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# Reporting interventions in trials evaluating cognitive rehabilitation in people with Multiple Sclerosis: A systematic review

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**Abstract**

**Objective:** To determine the quantity and quality of description of cognitive rehabilitation for cognitive deficits in people with Multiple Sclerosis, using a variety of published checklists, and suggest ways of improving the reporting of these interventions.

**Data sources:** Ten electronic databases were searched, including MEDLINE, EMBASE, CINAHL and PsycINFO, from inception to May 2017. Grey literature databases, trials registers, reference lists and author citations were also searched.

**Review methods:** Papers were included if participants were people with multiple sclerosis aged 18 years and over, and if the effectiveness of cognitive rehabilitation in improving functional ability for memory, attention or executive dysfunction, with or without a control group, was being evaluated.

**Results:** Fifty-four studies were included in this review. The reporting of a number of key aspects of cognitive rehabilitation was poor. This was particularly in relation to content of interventions (reported completely in 26 of the 54 studies), intervention procedures (reported completely in 16 of the 54 studies), delivery mode (reported completely in 24 of

the 54 studies) and intervention mechanism of action (reported completely in 21 of the 54 studies).

**Conclusion:** The quality of reporting of cognitive rehabilitation for memory, attention and executive function for multiple sclerosis, across a range of study designs, is poor. Existing reporting checklists do not adequately cover aspects relevant to cognitive rehabilitation, such as the approaches used to address cognitive deficits. Future checklists could consider these aspects we have identified in this review.

**Keywords:** Cognitive rehabilitation, multiple sclerosis, systematic review, quality of reporting, description of interventions.

**Introduction**

Although the effectiveness of cognitive rehabilitation programmes for people with multiple sclerosis has been evaluated in previous trials[1-4] and systematic reviews,[5, 6] researchers have often not provided sufficient details of the interventions. Following the International Classification of Functioning, Disability and Health (ICF)[7] core sets for the focus of rehabilitation in relation to multiple sclerosis,[8] cognitive rehabilitation can be defined as a structured set of therapeutic cognitive activities designed to address cognitive deficits by using a range of approaches to improve individuals' everyday functional abilities and promote independence.

Precise and complete descriptions of interventions are needed in rehabilitation research to facilitate replication of the intervention by other researchers, and to enable implementation into clinical practice.[9] This has been emphasised by Michie and colleagues[10] who have stressed the need for greater transparency in reporting complex interventions, and have

underlined the need for the salient effective components or the 'active ingredients' to be clearly described in research studies.[10]

Two previous reviews found that information relating to treatment dose, delivery format and information about the staff who delivered the intervention[11] and session by session content[12] were poorly reported in trials of cognitive rehabilitation for a range of neurological conditions. Both reviews suggested developing a checklist for reporting interventions in a standardised way, as a standalone[11] or to be used as an adjunct[13] to the Template for Intervention Description and Replication (TIDieR)[14] checklist for researchers. As TIDieR is a general tool for pharmacological and non-pharmacological studies, specific aspects of cognitive rehabilitation (e.g., group size, take home activities) could be omitted even when following this checklist.

A major limitation of previous reviews and checklists is that by only including RCTs and a range of non-specific neurological conditions, the findings do not provide a comprehensive overview of research into cognitive rehabilitation for people with multiple sclerosis. The findings of Mitolo and colleagues[15] suggest there are potentially more studies that could inform the development of a reporting checklist for cognitive rehabilitation specifically for multiple sclerosis.

The limitations within existing systematic reviews implies a more exhaustive examination of what is currently reported about cognitive interventions for people with multiple sclerosis is needed. This would strengthen the validity of existing cognitive rehabilitation checklists. Therefore our primary aim was to conduct a systematic review specifically focused on the

description cognitive rehabilitation interventions used for people with multiple sclerosis. The focus was interventions targeting memory, attention and executive function, some of the most commonly reported problems in multiple sclerosis.[16-18] The secondary aims were to evaluate the quality of reporting of interventions, and to make recommendations on how to improve the reporting of cognitive interventions.

**Methods**

We conducted this review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[19] We only included studies with people aged 18 years and over, with any type of multiple sclerosis. We included studies involving participants with other neurological disorders (e.g. stroke) if a subgroup of people with multiple sclerosis could be identified or the sample had a substantial number (defined as at least 75% of the participants). We included studies that were a re-analysis or subgroup analysis, or a sub-study of an included primary study.

We included any study that evaluated interventions for memory, attention and executive function in people with multiple sclerosis, with or without a control group. We defined cognitive rehabilitation as a structured set of therapeutic cognitive activities that aimed to improve function and participation in daily activities.[7, 8] The interventions had to occur over more than one session, were delivered in any setting (e.g., hospital or home-based) and in any format (e.g., computer-based, face-to-face, group-based, blended and one-to-one interventions).

We included studies where the primary or secondary outcomes were measures of functional ability. These could be objective neurocognitive/neuropsychological measures (batteries/tests), or self-report measures that assess memory, attention and executive function problems in everyday life. We also included studies reporting outcomes assessing mood, fatigue and general function, to account for the relationship these variables have with self-reported cognitive impairments, and the effect that this has on quality of life.[17, 20] We did not restrict the search strategy by date or geographical location, but excluded studies not published in English.

We conducted searches across a number of electronic databases and set up alerts to highlight new papers published in-between the initial search and the analysis. We developed a search strategy for MEDLINE (Ovid) based on the aforementioned inclusion and exclusion criteria (see Supplementary Data File 1), and modified it for other databases.

The following ten databases were searched from time of inception to May 1st 2017: MEDLINE In-Process & Other Non-Indexed Citations (1946 to current); EMBASE (1974 to current); CINAHL (1982 to current); Applied Social Sciences Index and Abstracts (ProQuest) (1987 to current); ISI Web of Science: Social Sciences Citation Index (1956 to current); PsycINFO (1806 to current); Dissertations & Theses A&I (1743 to current); Dissertations & Theses - UK and Ireland (1716 to current); Allied and Complementary Medicine database (1985 to current); CAB Abstracts (1973 to current).

The reference lists of all included studies and previously published reviews[5, 6, 15] were searched for relevant studies. The Cochrane Central Register of Controlled Clinical Trials (CENTRAL) (The Cochrane Library, latest issue) was searched to identify other relevant systematic reviews. We hand-searched the UK Clinical Trials Gateway (https://www.ukctg.nihr.ac.uk/), NIHR Clinical Research Network database, and Networked Digital Library of Theses & Dissertations. We also searched the specialist register GreyNet (http://www.greynet.org/) for grey literature.

