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# Occupational therapy in multiple sclerosis (Protocol)

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# TABLE OF CONTENTS

[Intervention Protocol]

# Occupational therapy in multiple sclerosis

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## ABSTRACT

### Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

#### *Main objective*

To assess the benefits and harms of occupational therapy interventions for improving daily functioning, participation, and quality of life in people with multiple sclerosis.

#### *Secondary objectives*

To assess whether the effects of occupational therapy interventions differ according to the format of intervention delivery (individually versus group) and to the location of service delivery (outpatient, inpatient, or home-based therapy).

# BACKGROUND

## Description of the condition

Multiple sclerosis (MS), a progressive, inflammatory, demyelinating disease of the brain and spinal cord. It is the most common neurological condition that has a disabling effect on young and middle-aged adults (Barten 2010). In 2020, the estimated number of people living with MS worldwide was 2.8 million (36 per 100,000 people). Exact incidence numbers are lacking, but the estimated average incidence is 2.1 per 100,000 people per year, with substantial regional variation (MS International Federation 2020). This implies that every day, nearly 300 people are diagnosed with MS across the world. Although gender, age at diagnosis, and regional distribution seem to remain the same, prevalence of MS is increasing (Walton 2020). The average age of an MS diagnosis globally is 32 years, an age at which many people are planning families and building careers (Wijeratne 2021). Based on the disease course, the main phenotypes of MS are described: relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), secondary-progressive MS (SPMS), and progressive-relapsing MS (PRMS) (Klineova 2018). Globally, 12% are initially diagnosed with progressive MS and 85% with the relapsing-remitting type (3% is unknown) (Klineova 2018).

Although survival rates have increased in recent decades (Scalfari 2013), people affected by MS have a higher mortality rate and shorter lifetime expectancy of approximately 10 years compared with the general population (Oh 2018; Smyrke 2022).

Symptoms can vary across those living with the condition. Because of the presence of multiple lesions in the white matter of the brain and spinal cord (Dobson 2019), people with MS present functional difficulties such as fatigue, mobility challenges, cognitive difficulty, spasticity, and speech, urinary, and swallowing difficulties (Feinstein 2015; Kesselring 2005). Depression and anxiety are also commonly seen in people with MS across the disease course (Beckerman 2013; Boeschoten 2017; Koch 2008). Moreover, psychological symptoms, such as depression and anxiety, may impact functioning, Feinstein 2014; Morrow 2016, and quality of life of people with MS, Nourbakhsh 2016, and caregivers of people with MS (Chipchase 2001; Giordano 2012).

These functional and psychological impacts of MS consequently affect a wide variety of daily activities, engagements, and routines (Green 2017; Kratz 2017). Additionally, the progressive nature of the disease requires a long-term adaptation and coping process to deal with these challenges in people's everyday life (McCabe 2004). It is therefore important to deliver a variety of interventions and approaches across the spectrum of disease severity to enhance activity, participation, and quality of life (Conradsson 2018; Jansa 2022; Momsen 2022; Strupp 2014).

Occupational therapy is a key service providing clinical care to those living with MS (Chiu 2019; Rommer 2019); occupational therapists are identified as one of the healthcare professionals that are most important to people with MS (Chiu 2019). Despite this, the impact of occupational therapy for MS remains unclear.

## Description of the intervention

Occupational therapy is a client-centred health profession promoting health and wellbeing through everyday activities that people do as individuals, in families and with communities, including things people need to, want to, and are expected to do (World Federation of Occupational Therapists 2012).

The primary goal of occupational therapy is to enable people to participate in meaningful activities of everyday life. Occupational therapists work with people to optimise their ability to manage symptoms, to engage in daily activities, and to participate in a modified activity or environment (World Federation of Occupational Therapists 2012). In practice, occupational therapists assess which activities people want to improve or (re)start, such as paid work or going out with friends. Then, the occupational therapist and people with MS discuss the strategies to reach that goal and jointly agree on a treatment plan. This treatment may consist of training specific skills, advising alternative activity performance (e.g. rescheduling working hours), or suggesting changes in the environment (e.g. home modifications or adjustments to the workspace).

Occupational therapists provide their services for people with MS in clinical settings or in the community, including:

- outpatient or day treatment (located within private or public hospitals, community rehabilitation centres, or specialist rehabilitation centres);
- inpatient rehabilitation (in specialised rehabilitation units or hospital wards, where care is delivered 24 hours per day);
- home-based (at individuals' own homes) (Amatya 2019; Cason 2014).

Occupational therapists optimally support people where they live their lives (American Occupational Therapy Association 2016), therefore occupational therapy services are preferably delivered in and with the relevant context (at home, at work, or at school). From this perspective, it is relevant for this review to explore differences in outcomes when interventions are delivered in the diverse intervention settings.

As in other healthcare professions, services delivered to a person who is in a different physical location than the therapist, so-called 'telehealth', is an evolving field in occupational therapy (American Occupational Therapy Association 2013; Cason 2014; Little 2021; World Federation of Occupational Therapists 2014). Telehealth is a format of service delivery that can be used in all settings, rather than a distinct and separate intervention (Cason 2014).

Occupational therapists work with people on an individual basis, in group sessions, or a combination of those. The advantages of peer group support and encouragement may benefit treatment outcomes (Aterman 2022). On the other hand, individual-based models can target therapy outcomes more closely to the specific problems and needs of each person. It is therefore worthwhile exploring differences in outcomes between these approaches.

The specific intervention methods in occupational therapy may include conscious efforts to optimising therapeutic interactions with people (so-called 'therapeutic use of self'), to improve outcomes, including adherence to treatment; task-specific training (in occupational therapy this is referred to as occupation-based intervention); consultation; education; advocacy (assist the person in finding resources to be successful in activities and ensuring people's rights are respected, e.g. advocate for access to transportation or assistive devices) or problem-solving (Finlayson 2012; Taylor 2009).

The ways in which occupational therapy services are provided differ across countries as well as setting. Also, the period and frequency of service delivery may vary substantially between countries, settings, and specific programmes.

### How the intervention might work

Occupational therapists enable individuals who need help to perform their daily tasks, or occupations, in a way that allows them to participate as optimally as possible in the context where they work, live, and socialise. Because of the client-centred approach, and the emphasis on everyday life, it is expected that a focused intervention for people with MS would improve (social) participation, daily functioning, and quality of life.

To generalise to daily life, the occupational therapist works in real-life contexts and focuses the treatment on that what is meaningful to the people they work with.

Occupational therapy interventions focus on three levels (Finlayson 2012):

- the person (support symptom (self-)management, improve activity performance, promote problem-solving, enhance coping, etc.);
- the activity (optimise methods of activity performance, modify routines and habits, adjust activity demands, etc.);
- the environment (educate caregivers, adapt home, work, or school environment, facilitate social and supportive networks, advise on and train the use of assistive devices, etc.).

These interventions are designed to support restoration of functions, adaptation processes, compensation or remediation of losses, and prevention of complications and functional decline.

Occupational therapy focuses on causing changes to a person and/or their contexts and/or their activities to achieve health and wellbeing. Meaningful activities and engagement in these activities are central causal assumptions underpinning processes of change in occupational therapy (Finlayson 2012; Pentland 2018). Mechanisms of impact of occupational therapy at the level of the individual include physical, cognitive, and social skills, emotional regulation, adapting to difficult or challenging life experiences (resilience), ability to make choices and to use assets and capabilities (self-management), and belief in one's ability to perform meaningful activities (self-efficacy) (Pentland 2018). Impact on the social context may include family members' and carers' coping and support.

### Why it is important to do this review

In the recently published worldwide, multi-stakeholder Priority Setting project, two domains relevant to occupational therapy were ranked within the top five priorities for future research in multiple sclerosis (Celani 2022):

- the efficacy of multidisciplinary care by teams of different social and health professionals in improving health outcomes and experiences for people with MS;
- the impact of psychological health on disease progression in people with MS.

