the short-term. This finding appears to be roughly comparable to other systematic reviews of telephone therapies in chronic and neurological populations (Hailey et al., 2011; Johansson & Wild, 2011; Leach & Christensen, 2006), which also offer tentative evidence for the potential effectiveness of the intervention.

Where follow-up data were available, initial gains were not sustained in the long-term after the termination of telephone-psychotherapy. The results suggest there is some mostly poor quality evidence that providing T-CBT over T-SEFT will have small benefits on short-term QOL.

Overall, the majority of trials were of poor quality, with no studies fully adhering to the CONSORT guidelines (Moher, Schulz, & Altman, 2001). Mostly of small and moderate sample sizes, the majority of RCTs had high or unclear risks of selection.
bias and performance bias. Just over half had a low risk of detection bias. However, attrition, reporting and other biases were relatively low. All studies had at least one high or unclear risk of bias.

Like other systematic reviews, there is risk of potential publication bias. Any RCTs without positive results may not have been picked up by the search strategy. However, funnel plots of multiple comparisons were symmetrical, suggesting this may not be the case. The results of this study support the notion that many psychological variables in MS are correlated, as telephone-psychotherapy produced similar effects across different outcomes. Other psychosocial and functional outcomes may respond to similarly to telephone-psychotherapy. Due to limited data, sub-analysis based on subtype of MS diagnosis, frequency of telephone calls, or theoretical approach of therapy were not conducted. Future research, once more primary studies have been conducted in this area, may address these areas in hope of exploring what formats of therapy are most effective for whom.

Almost all studies were based on a specific psychological theory or model, commonly motivational interviewing or cognitive behaviour therapy, and demonstrate a similar small effect on psychological outcomes. However, the intervention in one trial (Finlayson et al., 2011) only very briefly alluded to cognitive-behavioural principles and it was not explicit. Nevertheless, one could cautiously conclude that the specific theoretical modality of the telephone-support offered does not impact significantly upon outcome, much like face-to-face psychotherapy (Wampold et al., 1997). Although little evidence exists, it may be the case that, like face-to-face therapy (Norcross, 2002), telephone-psychotherapy relies upon therapeutic alliance for outcome change. Evidence for this comes from a study where better therapeutic
alliance was found to predict better outcomes in telephone-psychotherapy for people with MS and depression (Beckner, Vella, Howard, & Mohr, 2007). Therapeutic alliance may feasibly be modified by frequency and intensity of telephone calls.

Overall, the current literature on telephone-psychotherapy for people with MS is sparse and methodologically poor, with most trials not adhering to CONSORT guidelines (Moher et al., 2001). However, in terms of clinical impact, the literature thus far indicates that telephone-psychotherapy interventions can have small-to-moderate short-term effects on mental and physical well-being. Nevertheless, more well-conducted and reported RCTs following published guidance in this area are needed. Although not possible in this review due to small sample sizes and lack of information of diagnosing criteria, future reviews may also attempt to conduct sub-group analyses by MS sub-type or level of disability, theoretical approach and frequency/intensity of telephone support. Given potential advantages in terms of increased accessibility and reduced cost in telephone-based psychotherapy, findings to date warrant further investigation.
References


Appendix 1. Example search strategy

Example of the search strategy employed by the review with the EMBASE database

1. multiple sclerosis.mp
2. Multiple Sclerosis (subject heading)
3. 1 or 2
4. tele$.mp
5. phone.mp
6. Telemedicine/ or Telecommunication/ or teleconsultation (subject headings)
7. 4 or 5 or 6
8. RCT
9. randomi*ed
10. Controlled Clinical Trial (subject heading)
11. 8 or 9 or 10
12. 3 and 7 and 11