The first author (JMM) judged the eligibility of the studies by assessing the titles and abstracts against the pre-defined inclusion criteria. We developed a hierarchy (Supplementary Data File 2) for exclusion. Two reviewers (JMM and OAK) obtained full text copies of all potentially relevant studies or studies where there was uncertainty regarding their inclusion, and independently assessed whether they met the inclusion criteria. Any disagreements were resolved by discussion with a third reviewer (RdN).

Two reviewers (JMM and OAK) extracted data pertaining to the theory and underlying assumptions of the interventions, and descriptions of cognitive rehabilitation. We also included relevant items from checklists identified in the literature and applicable to cognitive rehabilitation research. We included items from the TIDieR checklist, systematic reviews by Martin[12] and van Heugten,[11] American Psychological Society's publication manual's Journal Article Reporting Standards[21] and Western Journal of Nursing Research[22] checklist for the reporting of interventions. Where multiple reports contained varying descriptions of the content of the same interventional study, this was recorded. Data from

multiple reports were not combined into a single data collection form, nor was information from multiple forms combined at this stage.

The various components of the intervention described in each paper were coded against the checklists and frameworks. Content was recorded as complete (based on the description provided for each item), partially reported, or missing. A third reviewer (RdN) checked a random selection (10%) of the data entered. Where corrections were required, we conducted a full audit trail to understand why the error had occurred. As the aim of the review was to report on how interventions were reported, we did not contact study authors to request additional or missing data. A narrative synthesis process [23] was followed for data analysis.

**Results**

Figure 1 provides a flowchart illustrating the search process. Supplementary Data File 3 provides details of the 54 included studies. The cognitive domains targeted in the rehabilitation programmes of the included studies are presented in Table 1.

Where similar items from different checklists were identified (that is, describing the same reporting information) the results of the coding/data extraction were merged (Supplementary Data File 4). Table 2 presents a summary of the findings of the quality of reporting of the included studies based on the merged checklist items.

**Overall quality of reporting of interventions**

Information relating to the characteristics of the participants (such as baseline demographic and clinical characteristics) was reported completely in the majority of the included papers (n=51; 94%).

Intervention details that were reported partially complete

*Who delivered the intervention?*

The individuals who delivered the intervention were mostly described by their professional training (n=19; 82%), with the majority being rehabilitation psychologists, psychologists or neuropsychologists.

If the individual who delivered the intervention was reported to have received training (n=4; 17%), no further information was provided. For example, one paper reported that "the facilitator (interventionist) was a master's prepared nurse carefully trained prior to the initiation of the study".[2 (p. 884)] None of the papers provided any details regarding the therapists' competency level to deliver the intervention.

*The intervention 'dose'*

The frequency of sessions (n=50; 93%), total number of sessions (n=33; 61%), and duration of the intervention (n=50; 93%) was often reported. However, the actual dose (what actually happened) was missing. Only 17 (32%) papers provided this information (e.g., in the form of descriptive statistics).

*The key elements of the intervention, including active ingredients and mechanism of action*

Only two papers made specific reference to the active ingredients of the intervention. For example one paper reported the following: “The only difference between the groups was that only the treatment group was exposed to the active ingredients of the mSMT (imagery and context)”.[24 (p. 2067)] Twenty-one (39%) papers reported the key elements of the intervention and the intended mechanism of action, but did not make explicit mention of active ingredients. For example, one paper defined the intervention as: “ProCog-SEP program […] based on exercises drawn from facilitation/reorganization theories. This technique is defined by the use of preserved functions. It aims to teach the patient to use facilitation strategies to help these preserved functions, like mental imagery, or semantic cues”.[25 (p. 554)]

The majority (n=29; 54%) of the studies indicated the cognitive rehabilitation strategy, but did not specify the intended mechanism of action or goal of the key elements. For example one paper-reported: “[…] this investigation focused specifically on training processing speed and working memory, the most fundamental cognitive deficits for multiple sclerosis patients”.[26 (p. 114)]

*Procedures*

Specific details about the procedures (e.g., ‘the methods section of a recipe’) as described in the TIDieR[14] checklist were only complete in 16 (30%) papers. This information was incomplete in 36 (67%) of the papers. Information that was often incomplete or missing included session-by-session content and the format of the sessions.

*Materials*

The intervention materials were reported completely in 12 (22%) papers. For instance, one paper included an example of the patient score sheet used for one of the rehabilitation sessions. In 32 (59%) papers the materials were not mentioned specifically, but could be inferred from the procedures. Ten (18%) papers did not provide this information.

Intervention details that were reported poorly

*Intervention mode of delivery*

The mode of intervention delivery (delivered individually or in a group) was often not clear. Only 24 (44%) papers mentioned this explicitly. In eight (15%) papers the delivery mode could be deduced if information about the setting (e.g., home-based) or format (e.g., computer-based) was reported. For example, one paper reported that the intervention was delivered in the participants' homes, therefore, we assumed that the intervention was individually delivered. Details pertaining to the intervention mode of delivery were not reported in 22 (41%) papers.

*Specific to group interventions*

The minimum and maximum number of people in the groups was only reported in one of the 14 group-based or blended studies. Four (29%) studies reported the maximum number of people in each group. The group size was not reported in nine (64%) papers.

**Multiple study reports**

There were mixed findings when the quality of reporting was compared across several studies reporting the same intervention. For example, more details about the procedures (including how missed sessions were dealt with), the intervention dose, the location, who

delivered the intervention (i.e., professional skills and intervention-specific competencies) were provided in the one-year follow-up to the *Sclerosi Multipla Intensive Cognitive Training (SMICT)* trial[27] than in the original study[28] or the two-year follow-up study.[29] However, the quality of the reporting for another trial was observed to be consistent when comparing the primary study[30] to subsequent sub-group[31] and secondary analysis[32] of the Story Memory Technique (mSMT) intervention.