Within multidisciplinary care, the National Institute for Health and Care Excellence (NICE) recommends including occupational therapists as one of the "professionals who can best meet the needs of the person with MS and who have expertise in managing MS" (NICE 2019), p.11).

Providing a response to the latter research priority may also include how important psychological support can be for 'invisible symptoms' like fatigue, pain, bowel/bladder dysfunction, sexual dysfunction, and vision changes (Celani 2022). Occupational therapy can play an important role in managing the visible and invisible symptoms and in living a satisfactory life, despite these symptoms.

Although occupational therapy for people with MS is well-established, the evidence for its effectiveness has yet to be assessed through synthesis of the existing evidence. The latest Cochrane Review was carried out in 2003 and could draw no conclusions as to whether occupational therapy for people with MS was effective (Steultjens 2003). That review only found one randomised controlled trial. No updates have been performed since then. The current review protocol is not a direct update of the review of Steultjens 2003, given the extent to which the methods will have to change to reflect current standards.

The research and evidence-base appear to have grown significantly in recent decades, as can be seen from a scoping review in the area (Quinn 2021). The scope of work of occupational therapists has also changed since 2003, with a shift from the biomedical point of view to a more client-centred and holistic approach (De-Bernardi-Ojuel 2021; Quinn 2021; Yu 2014a; Yu 2014b). The focus is no longer merely on the individual with MS but also on their caregiver(s) and physical and social context, and optimising participation through home-based and community approaches (e.g. Finlayson 2008; Finlayson 2009; Ortiz-Rubio 2016). The review of Cochrane Reviews on rehabilitation for people with MS only included the Cochrane Review on occupational therapy interventions for people with MS by Steultjens and colleagues (2003) (Amatya 2019).

The review of Khan 2015 on telerehabilitation for people with MS includes interventions provided by occupational therapists. However, as these are only interventions using telecommunication technology, this is not an exhaustive overview of occupational therapy interventions in MS. No other published or ongoing Cochrane Reviews are related to the current review proposal.

There is a clear need for more synthesised evidence in occupational therapy and MS to support therapists who want to ensure that their practice is evidence-based. There is an urgent need for occupational therapists, other healthcare practitioners, and people with MS to have an impartial way of making decisions. Researchers would also benefit from having a recent review as it would identify gaps in knowledge and suggestions for future research in occupational therapy for people with MS.

Other beneficiaries of this review include MS caregiver(s), policymakers, guideline developers, health insurance organisations, etc.

## OBJECTIVES

### Main objective

To assess the benefits and harms of occupational therapy interventions for improving daily functioning, participation, and quality of life in people with multiple sclerosis.

### Secondary objectives

To assess whether the effects of occupational therapy interventions differ according to the format of intervention delivery (individually versus group) and to the location of service delivery (outpatient, inpatient, or home-based therapy).

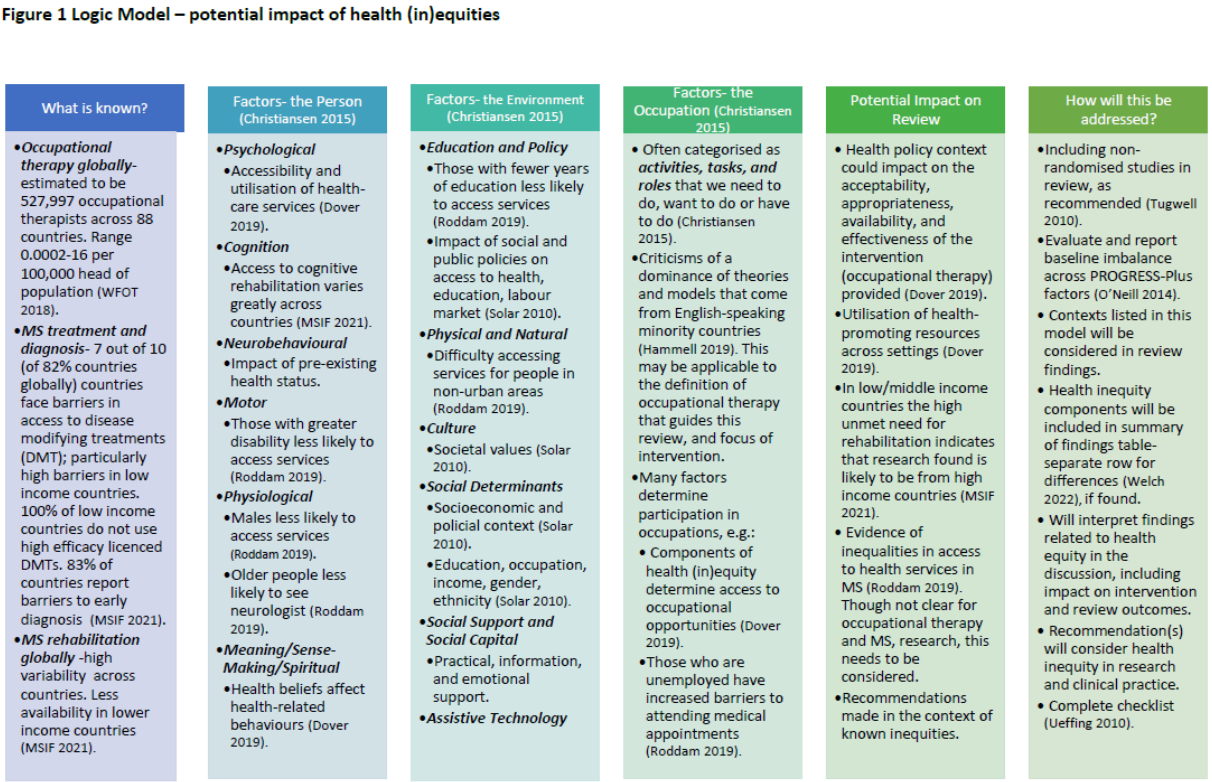
## METHODS

### Criteria for considering studies for this review

#### Types of studies

We will include all randomised and non-randomised controlled studies addressing occupational therapy for people with MS, including the first phase of cross-over studies (to avoid carry-over effects from the initial intervention phase). Non-randomised studies are eligible because of the anticipated dearth of published randomised controlled trials (RCTs) (Quinn 2021). Besides, as described in the recommendations and Figure 1 (Reeves 2022; Tugwell 2010), non-randomised studies of interventions (NRSI) will help to ensure that the team has conducted and written an equity-oriented systematic review, focusing on 'fitness of purpose' of the included evidence.

**Figure 1. Logic Model – potential impact of health (in)equities.**




To be included, non-randomised studies should be prospective and have a comparison group, such as controlled clinical trials, cohort studies (including, if available, case-cohort or nested case-control studies). We will exclude retrospective studies with a comparison group, such as retrospective cohort studies or case-control studies. We will also exclude studies without comparison, such as case series.

We will include all finalised studies regardless of their publication status and language of publication. We will keep a list of ongoing studies and studies without full written reports.

#### Types of participants

We will include studies reporting on people over the age of 18 who are diagnosed with MS (as described in each study). The review will include all types of MS and all disease durations.

We will exclude studies including people with mixed diagnoses unless results are reported separately for the subgroup of people with MS, or if the proportion of people with MS is at least 75% of the total population. We will conduct a sensitivity analysis to examine whether this decision impacts our results.

#### Types of interventions

We will include studies in which authors report that they examined 'occupational therapy', that is an occupational therapy intervention or an intervention delivered by an occupational therapist. When this is not clear, we will include studies on interventions that aim to support people with MS to perform or cope with their daily roles and tasks, according to the definition of occupational therapy in the Background section (World Federation of Occupational Therapists 2012). We will include studies performed in hospital, rehabilitation, and community settings. There will be no restrictions regarding

intensity (frequency (sessions per week), length of session (minutes), and intervention duration (days/weeks)) or mode of delivery.

