The effects of clinical interventions on health-related quality of life in multiple sclerosis: a meta-analysis
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CRD summary
The authors of this review concluded that positive effects in terms of health related quality of life varied between the different types of intervention for patients with multiple sclerosis. The authors' conclusions should be treated with caution given potential for bias and variation within intervention type groupings.

Authors' objectives
To assess the effects of health care interventions designed to improve health-related quality of life (HRQL) of patients with multiple sclerosis (MS).

Searching
The authors searched MEDLINE (1948 to September 2011), EMBASE (1980 to September 2011), CINAHL (1960 to September 2011) and the Cochrane Central Register of Controlled Trials (CENTRAL; date not reported). Studies published in languages other than French or English and unpublished or grey literature were excluded. Search terms were reported.

Study selection
Parallel group randomised controlled trials (RCTs) of any intervention, apart from disease modifying therapies and corticosteroids, were eligible for this review. Any control group was acceptable. Trials needed to include people aged 18 or over with clinically definite MS of any severity, type or presence of medical co-morbidities. Those who had had an MS attack one month prior to study entry or were part of a study with other disease populations were excluded. Trials needed to include HRQL as a primary or secondary outcome assessed by the patient themselves. Only HRQL instruments with a single index were included.

Studies were published in North America, Europe and Australia. Mean age of participants ranged from 33 to 59 years. The Expanded Disability Status Scale scores of participants ranged from 0 (no disability) to 9.5 (bedridden). Intervention types included: complementary and alternative medicine, self-management or self-efficacy, exercise/rehabilitation, cognitive training, medication for symptom management and psychological interventions for mood. Most trials were not compared to an active intervention. The most commonly used measure of HRQL was Short Form-36.

Two reviewers independently screened studies for inclusion in the review with any disagreements resolved by discussion.

Assessment of study quality
The quality of trials was assessed using the Cochrane risk of bias tool which consists of seven domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and any other potential sources of bias. Selective outcome reporting was not deemed relevant to this review.

Two reviewers independently assessed study quality.

Data extraction
HRQL was the only outcome of interest. When more than one HRQL measure was used in a trial, the one with the largest effect size was included in the meta-analysis. If HRQL was assessed on more than one occasion, only the first occasion after the intervention was selected. Follow up assessments were not included in the analysis. Effect sizes were calculated using Hedges' adjusted g which considered the difference in outcome between treatment groups and expresses the result as a standard deviation. Where necessary, authors were contacted for information to calculate standard deviations or these were estimated if no reply was received.
Each author independently extracted data from trials included in the meta-analysis.

**Methods of synthesis**

Trials were combined using a random-effects model of meta-analysis. Effect sizes were interpreted in the standard way: 0.2 (small), 0.5 (moderate) and 0.8 (large). Heterogeneity was assessed using the $I^2$ statistic with $I^2>50\%$ (at p value less than 0.10) considered to represent substantial heterogeneity. Publication bias was assessed through Egger's test and via inspection of funnel plots.

**Results of the review**

Thirty-nine trials were included in the review (2,952 participants). Sample size ranged from five to 133 per group. Most of the included studies were of moderate or high quality with low risk of bias. Further details were provided in the article. Twenty-six trials had HRQL as a secondary outcome and of these 19 had concordance between the primary and secondary outcome measures. Most of the trials did not have adequate power to detect a small or moderate effect on HRQL.

Complementary and alternative medicine (seven trials): The pooled effect size was 0.16 (95% CI: -0.06 to 0.40, $I^2=0\%$).

Self-management or self-efficacy (seven trials): The pooled effect size was 0.24 (95% CI: 0.10 to 0.38, $I^2=0\%$).

Medication for symptom management (six trials): The pooled effect size was 0.35 (95% CI: 0.02 to 0.68, $I^2=70\%$).

Exercise / rehabilitation (13 trials): The pooled effect size was 0.43 (95% CI: 0.29 to 0.57, $I^2=0\%$).

Cognitive training (three trials): The pooled effect size was 0.38 (95% CI: -0.26 to 1.02, $I^2=82.6\%$).

Psychological interventions for mood (three trials): The pooled effect size was 0.68 (95% CI: 0.45 to 0.91, $I^2=0.9\%$).

There was no indication of publication bias.

**Authors’ conclusions**

The magnitude of positive effect on HRQL for patients with MS varied between the different types of intervention with the smallest effects observed for self-management and complementary and alternative medicine, followed by medication, then cognitive training, exercise and the largest seen for psychological interventions to improve mood.

**CRD commentary**

This review was underpinned by clear inclusion criteria and a search of a range of sources. Articles published in languages other than English and French were excluded which introduced the possibility of language bias. Unpublished and grey literature was also excluded which raised the possibility of excluding relevant studies. Quality was assessed using an appropriate tool and results presented. Most trials were unblinded given the nature of the intervention and all outcomes were patient assessed which could have caused bias.

More than one reviewer was involved in the processes of study selection, data extraction and quality assessment which minimises the possibility of error and bias. Meta-analysis appeared appropriate given trial homogeneity for most intervention groups. However, there was considerable diversity in interventions, comparators and outcomes scales which could affect generalisability. The medication intervention type also had substantial statistical heterogeneity.

The authors' conclusions should be treated with caution given potential for bias and variation within intervention type groupings.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that new studies were needed where HRQL is the primary outcome. If it was a secondary outcome the trial should be powered to detect an effect on HRQL should one exist. Interventions should be designed using theory and or evidence to guide their components.
Funding
Fonds de la Recherche en Sante du Quebec; Multiple Sclerosis Society of Canada; Physiotherapy Foundation of Canada.

Bibliographic details

PubMedID
23235779

DOI
10.1177/1352458512445201

Original Paper URL
http://msj.sagepub.com/content/18/12/1686.abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Humans; Multiple Sclerosis /psychology /therapy; Quality of Life /psychology; Randomized Controlled Trials as Topic

AccessionNumber
12013005389

Date bibliographic record published
06/03/2013

Date abstract record published
31/05/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.