**Comparison of the quality of reporting across different reporting checklists**

Studies that did well on one checklist and not on others

Three papers[26, 33, 34] performed 'well' (that is, provided more complete descriptions of the intervention, based on the description provided for each item, where applicable) on the TIDieR checklist. Two papers[33, 34] reported the materials, procedures and tailoring of the intervention completely. All three papers provided partial information for who delivered the intervention. For example, papers mentioned research assistant or neuropsychologist but did not mention what, if any, training they received or how many people delivered the intervention. All three papers did not report whether the intervention was modified (e.g., changes to the intervention provider or intervention material) during the study. For all papers, partial information was reported for the intervention dose, the skills and qualifications of the person who delivered the intervention. All three papers performed poorly on the Western Journal of Nursing checklist[22], particularly for items relating to the conceptual frameworks of the intervention, intervention materials, intervention procedural items (e.g., the timing of the intervention delivery) and intervention variations. These items were the most poorly reported across all checklists.

Studies that performed well on all checklists

None of the studies performed well on all checklists, but two papers[1, 2] were close to achieving this.

Studies that did not perform well on any of the checklists

Forty-four (82%) papers provided incomplete or missing reports of the session by session content of the interventions (for example, these four papers[31, 35-37]). There was no obvious reason for this, nor commonality between the studies in this group, for instance, in terms of mode of delivery (group or individual) or type of study (primary or secondary/sub-group analyses of a primary study.

**Discussion**

We examined how cognitive rehabilitation for memory, attention and executive function for people with multiple sclerosis is reported in scientific journals. The review showed that, overall, the reporting of the content of cognitive rehabilitation was poor. Specifically, we found that a number of key details needed to aid replication of the study were either reported incompletely or were missing. Information that was partially reported was: the key elements of the intervention (including active ingredients and mechanism of action); the theory or conceptual framework for the intervention; details of the content, i.e., exactly what participants received; and the intervention 'dose'. Information that was reported poorly was: how the intervention was delivered; whether the intervention was delivered as planned; whether participants adhered.

There were no discernible differences in the quality of reporting of the same intervention across multiple study reports (i.e., primary study compared to follow-up and/or secondary analyses). In terms of the checklists used, none of the included papers performed well on all the checklists, with items from the Western Journal of Nursing checklist[22] tending to be reported incompletely or not at all.

Our findings are comparable with previous research that found 50 to 70 percent of non-pharmacological interventions were poorly reported.[38-40] Specifically, information relating to the theory/aims of the intervention,[12] the content and intervention procedures,[11, 12, 38, 40] the materials used,[12, 38, 40] fidelity and adherence[11] was omitted from published studies.

Complete descriptions of interventions are needed to enable replication by other researchers, and for implementation into clinical practice.[9] This viewpoint is supported by Cicerone,[41] who also argues that imprecise descriptions may lead to disagreements when interpreting the research evidence. Michie and colleagues[10] argue for the 'active ingredients' of the intervention needing to be described clearly in research studies.[10] 'Active ingredients' of a complex intervention are the components of the intervention that are "essential to achieving good outcomes for those targeted by the intervention".[10 (p. 40)] We acknowledge that in complex interventions, some of the 'active' ingredients can only be hypothesised based on theory or previous research literature. In our review, only two papers[24, 32] made specific reference to the active ingredients of their intervention, whilst 18 papers provided information on the intended mechanism of action. This is closely linked with the theory/conceptual framework upon which the interventions are based (only reported completely in 54% of the included studies). Cognitive rehabilitation is driven by

cognitive, emotion, behavioural and learning models and theories.[42, 43] However, the actual contribution of each ingredient to the overall effect of the treatment can only be understood if each of those ingredients were assessed and reported. This might be beyond the scope of some studies, and hence is not featured in many of the papers.

There is evidence that checklists can improve the quality of reporting of interventions.[44-47] However, in a recent scoping review of systematic reviews of adherence to reporting guidelines by Samaan and colleagues,[39] of the 50 included reviews, 43 (86%) reported poor levels of adherence to reporting guidelines. The authors provided a number of recommendations to improve adherence, including the use of *appropriate* reporting guidelines. Taken together with the existing literature, the findings from this review provide further evidence for the need for more domain/intervention-specific checklists.[9, 11, 12, 38-40]

Several issues came to light during the data extraction and coding process, based on the checklists used. Disparities in coding of different checklist items could be attributed to whether or not an item description was provided, and the level of description/detail provided. Where no item descriptions were supplied, it was left to the reviewers to determine what was required for a specific checklist item. Thus, items on a checklist should be accompanied with a clear and detailed description, as well as with examples.

The coding process that was undertaken in this review highlighted the need for a checklist that is user-friendly, in terms of the number of items contained within it and the way in which items are presented. We suggest a one-page checklist, whereby a tick-box is used to indicate whether a particular aspect of the intervention content has been reported.

The checklists used in this review tended to describe intervention components, such as 'dose' in more medical terminology, which would not be appropriate for some rehabilitation interventions. For example, the Journal Article Reporting Standards[21] checklist includes an item that asks researchers to report how long any effects of the intervention were intended to last. The terminology of our proposed checklist should be appropriate for cognitive rehabilitation, such as the maintenance of strategies or skills targeted in the intervention, as suggested by Sohlberg and Mateer.[48] This may help towards ameliorating the difficulty researchers face using multiple checklists in tandem to report on different aspects of their research.

Our review follows Moher and colleagues'[49] recommended steps for developing health research reporting guidelines and previous reviews by van Heugten and colleagues[11] and Martin and colleagues.[12] These two reviews examined the content of cognitive rehabilitation interventions for a range of neurological conditions, including multiple sclerosis. They also considered several cognitive domains (memory, attention, executive function, language, awareness, visuospatial functioning and apraxia) and found the overall quality of reporting was poor. This current review built on the findings of these reviews, but is unique as it focused solely on studies of the cognitive rehabilitation of memory, attention and executive function for people with multiple sclerosis.

In light of the evidence presented, a domain-specific reporting checklist (i.e., that is *appropriate*) may facilitate better reporting of the content of cognitive rehabilitation for people with multiple sclerosis. For example, the checklist could include the rehabilitation

setting (inpatient, outpatient, home-based), the practical details needed to administer the key elements of the intervention (following fundamental approaches to cognitive rehabilitation to restore cognitive function, the use compensatory strategies and devices, or environmental modifications[50]), and the materials used by both facilitators and participants.