We will allow co-interventions, such as disease-modifying treatments, regular physical therapy, or others, if they are provided to both the intervention and comparison groups. We will exclude studies addressing multidisciplinary programmes unless they specifically evaluated the unique contribution of occupational therapy in the multidisciplinary approach.

We will include studies that compared occupational therapy with no intervention, standard care/practice, or an active control. We will also include studies directly comparing occupational therapy with another intervention such as a behavioural, physical, or pharmacological intervention.

### Types of outcome measures

Outcomes in occupational therapy are person-driven and measured in terms of satisfaction derived from activity performance, participation and/or improvement in engagement in activity performance and participation (World Federation of Occupational Therapists 2017).

We will include studies that report on any of the outcomes listed below. We expect a wide range of instruments to have measured these outcomes. We will include all variants of instruments and outcome measures; however, by preference we will use the instruments listed below for each outcome.

We will include up to four prespecified time points of measurement for each outcome, including baseline, postintervention, and any follow-up measurement reported (mid-term: up to six months follow-up; long-term: the longest follow-up after six months).

#### *Primary outcomes*

##### Daily functioning

Canadian Occupation Performance Measure (COPM) evaluates individual person-identified outcomes in the areas of self-care, productivity, and leisure (Carswell 2004; Law 1990). First, the most important problems are identified, then people score how they perceive their ability and satisfaction with that performance. Two final scores are obtained: one for performance and one for satisfaction with performance, both on a scale from 1 to 10, with higher scores representing better performance or higher satisfaction. Suggested thresholds for clinically important change (in an outpatient population) range between 0.9 and 1.9 (Eyssen 2011). Several studies have used COPM to describe occupational performance in people with MS (Karhula 2013; Månsson Lexell 2006; Pérez de Heredia-Torres 2020).

##### Quality of life

Multiple Sclerosis Impact Scale (MSIS-29) evaluates the physical (20 items) and psychological (9 items) impact of MS from the perspective of the person with MS (Hobart 2001). All items use the Likert scale scoring format (range 1 to 5). Sum scores for the two subscales are converted to a 0-to-100 scale, with higher scores representing more impact. The suggested threshold for a clinically significant change in physical impact is 7.5 points (Phillips 2014). MSIS-29 is one of the core outcome measures for quality of life of exercise studies in people with MS (Paul 2014).

##### Adverse effects

To assess adverse effects, we will use an exploratory approach (Peryer 2022). We will therefore report the type and frequency of any reported adverse events occurring during the trial or follow-up (across intervention groups), for example, but not limited to: falls, need for medical intervention, need for hospitalisation, MS relapse or exacerbation, mortality or morbidity. When no adverse events are reported in the study, we will report this as such.

#### *Secondary outcomes*

##### Participation

Impact on Participation and Autonomy (IPA) Questionnaire evaluates person-perceived participation (31 items) and perceived problem (8 items) for eight subdomains (Cardol 1999; Cardol 2001). Perceived participation items are scored from 1 = excellent to 5 = very poor. Perceived problem items are graded from 0 (no problem) to 2 (severe problem). The sum score for each domain can be calculated, with a higher score representing a greater perceived restriction in participation or problem. IPA has been used to predict participation and autonomy in 194 people with MS (Karhula 2019).

##### Resilience

Connor-Davidson Resilience Scale (CD-RS) measures how well a person can cope with stress. It consists of 25 items, each scored from 0 to 4. Sum scores range from 0 to 100, with higher scores reflecting greater resilience (Connor 2003). Several studies have used the CD-RS to explore resilience in MS (Broche-Pérez 2022; Koelmel 2017; Swanepoel 2020).

##### Self-efficacy

Multiple Sclerosis Self-Efficacy Scale (MSSE) measures self-efficacy specifically in individuals with MS (Chiu 2015; Schwartz 1996). The original version contained 24 items, but the revised version retained 18 items scored from 10 to 100 (anchored by 10 = very uncertain, 50 = moderately certain, and 100 = very certain). There are two subdomains: Function and Control (9 items each). MSSE is used to study self-efficacy in people with MS (Kayes 2011; Sinnakaruppan 2010).

##### Self-management

Multiple Sclerosis Self-Management Scale (MSSM) addresses self-management knowledge and behaviour among individuals with multiple sclerosis (Bishop 2007; Bishop 2011). The scale has 24 items and 5 factors (healthcare provider relationship/communication, treatment adherence/barriers, social/family support, MS knowledge & information, and health maintenance behaviour). Items are scored on a Likert-type scale ranging from 1 (completely disagree) to 5 (agree completely). Higher scores mean better self-management. MSSM is used to study self-management in MS (Efendi 2022; Wilski 2016).

##### Mood

Hospital Anxiety and Depression Scale (HADS) measures feelings of anxiety and depression without reference to the source of the complaints (Bjelland 2002; Zigmond 1983). It consists of 14 items: 7 each for the two subscales of depression and anxiety. Each item is scored on a 4-point scale (0 to 3). Total scores for the subscales range from 0 to 21, with higher scores representing more depression and anxiety. Scores between 0 and 7 for each subscale are within normal ranges. HADS is frequently used as a screening

tool for depression in MS and to describe relationships with other domains, like participation (Allataifeh 2020; Wu 2021).

#### Impact on caregivers

Caregiver Strain Index (CSI) examines subjective and objective elements of caregiver strain and contains 13 items to be scored 0 (no), 1 (sometimes), or 2 (on a regular basis) (Robinson 1983). Thornton and Travis adapted the CSI for relevance to long-term caregivers, which also improved its psychometric properties (Thornton 2003). Several studies have used CSI to describe the perspective of caregivers of people living with MS (García-Domínguez 2019; Sarhan 2022).

## Search methods for identification of studies

Searches will be motivated directly by the eligibility criteria set. We will conduct an extensive computerised search in order to minimise publication bias, language bias, and to identify as much relevant literature as is possible. The Participant, Intervention, Comparison, and Outcomes (PICO) for the search have been defined by the eligibility criteria. The planned search will draw on appropriate subject headings and text words based on the eligibility criteria.

We will keep a detailed record of the search process which we will report in the review publication to allow for replication. This will include the sources searched, when the search was conducted, by whom, and the search terms used (Lefebvre 2022). We will follow the guidance from the PRISMA-Search (PRISMA-S) Extension in the reporting of the search (Rethlefsen 2021).

Prior to review publication, we will re-run the search to identify any recent additions to databases and registers. Any new findings will be incorporated prior to publication of the Cochrane Review.

The search strategy will have three key concepts: multiple sclerosis (P), occupational therapy (I), and study design. The planned search will include both randomised and non-randomised controlled studies (all controlled trials). We will not include a comparator in the search terms, as this may lead to the inadvertent exclusion of relevant records. To increase precision and generalisability of the review results, the search will not be restricted by date or language.

### Electronic searches

We will complete systematic searches of the following electronic databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1946 to present), Embase (1974 to present), CINAHL (Cumulative Index to Nursing and Allied Health Literature; EBSCOhost; 1982 to present), PsycINFO (1800 to present), Web of Science.

The search strategy, developed in consultation with an Information Specialist, can be found in Appendix 1 (Avau 2021). We will keep a record of the database searched, along with the interface used, and the date ranges of the search (from inception to search date). If there are any changes that differ from what is reported in the protocol, we will report this in the 'Differences between protocol and review' section of the review.

### Searching other resources

We will screen the reference lists of included studies. We will also screen reference lists of similar reviews that have been conducted in the area. We will examine any retraction statements and errata of included studies.