A strength of our systematic review is the inclusion of a variety of study designs in the search strategy. This provides a more comprehensive examination of the quality of reporting of cognitive rehabilitation in multiple sclerosis compared to previous reviews. However, one potential limitation of the review is that we only included published studies of interventions for memory, attention or executive dysfunction. While 70% of published cognitive rehabilitation studies in multiple sclerosis target the cognitive domains of memory, attention and executive function[15], we acknowledge that the studies we included may not be representative of all cognitive rehabilitation research in multiple sclerosis.

**Clinical messages**

- Most studies do not adequately report key aspects of cognitive rehabilitation for memory, attention and executive function for people with multiple sclerosis. This may prevent implementation of cognitive rehabilitation clinically.
- Current reporting checklists may be too general, or use terminology that may not be appropriate for cognitive rehabilitation but more suited to drug trials. Therefore, modifications to these or new checklists need to take into account clinicians who deliver cognitive rehabilitation.

## Conflict of interest

RdN is an author of one study that was included in this review.


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**Figures and Tables**

**Figure 1.** PRISMA Flowchart of Systematic Review Search Results

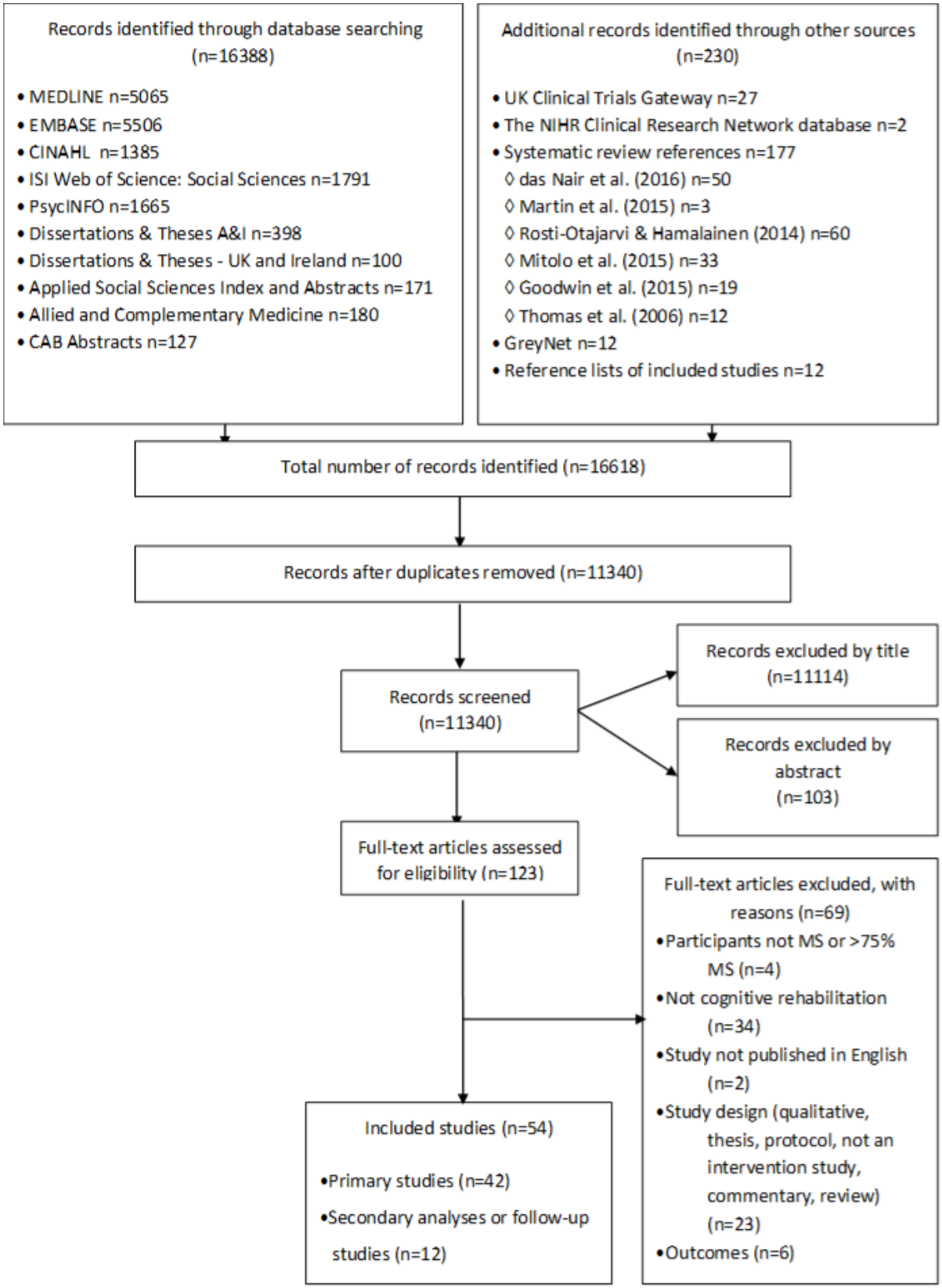


**Table 1.** Characteristics of included studies by delivery mode and cognitive domain targeted in the intervention

| **Cognitive Domain** | **Delivery Mode** | | |
|---|---|---|---|
| | Individual | Group | Blended |
| Memory only | Allen (1998)[43], Ernst (2012)[32], Ernst (2013)[31], Gentry (2008)[51], Pedulla (2016)[59], Vogt (2009)[66] | Carr (2014)[1], Chiaravalloti (2012)[28] | Martin (2014)[68] |
| Attention only | Amato (2014)[24], Cerasa (2013)[27], Plohmann (1994)[60], Plohmann (1998)[61], Rosti-Otajarvi (2013)[40] | - | - |
| Executive function only | Birnboim and Miller (2004)[44], Fink (2010)[33] | - | Hanssen (2015)[54] |
| Combination | Altun (2015)[23], Bonavita (2015)[25], Brenk (2008)[45], Charvet (2015)[22], Campbell (2016)[51], De Giglio (2015)[29], De Giglio (2016)[30], Ernst (2015)[21], Filippi (2012)[20], Gich (2015)[52], Hancock (2015)[53], Hildebrandt (2007)[3], Janssen (2015)[34], Jonsson (1993)[55], Lincoln (2002)[57], Mantynen (2014)[35], Mattioli (2010)[36], Mattioli (2012)[37], Mattioli (2014)[38]; Mattioli (2016)[39]; Mendozzi (1998)[58]; Parisi (2014)[46], Perez-Martin (2007)[52], Rosti-Otajarvi (2013)[41], Sastre-Garriga (2011)[63], Shatil (2010)[6], Solari (2004)[4] | Brissart (2013)[26], Chiaravalloti (2005)[47], Chiaravalloti (2013)[48], Chiaravalloti and DeLuca (2015)[49], Dobryakova (2014)[50], Leavitt (2014)[56], Shevil and Finlayson (2010)[42], Tesar (2005)[65] | Pusswald (2014)[62], Stuifbergen (2012)[2] |