We will search the following clinical trial registers: ISRCTN registry (www.isrctn.com/), ClinicalTrials.gov (www.clinicaltrials.gov/), and the World Health Organization International Clinical Trials Registry Platform (www.who.int/clinical-trials-registry-platform). In most countries there is no legislation in place that requires the registration of non-clinical trials of investigational medicinal products (CTIMPs). There is, however, an increasing awareness of the importance of registering all interventional trials, therefore we hope to find ongoing and unpublished trials through this method. We will contact the Restoring Invisible and Abandoned Trials (RIAT) support centre during this process if necessary.

We will also undertake a search of the grey literature, specifically research theses, reports, and conference abstracts. Specifically, we will search the Institute for Scientific and Technical Information database, which allows access to all records in greynet.org and all records previously hosted on the System for Information on Grey Literature database. In addition, we will further search grey literature through the Healthcare Management Information Consortium database, the National Technical Information Service, and PsycEXTRA.

We will search research newsletters of multiple sclerosis societies, and send letters of request for information directly to researchers/research teams.

We will use URLs of all websites, and keep a record of sources accessed. We will also record reference lists searched and investigators contacted as part of the search process.

## Data collection and analysis

We will use EndNote reference manager software to manage the retrieved records (EndNote). We will produce a PRISMA diagram with an overview of the search results, including 1) the total number of records retrieved from all database sources; 2) the number of records that are included and excluded at each stage of the screening process, with reasons for exclusion of the excluded studies; and 3) the number of records from all other sources.

### Selection of studies

We will use Covidence to support the review process (Covidence). We will take the following steps when selecting studies.

1. Merge records from all sources. One person will merge the studies from all sources into one database and duplicates will be removed. To deduplicate, we will follow the steps described by Bramer 2016, using EndNote software.
2. Pilot the eligibility criteria. This will involve two people screening the same set of 50 records working independently. Once the records have been screened, the two people will consult and assess the level of agreement. Amendments will then be made if the criteria are not sufficiently clear following this.
3. Screen abstract and title. Two review authors will independently screen the abstract and title using the eligibility criteria. The two review authors will discuss disagreements; if no consensus can be reached, a third person will be consulted to resolve any disputes.

4. Review full text for eligibility.
   a. Retrieve the full texts of all records deemed potentially relevant. The two review authors will screen these using the same eligibility criteria.
   b. Link together multiple reports of the same study. By seeking detail through trial registration numbers or contacting the authors of the reports, we will bring together the key authors or multiple papers that report on the same trial to decide on inclusion. This will be done in order to reduce potential bias from including more than one source of the same trial. The studies, rather than study reports, are the record of interest.
   c. If needed, for example if it is unclear if a study has been conducted by an occupational therapist or if the intervention is occupational therapy, or if we are unsure what outcomes have been used, we will correspond with trial investigators.
5. Make final decision on inclusion. This will be decided by two people working independently. Disputes will be managed through a live online meeting with all review authors to enable resolution of any uncertainties or misunderstandings.
6. Record any ongoing trials that fit our inclusion criteria.

The review authors involved in study selection will have no conflict of interest (e.g. they will not have worked on or published any study that could meet the review eligibility criteria). At least one review author is familiar with the review area (i.e. occupational therapy or MS, or both); the other review authors will not need to be content experts.

**Data extraction and management**

As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022a), we will extract the following data, where available. Two members of the review team will extract the data independently.

- Source: study ID; report ID; review author ID; citation and contact details; funding details.
- Eligibility: confirm eligibility or reason for exclusion.
- Participants: age; sex; occupation; year of diagnosis; MS phenotype; degree of disability; total number randomised; diagnostic criteria; comorbidity; race/ethnicity; geographical area, inclusion and exclusion criteria.
- Outcomes (collected and reported): critical outcomes and important outcomes; specific outcome measure or person-reported outcome used. We will report outcome definitions, along with units of measurement, and upper and lower limits, where applicable.
- Study design: RCT/controlled clinical trial (CCT); total study duration.
- Adverse events.
- Intervention: description of the intervention (including intervention details), description of the comparison interventions, intervention setting, geographical location, professional delivering the intervention, caregiver involvement; number of intervention groups; duration and frequency of the intervention and follow-up; blinding; integrity/fidelity of the intervention. We will use the Template for Intervention Description and Replication (TIDieR) for the description of studies (Hoffmann 2014).
- Results: number of participants allocated to each group; numbers included in the analysis; summary data for each group; estimate of effect with confidence interval and P value; subgroup analyses.

Potential effect modifiers include disease duration, baseline level of disability, age, comorbidity, baseline functional performance, social support. We will extract these from studies when available (Karim 2021; Marrie 2017).

We will contact study authors when data are missing. Each person involved in data extraction will use an electronic data extraction form, which will include space for extraction of all of the above data. The data extraction form will be piloted on six studies by two review authors in order to ensure uniformity of extraction and reliability of the form across review authors. Following this, experiences will be discussed with the two review authors and changes will be made accordingly. Any disagreements in data extraction will be discussed in online meetings, with a third member of the review team involved if necessary. This team member (and those extracting the data) will have no conflict of interest (i.e. publications or ongoing research in the area of occupational therapy and MS).

In addition to the data extraction form, we will include a 'Characteristics of included studies' table with the study methods, participants, interventions, outcomes, and any additional brief notes for each study.

We will also include a 'Characteristics of excluded studies' table with all studies that were reviewed at full text but not included in the review. Decisions made about eligibility will be clearly documented. Furthermore, we will include a 'Characteristics of ongoing studies' table to facilitate future updates of the review.

**Assessment of risk of bias in included studies**

We will use the Cochrane RoB 2 tool to assess the risk of bias in the included RCTs (Sterne 2019). For included cross-over trials, we will only include the first period when both groups start at the same time, therefore we will also use RoB 2 for cross-over trials. Importantly, this tool assesses the risk of bias per outcome and not per study (Higgins 2022b). We will record the key information used to decide on the level of risk assigned to each study. As outlined in the tool, we will assess five domains for risk of bias:

- the randomisation process;
- deviations from the intended intervention;
- missing outcome data;
- measurement of the outcome;
- selection of the reported result.

We will assess the risk of bias in each domain and the overall risk of bias as 'low risk', 'some concerns', or 'high risk' (Sterne 2019). We will focus on the effect of assignment to the interventions at baseline, regardless of whether the interventions are received as intended (the 'intention-to-treat effect') (Higgins 2022b).

For included non-randomised studies, we will use the Risk of Bias In Non-randomised Studies of Interventions (ROBINS-I) tool to determine risk of bias for each outcome (Sterne 2016). This tool consists of seven domains of concern (domains 2 to 5 of RoB 2 in addition to confounding, selection bias, and measurement classification of interventions), and categorises studies as 'low risk', 'moderate risk', 'serious risk', or 'critical risk' of bias, for each outcome.

Two review authors (COM and one other review author without conflict of interest) will perform the risk of bias assessment independently, using the RoB 2 Excel templates. Any disagreements will be discussed and resolved via consensus. A record of disagreements and outcomes, along with the rationale for final decision, will be kept by the review team. As advised in the *Cochrane Handbook* when assessing overall risk of bias (Higgins 2022b), we will ensure that the overall results have at least the same risk of bias (if not more severe) than any of the individual domains assessed.

We will use Covidence to support and record the risk of bias assessment of included studies (Covidence). We will include a risk of bias table with all decisions made in relation to risk of bias in each domain, along with a rationale for our decisions. This information will be available for each study and outcome included in the review.

### Measures of treatment effect

The data to be included in the meta-analysis will be continuous and may not be collected using the same measurement scale. As such, the effect measure for the analysis will be the standardised mean difference (SMD). This will provide an absolute measure of treatment effect between groups (occupational therapy and control). The SMD allows for comparison across studies and provides an expression of the size of the effect of the intervention, relative to study variability (Suero 2021). We will use data from endpoints of studies.

If we find that the same continuous outcome is used across studies, we will use the mean difference (MD). For dichotomous outcomes, we will use the risk ratio (RR). We anticipate that data may be sparse due to a small number of studies and participants. For this reason, we will use Mantel-Haenszel methods, as they have stronger statistical properties when data are sparse using a random-effects meta-analysis method (Deeks 2022). We will calculate confidence intervals (CI) as a measure of precision.

The review team will make an overall decision on the appropriateness of meta-analysis following data extraction, review of the availability of usable data including clinical characteristics of the studies (participants, interventions, and outcomes), and assessment of risk of bias of the included studies.

### Unit of analysis issues

If studies compare occupational therapy with more than one comparison group, we will select the group that is most similar to usual care as our main control group.

As cross-over trials are not suitable for the intervention of our review due to anticipated long-lasting effects, we will only consider the first period of such trials. Subsequently, we will treat cross-over trials as standard RCTs, including analysis.

### Dealing with missing data

Where possible, we will assess the extent of data missing from included studies. It is expected that any missing data will be missing at random. We will record the amount of data missing, the distribution of missing data across study arms, and the reasons provided for the missing outcomes. If studies have used imputation for missing data, then the review team will decide whether the assumptions made are plausible or if they had the potential to bias the study results, using existing guidance in this area (Jakobsen 2017).

If it is not possible to obtain the missing data from the study authors, a small amount of missing data may be imputed by the review team. We anticipate the data most likely to be missing to be the standard deviation (SD). If SD is missing, we will take the SD of a similar trial (or the mean SD of all included trials). This approach has been found to be appropriate and obtains approximately correct results (Furukawa 2006). If a large amount of summary data is missing, it will not be imputed, and the study will not be included in meta-analysis; however, the study will be included in the systematic review.

We will make a note of any data that have been imputed, along with the rationale and decision for the imputation. We will also conduct a sensitivity analysis to assess the impact of imputed data on the overall results. We will address the potential impact of missing data in the Discussion section of the review.

### Assessment of heterogeneity

We will initially assess heterogeneity using visual inspection of the forest plot, and $Chi^2$ test included in the plot. We will then quantify heterogeneity using the $I^2$ estimate. We will also provide a narrative description of any heterogeneity across included studies and the potential causes of it.

If we identify very high levels of unexplained heterogeneity in the meta-analysis, for example if studies are too dissimilar to compare or if the $I^2$ is above 90%, we will not complete the meta-analysis, as it would not be appropriate.

### Assessment of reporting biases

We will evaluate the possibility of non-reporting bias by means of contour-enhanced funnel plots, if meta-analyses include at least 10 studies (Peters 2008).

### Data synthesis

We will use Review Manager Web to conduct analyses (RevMan Web 2022).

Given the broad nature of the intervention (occupational therapy) in this review, and the resultant likelihood of increased heterogeneity from a clinical (e.g. differences in intervention, intensity, duration) and methodological (e.g. differences in outcomes, trial design), we will use a random-effects model in the meta-analysis. We will take a two-step approach for each study, whereby we will calculate a uniform measure of effect (SMD, RR, or MD + 95% CI). We will then pool the results of individual studies.

We have selected outcomes and effect measures for the analysis (see Criteria for considering studies for this review). If a meta-analysis is deemed appropriate (based on studies included in the review), the inverse variance method will be used. Using this approach, each study will be weighted as the inverse of their effect estimate. We will present a forest plot to summarise the results of the meta-analysis.

For cross-over-trials, we will use the first phase only and analyse as parallel RCT evidence.

In a separate analysis, we will assess non-randomised studies in detail with respect to the PICO elements before data synthesis, as suggested in Section 24.6.2 of the *Cochrane Handbook* (Reeves 2022). We will only pool the results of non-RCTs if the overall risk of bias is low to moderate and adjusted results are presented for at least baseline level of disability, disease duration, and comorbidity (Karim 2021; Marrie 2017). We will use the inverse method employing random-effects meta-analysis (Deeks 2022).

Any data that cannot be included in meta-analysis will be reported in a narrative form and summarised in tabular format, using Synthesis Without Meta-analysis (SWiM) guidelines (Campbell 2020).

### Subgroup analysis and investigation of heterogeneity

If possible, we will conduct two subgroup analyses that are of clinical importance to the review question. Firstly, we will investigate any differences in the format of intervention delivery, specifically occupational therapy that is delivered in an individual format or in a group format. The second subgroup analysis will look at differences in the effects of the intervention across the locations of service delivery: inpatient, outpatient or day treatment and home-based settings. Both analyses are of importance to clinicians (see Description of the intervention). We will require a minimum of two studies for each subgroup analysis. Subgroups will be assessed using the statistical algorithms for subgroup differences in Review Manager Web (Deeks 2022).

### Sensitivity analysis

We will conduct a sensitivity analysis excluding studies with high risk of bias to explore the influence of risk of bias on the overall conclusions made and precision of the results. Specifically, sensitivity analysis will be applied through the exclusion of studies that are considered to have an overall high risk of bias (as per Cochrane RoB 2 tool) and serious or critical risk of bias for non-randomised trials (as per the ROBINS-I tool). We will report the results in a summary table. We will use Review Manager Web to conduct the sensitivity analysis (RevMan Web 2022).

### Summary of findings and assessment of the certainty of the evidence

#### *Summary of findings*

We will present the results of the review in a summary of findings table. We will produce the table using GRADEpro GDT software (GRADEpro GDT). As suggested by Sinnakaruppan 2010, we will include in the table the key information from the review for each outcome: the number of studies and the number of participants included in the analysis and the absolute and relative magnitude of effect measured. The key comparison, treatment as usual or usual care, will be described in the table along with the outcomes that are of most importance to this review: daily functioning, quality of life, and adverse events. Baseline and postintervention measurement will be prioritised in the summary of findings table. We have made every effort here to prespecify the most important outcomes. However, if during the review process, it is necessary to include an additional outcome in the summary of findings table that is not listed in the protocol, we will provide the rationale for its inclusion in the review (Kirkham 2010).

If meta-analysis is not possible, then we will take a narrative approach to the presentation of the results of the review. We will present a GRADE assessment of the overall certainty of the body of evidence. We will include the rationale for any assumed risk presented, along with the source. We will include explanations, using the guidance provided by Santesso 2016.

#### *Certainty of evidence*

Two review authors will rate the certainty of evidence for each outcome based on the five GRADE domains: risk of bias (within and across studies), consistency of effect, imprecision, indirectness, and publication bias (Atkins 2004; Guyatt 2008; Guyatt 2011). The evidence for each outcome will be categorised as high, moderate, low, or very low. We will justify and document each rating using GRADEpro GDT (GRADEpro GDT). We will follow the guidance provided in Chapter 14 of the *Cochrane Handbook* (Schünemann 2022): results of the RoB 2/ROBINS-I assessments feed directly into the GRADE assessment domain risk of bias: 'low' risk of bias would indicate 'no limitation'; 'some concerns' would indicate either 'no limitation' or 'serious limitation'; and 'high' risk of bias would indicate either 'serious limitation' or 'very serious limitation'. 'Critical' risk of bias on ROBINS-I would indicate extremely serious limitations in GRADE.

#### *Consideration of equity*

A logic model (see Figure 1) has been developed to understand the potential impact of health equity on the intervention. The model has been developed based on an occupational therapy model of practice (Christiansen 2015), existing framework of health inequity (Dover 2019), and World Health Organization social determinants of health (Solar 2010). The model describes what is known about health equity that may be important for the review. It then lists health equity components under the headings of a commonly used model of occupational therapy practice (Christiansen 2015; Hammell 2019; MSIF 2021; Roddam 2019; World Federation of Occupational Therapists 2018).