**Table 2.** A summary of the reporting quality of the 54 included studies for selected reporting items

| Broad aspect of reporting | No. (%) of studies in which item was reported completely* | No. (%) of studies in which item was not clearly reported* | No. (%) of studies in which item was not reported | No. (%) of studies in which item was not applicable** |
|---|---|---|---|---|
| Demographic and clinical characteristics of the participants | 51 (94%) | 0 | 3 (6%) | n/a |
| Theory/conceptual framework upon which the intervention is based | 29 (54%) | 21 (39%) | 4 (7%) | n/a |
| Key elements of intervention, including active ingredients and mechanism of action | 21 (39%) | 29 (54%) | 4 (7%) | n/a |
| Details of the intervention content i.e., what participants received | 26 (48%) | 24 (44%) | 4 (7%) | n/a |
| Specific details about the procedures | 16 (30%) | 36 (66%) | 2 (4%) | n/a |
| Level of professional training of the person who delivered the intervention | 6 (11%) | 13 (24%) | 4 (7%) | 31 (57%)** |
| Number of people who delivered the intervention | 5 (9%) | 3 (6%) | 15 (27%) | 31 (57%)** |
| Individual delivering intervention received training specific to the intervention | 0 | 4 (7%) | 19 (35%) | 31 (57%)** |
| Competency to deliver intervention assessed and achieved | 3 (7%) | 10 (18%) | 10 (18%) | 31 (57%)** |

| Broad aspect of reporting | No. (%) of studies in which item was reported completely* | No. (%) of studies in which item was not clearly reported* | No. (%) of studies in which item was not reported | No. (%) of studies in which item was not applicable** |
|---|---|---|---|---|
| Delivery mode: Individual or group | 24 (44%) | 8 (15%) | 22 (41%) | n/a |
| The intervention 'dose': intended and actual | 17 (31%) | 35 (65%) | 2 (4%) | n/a |
| Materials | 12 (22%) | 32 (59%) | 10 (19%) | n/a |
| Assessment of fidelity (specifically referring to delivery of the intervention by the facilitator, therapist, etc.) | 3 (13%) | 8 (15%) | 14 (27%) | 31 (57%)** |
| Adherence/compliance of participants to intervention | 9 (17%) | 6 (12%) | 37 (71%) | n/a |

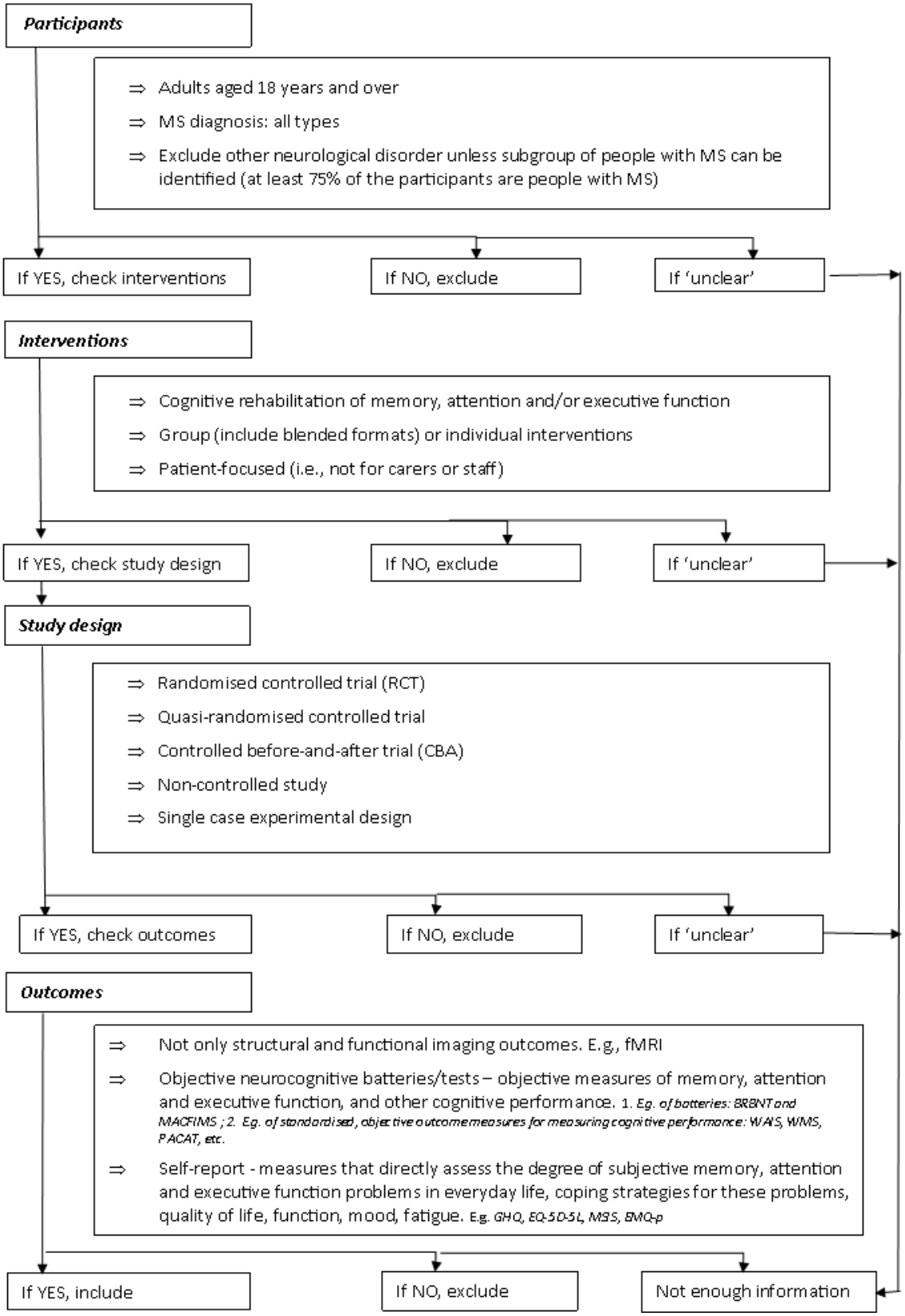
Note: *Assessed against the description of the reporting item for the checklists used; **not applicable for computer-based interventions.