The impact of these components on the review have been listed, along with how this will be addressed in the review. Specifically, we will:

- include non-randomised studies in review (Tugwell 2010);
- extract data relating to participant factors which may result in inequitable access to interventions using the PROGRESS-Plus framework (O'Neill 2014). This will include extracting data related to place of residence, race/ethnicity, language, occupation, gender, religion, socioeconomic status, social capital, and data related to personal characteristics potentially associated with discrimination (e.g. age or disability). The logic model developed describes how some of these factors may impact on health equity;
- evaluate baseline imbalance across PROGRESS-Plus factors (O'Neill 2014);
- include health inequity components in summary of findings table. We will include a separate row for differences, if found (Welch 2022);
- interpret findings related to health equity in the discussion, including impact on intervention and review outcomes (Welch 2022);
- consider health inequity in research and clinical practice in recommendations provided;

- use the Equity Checklist for Systematic Review Authors (Ueffing 2011), and report on this along with the findings of the review.

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- Sign-off Editor (final editorial decision): Robert Boyle, Cochrane's Editorial Board, Imperial College London, UK
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Samuel Hinsley, Central Editorial Service
- Editorial Assistant (conducted editorial policy checks and supported editorial team): Leticia Rodrigues, Central Editorial Service
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- Peer reviewers (provided comments and recommended an editorial decision): Cara L Brown, College of Rehabilitation Sciences, University of Manitoba (clinical review), Herbert Karpatkin, Physical Therapy Department, Hunter College (clinical review), Iván Pérez-Neri, National Institute of Neurology and Neurosurgery Manuel Velasco Suárez (consumer review), Assoc Prof Vanessa Jordan (methods review). One additional peer reviewer provided search peer review but chose not to be publicly acknowledged.

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# APPENDICES

## Appendix 1. Search strategy: search strings for different databases

Appendix 1 Search strategy

MEDLINE/PUBMED

| |
|---|
| #53 #51 AND #52 |
| #52 (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals [mh] NOT humans [mh]) |
| #51 #19 AND #50 |
| #50 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 |
| #49 Rehabilitat*[Title/Abstract] |

*(Continued)*

| |
|---|
| #48 "Rehabilitation"[Mesh] |
| #47 "energy conservation" [Title/Abstract] OR "energy management" [Title/Abstract] |
| #46 "joint protection"[Title/Abstract] |
| #45 dexter*[Title/Abstract] |
| #44 "assistive device*"[Title/Abstract] OR "assistive technolog*"[Title/Abstract] |
| #43 leisur* [Title/Abstract] |
| #42 "Self Care"[Title/Abstract] OR “self-efficacy*"[Title/Abstract] OR selfcare* [Title/Abstract] |
| #41 "Self Care"[Mesh] |
| #40 "Exercise Therap*"[Title/Abstract] |
| #39 "Exercise Therapy"[Mesh] |
| #38 Ergonomic*[Title/Abstract] |
| #37 "Ergonomics"[Mesh] |
| #36 Counseling[Title/Abstract] OR Counselling[Title/Abstract] |
| #35 "Counseling"[Mesh] |
| #34 "Health Literacy"[Title/Abstract] |
| #33 "Health Literacy"[Mesh] |
| #32 "patient education"[Title/Abstract] |
| #31 "Patient Education as Topic"[Mesh] |
| #30 Splint*[Title/Abstract] |
| #29 "Splints"[Mesh] |
| #28 "self-help device*"[title/abstract] |
| #27 "Self-Help Devices"[Mesh] |
| #26 "Daily Life Activit*"[title/abstract] |
| #25 ADL[title/abstract] |
| #24 "Daily Living Activit*"[title/abstract] |
| #23 "Activities of Daily Living"[Mesh] |
| #22 ergotherap*[Title/Abstract] OR ”ergo therap*”[Title/Abstract] |
| #21 “occupational therap*" [Title/Abstract] |

*(Continued)*

| |
|---|
| #20 "Occupational Therapy"[Mesh] |
| #19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 |
| #18 "Multiple Sclerosis"[Mesh:noexp] |
| #17 "encephalomyelitis"[Title/Abstract] OR "encephalo-myelitis"[Title/Abstract] |
| #16 "transverse myelitis"[Title/Abstract] |
| #15 "clinically isolated syndrome"[Title/Abstract] |
| #14 "demyelinating disorder"[Title/Abstract] |
| #13 adem[Title/Abstract] |
| #12 "demyelinating disease"[Title/Abstract] OR "Demyelinating Autoimmune"[Title/Abstract] |
| #11 "devic disease"[Title/Abstract] OR "Devic Syndrome"[Title/Abstract] OR "Devic's Syndrome"[Title/Abstract] OR "Devics Syndrome"[Title/Abstract] OR "Devic Disease"[Title/Abstract] OR "Devic's Disease"[Title/Abstract] OR "Devics Disease"[Title/Abstract] |
| #10 "optic neuritis"[Title/Abstract] |
| #9 "neuromyelitis optica"[Title/Abstract] OR "NMO spectrum disorder"[Title/Abstract] |
| #8 "multiple sclerosis"[Title/Abstract] |
| #7 "Myelitis, Transverse"[Mesh] OR "Transverse Myelopathy"[Title/Abstract] |
| #6 "Encephalomyelitis, Acute Disseminated"[Mesh] |
| #5 "Demyelinating Autoimmune Diseases, CNS"[Mesh:noexp] |
| #4 "Optic Neuritis"[Mesh] |
| #3 "Demyelinating Diseases"[Mesh:noexp] |
| #2 "Multiple Sclerosis, Relapsing-Remitting"[Mesh] |
| #1 "Multiple Sclerosis, Chronic Progressive"[Mesh] |

CENTRAL

| |
|---|
| #49 #18 AND #48 |
| #48 {OR #19-#47} |
| #47 rehabilitat*:ti,ab,kw |
| #46 MeSH descriptor: [Rehabilitation] explode all trees |

*(Continued)*

| |
|---|
| #45 "energy conservation":ti,ab,kw OR "energy management":ti,ab,kw |
| #44 "joint protection":ti,ab,kw |
| #44 dexter*:ti,ab,kw |
| #43 "assistive device*":ti,ab,kw OR "assistive technolog*":ti,ab,kw |
| #42 leisur*:ti,ab,kw |
| #41 "self care":ti,ab,kw OR "self-care":ti,ab,kw OR “self-efficacy*" ti,ab,kw |
| #40 MeSH descriptor: [Self Care] explode all trees |
| #39 "exercise therap*":ti,ab,kw |
| #38 MeSH descriptor: [Exercise Therapy] explode all trees |
| #37 ergonomic*:ti,ab,kw |
| #36 MeSH descriptor: [Ergonomics] explode all trees |
| #35 counseling:ti,ab,kw OR counselling:ti,ab,kw |
| #34 MeSH descriptor: [Counseling] explode all trees |
| #33 "health literacy*":ti,ab,kw |
| #32 MeSH descriptor: [Health Literacy] explode all trees |
| #31 MeSH descriptor: [Patient Education as Topic] explode all trees |
| #30 "patient education":ti,ab,kw |
| #29 splint*:ti,ab,kw |
| #28 MeSH descriptor: [Splints] explode all trees |
| #27 "self-help device*":ti,ab,kw |
| #26 MeSH descriptor: [Self-Help Devices] explode all trees |
| #25 "daily life activit*":ti,ab,kw |
| #24 ADL:ti,ab,kw |
| #23 "daily living activit*":ti,ab,kw |
| #22 MeSH descriptor: [Activities of Daily Living] explode all trees |
| #21 ergotherap*:ti,ab,kw OR "ergo therap*" ti,ab,kw |
| #20 "occupational therap*":ti,ab,kw |
| #19 MeSH descriptor: [Occupational Therapy] explode all trees |