**Supplementary data**

**Supplementary Data File 1**. MEDLINE In-Process & Other Non-Indexed Citations (Ovid) search strategy

1. exp Multiple Sclerosis/
2. exp demyelinating autoimmune diseases, cns/
3. "autoimmune diseases of the nervous system"/
4. multiple sclerosis.ab,ti.
5. 1 or 2 or 3 or 4
6. exp *Cognition Disorders/ or exp *Cognition/
7. exp *Cognitive Dissonance/
8. exp *Mild Cognitive Impairment/
9. exp *Metacognition/
10. exp *Awareness/
11. exp *Attention/
12. exp *Memory/ or exp *Memory Disorders/
13. mental processes/ or exp *executive function/
14. (cogniti* or neuropsychol* or memor* or attenti* or execut* or metacognit* or aware* or concentrat*).ab,ti.
15. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. 5 and 15
17. exp *Neurological Rehabilitation/ or exp *Rehabilitation/ or exp *Rehabilitation Research/
18. exp *Cognitive Therapy/
19. exp *Neuropsychology/
20. exp Therapy, Computer-Assisted/
21. exp Computers/
22. exp Neuropsychological Tests/
23. (interven* or train* or re?train* or computer?assisted therap* or rehabilit* or neurorehab* or neuropsych* rehab* or restitut* or remediat* or restorat* or retrain* or train* or recover* or treat* or guid* or instruct* or teach* or stimulat* or exerci* or strateg* or counsel* or therap* or intervent* or manage*).ab,ti.
24. 17 or 18 or 19 or 20 or 21 or 22 or 23
25. (attent* or memor* or cognit* or cogniti* disorder* or concentrat* or awar* or alert* or distract* or executive function).ab,ti.
26. 24 and 25
27. 16 and 26

**Supplementary Data File 2.** Hierarchy for Excluding Studies



**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Allen, 1998[53] | Before and after | Non-specific MS | Memory | 39.6 (8.71) | Individual, computer-based | Computer-based imagery-based mnemonic strategy training | 1 |
| Altun,2015[54] | Before and after | RRMS | Attention, sustainable attention, information processing speed, and verbal and visual memory | 36 (7.19) | Individual, Computer-based | Different screens used, based on cognitive domains. For example, memory screen had tasks such as identification of objects and deduction exercises. | 1 |
| Amato, 2014[55] | RCT | RRMS | Attention | 18–55 years (inclusion criteria) | Individual, home-based, computer-based | Based on the Attention Processing Training program (APT). Focus is on restorative exercises | 1 |
| Birnboim, 2004[56] | Before and after | Non-specific MS | Executive function | 45.5 (9.25) | Individual, computer-based | Strategy training, awareness and learning application to daily life. Computer-based | 1 |
| Bonavita, 2015[57] | CBA | RRMS | Attention and information processing speed | 49 (8) | Individual, computer-based | Short-term cognitive training based on Reckon | 1 |
| Brenk, 2008[58] | CBA | Non-specific MS | Non-specific, but targets memory and attention | 43.5(8.9) | Individual | Non-specific cognitive training (restitution) | 1 |
| Brissart, 2013[25] | CBA | RRMS | Memory and executive function | 42.5 (5.17); | Group | Group proctor-SEP Cognitive Program - aims to teach the patient to use facilitation strategies to help preserved functions | 1 |
| Campbell, 2016[51] | RCT | RRMS, SPMS | Working memory, visuospatial memory, divided attention | 47.37 (8.23) | Individual | Restitution. Cognitive training to improve/increase brain activation of specific brain areas and thus improve neural efficiency | 1 |
| Carr, 2014[1] | RCT | PPMS, SPMS, RRMS, benign | Memory | 34-72 | Group | Group memory rehabilitation programme combining restitution and compensation strategies | 1 |
| Cerasa, 2013[59] | RCT | RRMS | Attention | 31 (9.2) | Individual, home based, computer-assisted | Software reckon -computer-based intensive attention training program | 1 |
| Charvet, 2015[60] | RCT | RRMS | Working memory and processing speed | 19-55 years | Individual | Computer-based, active adaptive cognitive remediation program focusing on training common areas of impairment in multiple sclerosis | 1 |

**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Chiaravalloti, 2005[30] | RCT | RRMS, PPMS and SPMS | Memory and learning | 45.14 (13.78) | Group | Story Memory Technique (mSMT) focusing on approving the acquisition of info through context and imagery) into long-term memory | 1 |
| Chiaravalloti, 2012[31] | RCT | RRMS | Memory | 49.25 (9.33) | Group | Engagement of imagery procedures to facilitate learning + use of context to organize incoming information | 2 |
| Chiaravalloti, 2013[24] | RCT | RRMS, PPMS, SPMS, PRMS | Memory and learning | Inclusion criteria; age 30–70 year. I: 48.13 (10.17); | Group | Modified Story Memory Technique (mgmt.) focusing on approving the acquisition of info through context and imagery) into long-term memory | Similar studies as Chiaravalloti 2012, Dobryakova 2014 and Leavitt 2012 |
| Chiaravalloti, 2015[61] | RCT | RRMS, PPMS, SPMS, PRMS | Memory and learning | 48.13 (10.17) | Group | Modified Story Memory Technique (mSMT) focusing on approving the acquisition of info through context and imagery) into long-term memory | 2: Post-hoc analysis of Chiaravalloti et al., 2013 |
| De Giglio, 2015[62] | RCT (waiting list control) | RRMS | Attention, working memory, processing speed and executive function | 43.9 (8.4) | Individual, home-based, computer | Computer and videogame-based training | 1 |
| De Giglio, 2016[63] | RCT (waiting list control) | RRMS | Attention, working memory, processing speed and executive function | 43.2 (8.2) | Individual, home-based, computer | Computer and videogame-based training | 2: Further analyses of De Giglio 2015 |
| Dobryakova, 2014[64] | RCT | RRMS and PPMS | Memory and learning | 40 (5.66) | Group | Modified Story Memory Technique (mSMT) focusing on approving the acquisition of info through context and imagery) into long-term memory | 3: Follow-up of Chiaravalloti (2013) |
| Ernst, 2012[65] | CBA | RRMS | Autobiographical memory | 37.25 (5.5) | Individual | Mental visual imagery (MVI)-based exercises - compensatory | 1 |

**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Ernst, 2013[66] | CBA | RRMS | Autobiographical memory | 42.96 (10.94); | Individual | An MVI (mental visual imagery)-based cognitive facilitation programme - compensatory | 1 |
| Ernst, 2015[35] | RCT | RRMS | Executive function, autobiographical memory | 42 (10.37) | Individual | Mental visual imagery (MVI)-based exercises | 1 |
| Filippi, 2012[67] | RCT | RRMS | Attention and information processing and executive functions | 44.8 (28-60); | Individual, computer-based | Domain-specific cognitive training. Computer software – reckon package | 1 |
| Fink, 2010[68] | CBA | RRMS | Executive function | 44.8 (8.2) | Individual | Ease executive deficits by self-training and receiving feedback | 1 |
| Gentry, 2008[69] | Before and after | RRMS, PPMS, SPMS, CPMS | Memory | 50 (37-73) | Individual, home based | PDA; compensatory assistive technology/strategy | 1 |
| Gich, 2015[70] | RCT | RRMS and SPMS | Memory and executive function | 45.5 (9.6) | Individual, computer-based | Cognitive rehabilitation programme based on the restoration of function | 1 |
| Hancock, 2015[26] | RCT | RRMS, SPMS, PPMS | Processing speed and working memory | 50.65 (6.32) | Individual, home-based, computer-based | Computerized cognitive training (Posit Science) | 1 |
| Hanssen, 2015[33] | RCT | PPMS, RRMS, SPMS | Executive function | 53.9 (33-70) | Blended | Goal attainment. Psychoeducation, learning strategies | 1 |
| Hildebrandt, 2007[3] | RCT | RRMS | Memory and working memory | 42 (25-55) | Individual, home-based, computer-based | Home-based cognitive training program, designed to increase frequency and intensity of training | 1 |
| Janssen, 2015[71] | RCT (waiting list control) | RRMS | Attention, working memory, executive functioning and processing speed | 30-59 (inclusion criteria); I=49.4396.4), C=44.96(8.8) | Individual | Cognitive training through multimodal videogame-based learning strategies: Hybrid-variable priority training (HVT) program | 1 |
| Jonsson, 1993[34] | RCT | RRMS, secondary CPMS and primary CPMS course | Memory and attention (concentration) | 46.1 (7.3); | Individual | Compensation (internal and external memory aids), substitution, direct training (puzzles, etc.) + neuropsychotherapy. | 1 |

**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Leavitt, 2014[32] | RCT | RRMS, PPMS, SPMS, PRMS | Memory and learning | 49.72 (9.98) | Group | Modified Story Memory Technique (mSMT) ) focusing on approving the acquisition of info through context and imagery) into long-term memory | 2: Sub-group analysis of Chiaravalloti 2012 |
| Lincoln, 2002[72] | RCT | SPMS, RRMS, including benign, PPMS | Range of cognitive deficits (dependent of participants' needs), including memory | 43 (10) | Individual | Identification of individual needs. Compensatory techniques includes training in use of external memory aids (diaries, calendars, note books) + internal memory aids (visual mnemonics) | 1 |
| Mantynen, 2014[73] | RCT | RRMS | Attention and working memory | Inclusion criteria age range 18-58. 43.5 (8.7); | Individual, computer-based | Strategy-oriented computer-based attention and working memory retraining, psychoeducation and teaching compensatory strategies | 1 |
| Martin, 2014[13] | RCT | Not stated | Memory | 45.2-48.3 | Blended: 2 individual sessions and 10 group sessions | Compensatory (external memory aids) or restitution (encoding and retrieval practice, and attention- retraining exercises e.g. Letter and number cancellation | 2 |
| Mattioli, 2010[28] | RCT | RRMS | Attention, information processing, executive function | 42 (41-53) | Individual, computer-based | RehaCom computer-based intensive training | 1 |
| Mattioli, 2012[74] | RCT | RRMS | Attention, information processing and executive function | 45.46(10.48) | Individual, computer-based | Intensive neuropsychological training | 1 |
| Mattioli, 2014[27] | RCT | RRMS | Attention/speeded information, executive function and memory | 45 (38-50) | Individual, computer-based | Domain-specific cognitive training (based on individual cognitive impairment) | 3: Follow-up 1 of Mattioli (2010) |
| Mattioli, 2016[29] | RCT | RRMS | Memory, attention/speeded information processing and executive function | 44.8 (8.69) | Individual, computer-based | Domain-specific cognitive training (based on individual cognitive impairment) | 3: Two year follow-up of Mattioli et al (2010) |
| Mendozzi, 1998[75] | Quasi-RCT | RRMS or secondary CPMS | Memory and attention | 45.38-47.92 | Individual, computer-based | Memory training (encoding) and attention tasks | 1 |

**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Parisi, 2014[36] | RCT | Non-specific MS | Attention, information processing and executive function | 43.6 (25-58) | Individual, computer-based | Domain-specific cognitive training. Computer software – reckon package | 3: Follow-up of Mattioli et al (2010) |
| Pedulla, 2016[76] | RCT | RRMS, SPMS | Working memory | 47.5 (9.3) | Individual, home-based, computer | Computer-based adaptive cognitive training | 1 |
| Plohmann, 1994[77] | CBA (waiting list control) | RRMS, CPMS | Attention | 39.7 (10.09) | Individual, computer-based | Retraining, restitution | 1 |
| Perez-Martin, 2017[52] | RCT | RRMS, PPMS, SPMS | Memory, attention, processing speed and executive function | 44.93 (9.89) | Individual, home-based, computer-based | Multi-domain computer-assisted cognitive rehabilitation supported by home-based work | 1 |
| Plohmann, 1998[78] | SCED | Primary CPMS, Secondary CPMS, RRMS | Attention | 44.6 (11.4) | Individual, computer-based | Four attention training programme; focus on two of most affected/diminished attention areas - specific + nonspecific training | 1 |
| Pusswald, 2014[79] | RCT | RRMS, SPMS, PPMS | Divided attention. Cog rehab included memory retraining | 42.6 (1) | Blended: Individual (home-based computer training) and group psychosocial counselling | Cognitive functional training + psychosocial counselling focusing on restitution training and compensation strategies | 1 |
| Rosti-Otajarvi, 2013a[80] | RCT | RRMS | Attention | 43.5 (8.7); | Individual, computer-based | Strategy-oriented computer-based attention and working memory retraining, psychoeducation and teaching compensatory strategies | 2: Secondary paper to Mantynen 2014 |
| Rosti-Otajärvi, 2013b[81] | RCT | RRMS | Attention and working memory | 18–59 | Individual | Strategy-oriented computer-based attention and working memory retraining, psychoeducation and teaching compensatory strategies | 3: Follow-up to Mantynen 2014 |
| Sastre-Garriga, 2011[82] | CBA | RRMS, PPMS, SPMS | Attention, executive function and memory | 50.73 (10.88) | Individual, computer-based | Intervention targeted worse affected cognitive domain. Training | 1 |