*(Continued)*

| |
|---|
| #18 {OR #1-#17} |
| #17 encephalomyelitis:ti,ab,kw OR "encephalo-myelitis" ti,ab,kw |
| #16 "transverse myelitis":ti,ab,kw OR "Transverse Myelopathy": ti,ab,kw |
| #15 "clinically isolated syndrome":ti,ab,kw |
| #14 "demyelinating disorder":ti,ab,kw |
| #13 adem:ti,ab,kw |
| #12 "demyelinating disease":ti,ab,kw OR "Demyelinating Autoimmune":ti,ab,kw |
| #11 "devic disease":ti,ab,kw OR"Devic Syndrome":ti,ab,kw OR "Devic's Syndrome":ti,ab,kw OR "Devics Syndrome":ti,ab,kw OR "Devic Disease":ti,ab,kw OR "Devic's Disease":ti,ab,kw OR "Devics Disease":ti,ab,kw |
| #10 "optic neuritis":ti,ab,kw |
| #9 "neuromyelitis optica":ti,ab,kw |
| #8 "multiple sclerosis":ti,ab,kw |
| #7 MeSH descriptor: [Myelitis, Transverse] explode all trees |
| #6 MeSH descriptor: [Encephalomyelitis, Acute Disseminated] explode all trees |
| #5 MeSH descriptor: [Demyelinating Autoimmune Diseases, CNS] this term only |
| #4 MeSH descriptor: [Optic Neuritis] explode all trees |
| #3 MeSH descriptor: [Demyelinating Diseases] this term only |
| #2 MeSH descriptor: [Multiple Sclerosis, Relapsing-Remitting] explode all trees |
| #1 MeSH descriptor: [Multiple Sclerosis] this term only |

EMBASE

| |
|---|
| #57 #53 NOT #56 |
| #56 #54 OR #55 |
| #55 (‘animal experiment’/de NOT (‘human experiment’/de OR ‘human’/de)) |
| #54((rat:ti,tt OR rats:ti,tt OR mouse:ti,tt OR mice:ti,tt OR swine:ti,tt OR porcine:ti,tt OR murine:ti,tt OR sheep:ti,tt OR lambs:ti,tt OR pigs:ti,tt OR piglets:ti,tt OR rabbit:ti,tt OR rabbits:ti,tt OR cat:ti,tt OR cats:ti,tt OR dog:ti,tt OR dogs:ti,tt OR cattle:ti,tt OR bovine:ti,tt OR monkey:ti,tt OR monkeys:ti,tt OR trout:ti,tt OR marmoset*:ti,tt) AND ‘animal experiment’/de) |
| #53 #51 AND #52 |

*(Continued)*

| |
|---|
| #52 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti |
| #51 #16 AND #50 |
| #50 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 |
| #49 rehabilitat*:ab,ti |
| #48 'rehabilitation'/exp |
| #47 'energy conservation':ab,ti OR 'energy management':ab,ti |
| #46 'energy conservation':ab,ti |
| #45 'energy conservation'/exp |
| #44 'joint protection':ab,ti |
| #43 dexter*:ab,ti |
| #42 'assistive device*':ab,ti OR 'assistive technol*':ab,ti |
| #41 'assistive technology'/exp |
| #40 'self help device'/exp |
| #39 leisur*: ab,ti |
| #38 'leisure'/exp |
| #37 'self care':ab,ti OR ‘self-efficacy*’:ab,ti |
| #36 'self care'/exp |
| #35 'exercise therap*':ab,ti |
| #34 'kinesiotherapy'/exp |
| #33 ergonomic*:ab,ti |
| #32 'ergonomics'/exp |
| #31 'counseling'/exp |
| #30 'health literacy':ab,ti |
| #29 'health literacy'/exp |
| #28 'patient education':ab,ti |
| #27 'patient education'/exp |

*(Continued)*

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|---|
| #26 splint*:ab,ti |
| #25 'splint'/exp |
| #24 'self help device*':ab,ti OR 'self-help device*':ab,ti |
| #23 'self help device'/exp |
| #22 ADL:ab,ti |
| #21 'daily living activit*':ab,ti OR 'daily life activit*':ab,ti |
| #20 'daily life activity'/exp |
| #19 ergotherap*:ab,ti OR 'ergo therap*':ab,ti |
| #18 'occupational therap*':ab,ti |
| #17 'occupational therapy'/exp |
| #16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 |
| #15 encephalomyelitis:ab,ti OR 'encephalo-myelitis':ab,ti |
| #14 'transverse myelitis':ab,ti OR 'Transverse Myelopathy':ab,ti |
| #13 'clinically isolated syndrome':ab,ti |
| #12 'demyelinating disorder':ab,ti |
| #11 adem:ab,ti |
| #10 'demyelinating disease':ab,ti OR 'Demyelinating Autoimmune':ab,ti |
| #9 'devic disease':ab,ti OR 'Devic Syndrome':ab,ti OR 'Devic's Syndrome':ab,ti OR 'Devics Syndrome':ab,ti OR 'Devic Disease':ab,ti OR 'Devic's Disease':ab,ti OR 'Devics Disease':ab,ti |
| #8 'optic neuritis':ab,ti |
| #7 'neuromyelitis optica':ab,ti |
| #6 'multiple sclerosis':ab,ti |
| #5 'transverse myelitis'/exp |
| #4 'acute disseminated encephalomyelitis'/exp |
| #3 'optic neuritis'/exp |
| #2 'demyelinating disease'/de |
| #1 'multiple sclerosis'/exp |

CINAHL

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|---|
| S54 S52 AND S53 |
| S53 (MH randomized controlled trials OR MH double-blind studies OR MH single-blind studies OR MH random assignment OR MH pretest-posttest design OR MH cluster sample OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR MH (placebos) OR PT (randomized controlled trial) OR AB (CONTROL W5 GROUP) OR MH (CROSSOVER DESIGN) OR MH (COMPARATIVE STUDIES) OR AB (CLUSTER W3 RCT)) NOT ((MH ANIMALS+ NOT MH HUMAN) OR (MH (ANIMAL STUDIES) NOT MH (HUMAN)) OR (TI (ANIMAL MODEL) NOT MH (HUMAN))) |
| S52 S17 AND S51 |
| S51 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 |
| S50 TI rehabilitat* OR AB rehabilitat* |
| S49 (MH "Rehabilitation+") |
| S48 TI "Energy management" OR AB "Energy management" |
| S47 TI "Energy Conservation" OR AB "Energy Conservation" |
| S46 (MH "Energy Conservation") |
| S45 TI "joint protection" OR AB "joint protection" |
| S44 TI dexter* OR AB dexter* |
| S43 TI ("assistive device*" OR "assistive technolog*" ) OR AB ("assistive device*" OR "assistive technolog*" ) |
| S42 TI leisure* OR AB leisure* |
| S41 (MH "Leisure Activities+") |
| S40 TI ( "Self Care" OR "Self-Care" ) OR AB ( "Self Care" OR "Self-Care" ) OR TI “self-efficacy*” OR AB “self-efficacy*” |
| S39 (MH "Self Care+") |
| S38 TI exercise therap* OR AB exercise therap* |
| S37 (MH "Therapeutic Exercise+") |
| S36 TI ergonomic* OR AB ergonomic* |
| S35 (MH "Ergonomics+") |
| S34 TI ( counseling OR counselling ) OR AB ( counseling OR counselling ) |
| S33 (MH "Counseling+") |
| S32 TI "Health Literacy" OR AB "Health Literacy" |

*(Continued)*

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|---|
| S31 (MH "Health Literacy+") |
| S30 TI patient education OR AB patient education |
| S29 (MH "Patient Education+") |
| S28 TI splint* OR AB splint* |
| S27 (MH "Splints+") |
| S26 TI ( self-help device* OR self help device* ) OR AB ( self-help device* OR self help device* ) |
| S25 (MH "Assistive Technology Devices+") |
| S24 TI Daily live activit* OR AB Daily live activit* |
| S23 TI ADL OR AB ADL |
| S22 TI Daily Living activit* OR AB Daily Living activit* |
| S21 (MH "Activities of Daily Living+") |
| S20 TI ergotherap* OR AB ergotherap* OR TI “ergo therap*” OR AB “ergo therap*” |
| S19 TI Occupational Therap* OR AB Occupational Therap* |
| S18 (MH "Occupational Therapy+") |
| S17 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 |
| S16 TI encephalomyelitis OR AB encephalomyelitis OR TI “encephalo-myelitis” OR AB “encephalo-myelitis” |
| S15 TI "transverse myelitis" OR AB "transverse myelitis" OR TI “Transverse Myelopathy” OR AB “Transverse Myelopathy” |
| S14 TI "clinically isolated syndrome" OR AB "clinically isolated syndrome" |
| S13 TI "demyelinating disorder" OR AB "demyelinating disorder" |
| S12 TI adem OR AB adem |
| S11 TI "demyelinating disease" OR AB "demyelinating disease" OR TI “Demyelinating Autoimmune” OR AB “Demyelinating Autoimmune” |
| S10 TI "devic disease" OR AB "devic disease" OR TI “Devic Syndrome” OR AB “Devic Syndrome” OR TI “Devic's Syndrome” OR AB “Devic's Syndrome” OR TI “Devics Syndrome” OR AB “Devics Syndrome” OR TI “Devic Disease” OR AB “Devic Disease” OR TI “Devic's Disease” OR AB “Devic's Disease” OR TI “Devics Disease” OR AB “Devics Disease” |
| S9 TI "optic neuritis" OR AB "optic neuritis" |
| S8 TI "neuromyelitis optica" OR AB "neuromyelitis optica" |
| S7 TI "multiple sclerosis" OR AB "multiple sclerosis" |

*(Continued)*

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| S6 (MH "Myelitis, Transverse") |
| S5 (MH "Encephalomyelitis, Acute Disseminated") |
| S4 (MH "Demyelinating Autoimmune Diseases, CNS") |
| S3 (MH "Optic Neuritis") |
| S2 (MH "Demyelinating Diseases") |
| S1 (MH "Multiple Sclerosis") |

PSYCHINFO

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|---|
| 65 48 AND 64 |
| 64 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 |
| 63 (phase adj3 (III or "3") adj3 (study or studies or trial*)).ab,ti. |
| 62 ((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ab,ti. |
| 61 ((pragmatic or practical) adj3 trial*).ab,ti. |
| 60 (pragmatic study or pragmatic studies).ab,ti. |
| 59 ((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ab,ti. |
| 58 ((open label or open-label) adj5 (study or studies or trial*)).ab,ti. |
| 57 allocated.ab,ti. |
| 56 (Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ab,ti. |
| 55 (control* adj3 (study or studies or trial* or group*)).ab,ti. |
| 54 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ab,ti. |
| 53 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ab,ti. |
| 52 (random* or sham or placebo*).ab,ti. |
| 51 exp Clinical Trials/ |
| 50 exp Randomized Controlled Trials/ |
| 49 (Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial Phase III).pt. |
| 48 15 AND 47 |

*(Continued)*

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| 47 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 |
| 46 "Rehabilitat*".ab,ti. |
| 45 exp Rehabilitation/ |
| 44 ("energy conservation" or "energy management").ab,ti. |
| 43 "joint protection".ab,ti. |
| 42 "dexter*".ab,ti. |
| 41 (assistive device* or assistive technolog*).ab,ti. |
| 40 leisure*.ab,ti. |
| 39 leisure time/ |
| 38 (Self Care or Self-Care).ab,ti. |
| 37 exp Self-Care/ |
| 36 "Exercise Therap*".ab,ti. |
| 35 exercise/ |
| 34 "ergonomic*".ab,ti. |
| 33 human factors engineering/ |
| 32 (counseling or counselling).ab,ti. |
| 31 exp Counseling/ |
| 30 Health Literacy.ab,ti. |
| 29 exp Health Literacy/ |
| 28 patient education.ab,ti. |
| 27 client education/ |
| 26 Splint*.ab,ti. |
| 25 exp Medical Therapeutic Devices/ |
| 24 "self-help device*".ab,ti. |
| 23 exp assistive technology/ |
| 22 "Daily Life Activit*".ab,ti. |
| 21 ADL.ab,ti. |
| 20 "Daily Living Activit*".ab,ti. |

*(Continued)*

| |
|---|
| 19 exp "Activities of Daily Living"/ |
| 18 "ergotherap*".ab,ti. |
| 17 "occupational therap*".ab,ti. |
| 16 exp Occupational Therapy/ |
| 15 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 |
| 14 encephalomyelitis.ab,ti. |
| 13 transverse myelitis.ab,ti. |
| 12 clinically isolated syndrome.ab,ti. |
| 11 demyelinating disorder.ab,ti. |
| 10 adem.ab,ti. |
| 9 demyelinating disease.ab,ti. |
| 8 devic disease.ab,ti. |
| 7 optic neuritis.ab,ti. |
| 6 neuromyelitis optica.ab,ti. |
| 5 multiple sclerosis.ab,ti. |
| 4 myelitis/ |
| 3 encephalomyelitis/ |
| 2 exp Optic Neuritis/ |
| 1 exp multiple sclerosis/ |

LILACS

Current guidance not to use

AMED

No CRG access

WHO International Clinical Trials Registry Platform

multiple sclerosis AND (occupational therapy OR rehabilitation)

Clinicaltrials.gov

occupational therapy | Multiple Sclerosis

## CONTRIBUTIONS OF AUTHORS

Conceptualisation: Daphne Kos, Isaline Eijssen, Sinéad Hynes, Geertruida Bekkering

Methodology: develop the strategy to search and select studies for inclusion in the review: Geertruida Bekkering, Leen De Coninck

Project administration and supervision: Daphne Kos

Validation: Geertruida Bekkering, Leen De Coninck

Writing - original draft of the protocol: Daphne Kos, Isaline Eijssen, Sinéad Hynes, Geertruida Bekkering, Leen De Coninck, Marja Koen

Writing - review and editing of the protocol: Daphne Kos, Isaline Eijssen, Geertruida Bekkering, Leen De Coninck, Ciara O'Meara, Marja Koen, Sinéad Hynes

## DECLARATIONS OF INTEREST

Daphne Kos is the first author of a study potentially eligible for inclusion (Kos et al, 2016). DK does not declare any commercial conflicts of interest.

Isaline CJM Eijssen is the first author of a study potentially eligible for inclusion (Eyssen et al, 2014). ICJME does not declare any commercial conflicts of interest.

Ciara O'Meara declares no conflicts of interest.

Leen De Coninck declares no conflicts of interest.

Geertruida E Bekkering declares no conflicts of interest.

Marja Koen declares no conflicts of interest.

Sinéad Hynes is the senior author of a study potentially eligible for inclusion (Reilly & Hynes 2018; Dwyer et al, 2020). SH does not declare any commercial conflicts of interest.

None of the review authors who are authors of eligible studies were involved in the development of the review protocol sections related to search methods and selection of studies. Furthermore, they will not be involved in data extraction, risk of bias assessment, or GRADE assessment of studies of which they were authors.

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- Vrije Universiteit Amsterdam, Amsterdam UMC, Amsterdam, Netherlands

  Salary for Isaline CJM Eijssen

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