**Supplementary Data File 3**. Characteristics of Included studies

| First author, year published | Study design | Type of multiple sclerosis (RRMS – relapsing remitting MS; PPMS – primary progressive MS; SPMS – secondary progressive MS; chronic progressive – CPMS; progressing relapsing - PRMS | Cognitive domain | Age of participants | Format of intervention delivery | Intervention technique | Study status – 1: primary study; 2: secondary/sub-group analyses; 3: follow-up study |
|---|---|---|---|---|---|---|---|
| Shatil, 2010[83] | CBA | RRMS and PRMS | Non-specific: it is composed of 15 evaluation tasks measuring a wide range of cognitive abilities such as memory, attention and eye-hand coordination | 43.75 (12.15) | Individual, computer-based, home-based | CogniFit Personal Coach (CPC), a home-based, computerized, individualized cognitive training program | 1 |
| Shevil, 2010[84] | Before and after | Non-specific MS | Memory, attention, information processing and executive function | 52.4 (10.3); range 26-70 | Group | Internal and external compensatory strategies (e.g. mnemonics, incorporating a day planner or digital recorder and organizing spaces). | 1 |
| Solari, 2004[4] | RCT | RRMS, PRMS, CPMS | Memory and attention | 46.2 (9.2) | Individual, computer-based | Rehacom ; computer-based memory and attention retraining | 1 |
| Stuifbergen 2012[2] | RCT | Non-specific MS | Attention, Memory, Problem solving, executive skills | 24-60; 47.95 (8.76) | Blended | MAPSS-MS : group sessions focusing on compensatory strategies + individual-based computer-assisted cognitive training program | 1 |
| Tesar, 2005[85] | RCT | RRMS and SPMS | Memory and learning | 45.3 (9.2) | Group, computer-based | Direct functional training + teaching of compensation strategies relevant to everyday life | 1 |
| Vogt, 2009[37] | Quasi-RCT | RRMS, SPMS and CPMS | Working memory | 43.2 (8.8); | Home-based, individual | High intensity, computer-based, working memory training - BrainStim | 1 |

**Supplementary Data File 4.** Data extraction of the content of the interventions of the included studies

| | |
|---|---|
| Information is reported completely, as per item description | |
| Information is reported incompletely, as per item description | |
| Information is not reported | |
| Reporting item not applicable | n/a |

| | Allen 1998[53] | Altun 2015[54] | Amato 2014[55] | Birnboim 2004[56] | Bonavita 2015[57] | Brenk 2008[58] | Brissart 2013[25] | Campbell, 2016[51] | Carr 2014[1] | Cerasa 2013[59] | Charvet 2015[60] | Chiaravalloti 2005[30] | Chiaravalloti 2012[31] | Chiaravalloti 2013[24] | Chiaravalloti 2015[61] | De Giglio 2015[62] | De Giglio 2016[63] | Dobryakova 2014[64] | Ernst 2012[65] | Ernst 2013[66] | Ernst 2015[35] | Filippi 2012[67] | Fink 2010[68] | Gentry 2008[69] | Gich 2015[70] | Hancock 2015[26] | Hanssen 2015[33] | Hildebrandt 2007[3] | Janssen 2015[71] | Jonsson 1993[34] | Leavitt 2014[32] | Lincoln 2002[72] | Mantynen 2014[73] | Martin 2014[13] | Mattioli 2010[28] | Mattioli 2012[74] | Mattioli 2014[27] | Mattioli 2016[29] | Mendozzi 1998[75] | Parisi 2014[36] | Pedulla 2016[76] | Perez-Martin, | Plohmann 1994[77] | Plohmann 1998[78] | Pusswald 2014[79] | Rosti-Otajarvi | Rosti-Otajärvi | Sastre-Garriga | Shatil 2010[83] | Shevil 2010[84] | Solari 2004[4] | Stuifbergen 2012[2] | Tesar 2005[85] | Vogt 2009[37] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Demographic and clinical characteristics of the participants | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Theory/conceptual framework upon which the intervention is based | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Key elements of intervention, including active ingredients and mechanism of action | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Details of the intervention content i.e., what participants received | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Specific details about the procedures | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Level of professional training of the person who delivered the intervention | n/a | n/a | n/a | n/a | n/a | | | n/a | | n/a | n/a | | | | | n/a | n/a | | | | | n/a | | | n/a | n/a | | n/a | | | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a | n/a | | n/a | | n/a | n/a | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a |
| Number of people who delivered the intervention | n/a | n/a | n/a | n/a | n/a | | | n/a | | n/a | n/a | | | | | n/a | n/a | | | | | n/a | | | n/a | n/a | | n/a | | | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a | n/a | | n/a | | n/a | n/a | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a |
| Individual delivering intervention received training specific to the intervention | n/a | n/a | n/a | n/a | n/a | | | n/a | | n/a | n/a | | | | | n/a | n/a | | | | | n/a | | | n/a | n/a | | n/a | | | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a | n/a | | n/a | | n/a | n/a | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a |
| Competency to deliver intervention assessed and achieved | n/a | n/a | n/a | n/a | n/a | | | n/a | | n/a | n/a | | | | | n/a | n/a | | | | | n/a | | | | n/a | n/a | n/a | | | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a | n/a | | n/a | | n/a | n/a | | n/a | | n/a | n/a | n/a | n/a | n/a | n/a |
| Delivery mode: Individual or group | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| The intervention ‘dose’: intended and actual | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Materials | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Assessment of fidelity | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adherence/compliance of participants to intervention | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |