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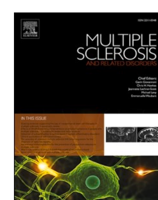

Original article

Complementary therapies for multiple sclerosis: Scoping review with evidence gap map

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ABSTRACT

Background: A systematic visual presentation of clinical research on complementary therapies for people with multiple sclerosis (pwMS) can support clinical decisions and guide future research.
Objectives: To identify the interventions and outcomes evaluated in systematic reviews (SRs) and randomized clinical trials (RCTs) of complementary therapies for pwMS.
Methods: Scoping review searching four databases for RCTs (any date) and SRs (since 2017). Results were presented in an evidence and gap map (EGM).
Results: The map displayed 63 complementary therapies, 30 outcomes of a core outcome set (COS) and 83 studies (46 SRs, 37 RCTs) published from 1977 to 2023. Most trials were small (26 (70.2%) had 100–200 participants) and conducted in Europe (n = 28; 75.6%). Natural products (n = 57 studies) and mind-body therapies (n = 12) were the most frequent groups of interventions. Cannabis (n = 24) and vitamins (n = 15) were the most frequent individual therapies. For 65.1% of the 63 listed interventions, there were no RCTs or SRs. Seventeen (56.7%) of the 30 core outcomes had fewer than five studies. Seven outcomes (23.3%) were not evaluated. The most frequent outcomes were ability to work/perform daily activities (n = 40 studies), safety (n = 37), health-related quality of life (n = 32), and fatigue (n = 31).
Conclusions: This overview of RCTs and SRs of complementary therapies for pwMS indicates that the available research is scarce, with many interventions and outcomes unevaluated. Future RCTs should be adequately powered to assess outcomes relevant to pwMS. Efforts should be made to integrate research from non-Western studies to inform decisions.

Abbreviations: COS, Core outcome set; EGM, Evidence and gap map; JBI, Joanna Briggs institute; MS, Multiple sclerosis; pwMS, People with multiple sclerosis; RCT, Randomised clinical trial; SR, Systematic review.

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1. Introduction

Complementary therapies are medical and healthcare systems, practices and products that are not generally considered part of conventional Western Medicine (National Center for Complementary and Integrative Health (NCCIH), 2021). They are widely used by people with MS (pwMS), with usage rates between 30.5% and 81% (Gotta et al., 2018; Huybregts et al., 2018; Kim et al., 2018; Silbermann et al., 2020). Our recent national survey, which was conducted by the Swiss Multiple Sclerosis Registry, found 48% of pwMS in Switzerland had used at least one complementary therapy in the past six months (Lopez-Alcalde et al., 2025). Common examples include supplements, exercise, specific diets, yoga, mindfulness, massage, homeopathy, and acupuncture (Gotta et al., 2018; Huybregts et al., 2018; Kim et al., 2018; Silbermann et al., 2020). The reasons for using complementary therapies among pwMS can differ, but they typically include improving quality of life and alleviating MS symptoms (Lopez-Alcalde et al., 2025).

The role of complementary therapies in MS management is being established through randomized controlled clinical trials (RCTs) (National Center for Complementary and Integrative Health (NCCIH), 2021). Some therapies might have the potential to alleviate MS symptoms (Silbermann et al., 2020). While not without risks, they may also serve as safer alternatives or effective adjuncts to pharmaceutical drugs, especially when conventional treatments carry a higher risk of adverse effects. Acupuncture, for instance, may relieve pain, and yoga improve cancer-related fatigue, both with typically low risk of side effects (Mentink et al., 2023).

Identifying systematic reviews (SRs) and RCTs on complementary therapies is essential to support informed decisions by pwMS. First, well-conducted RCTs and SRs provide the most rigorous evaluation of health interventions (Higgins et al., 2024). Second, some complementary therapies lack evidence, may interact negatively with pharmacological treatments, or even cause harm (Multiple Sclerosis International Federation, 2021; Institute, 2023), making rigorous evaluation critical. Third, there is an urgent need for reliable information about complementary therapies. Clinical guidelines on this topic are scarce, so healthcare professionals often lack sufficient information to guide their decisions. Additionally, many pwMS rely on untrustworthy online sources, increasing the risk of misinformation (Chang and Chang, 2015; Ng et al., 2016; Sharma et al., 2016).

Evidence and Gap Maps (EGMs) display evidence visually on a particular topic rather than synthesize findings in numbers (Saran and White, 2018; Bero et al., 2023; Miake-Lye et al., 2016). Our scoping review informed the development of an EGM of RCTs and SRs on complementary therapies for pwMS. This EGM serves as a comprehensive resource for pwMS, healthcare professionals, and researchers. By collecting and displaying SRs and RCTs, the map highlights existing evidence and knowledge gaps, supporting decision-making and guiding future research (Munn et al., 2022; Peters et al., 2020; Lorenc et al., 2018; Peters et al., 2022; Pollock et al., 2022; Khalil et al., 2022; Fisher et al., 2004). Its interactive format in four languages further enhances accessibility and usability.

This scoping review aimed to (1) identify SRs and RCTs evaluating the effects of complementary therapies on pwMS, (2) identify the complementary therapies and outcomes evaluated. The review findings informed the development of a core outcome set (COS) for trials of complementary therapies for pwMS, and an EGM visually presenting the RCTs and SRs found for each COS outcome. The review was part of the PEMS project (Participatory Evidence Synthesis in Multiple Sclerosis and complementary therapies) (López-Alcalde et al., 2025).

2. Methods

2.1. Ethics

The Cantonal Ethics Committee of Zurich stated that the project did not fall within the scope of the Human Research Act in Switzerland (Business Administration System for Ethics Committees (BASEC)-Nr. Req-2022–00,238; February 25, 2022).

2.2. Study design

Scoping review following Joanna Briggs Institute (JBI) methods (Munn et al., 2022; Peters et al., 2020; Peters et al., 2022) reported according to the Preferred Reporting Items for SRs and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018) (Appendix I). We followed a protocol pre-registered in Open Science Framework in May 2023 (López-Alcalde et al., 2023). This review used a participatory approach, involving academic and non-academic partners, particularly pwMS. See engagement methods in the review protocol (López-Alcalde et al., 2023).

2.3. Inclusion criteria

The review inclusion criteria followed the PCC (participants, concept, context) format (Munn et al., 2022).

2.3.1. Participants (P)

Adults (≥18 years) with MS regardless of demographics (e.g., age, sex, race, sociocultural context) or MS type or severity. We included studies exclusively considering pwMS. Studies on complementary therapies in mixed populations were excluded, even if MS data were disaggregated (e.g., SRs on acupuncture for pain in neurodegenerative diseases). Animal studies were excluded.

2.3.2. Concept (C)

The concept of interest for this review, that is, the topic that the scoping review explored (Peters et al., 2022), was the range of interventions and outcomes informed in SRs and RCTs evaluating the effects of complementary therapies in pwMS.

2.3.2.1. Eligible interventions. Complementary therapies are generally not considered part of conventional Western medicine and often used alongside it. Table 1 lists the eligible groups of complementary therapies, regardless of whether the studies labelled them complementary, integrative, or alternative, as these terms are used inconsistently (Ng et al., 2022). This list was compiled from relevant sources (Lorenc et al., 2018; Wieland et al., 2011; Mashola et al., 2021) and stakeholder input (see full methods in the review protocol). Table 2 details ineligible interventions.

2.3.2.2. Eligible outcomes. The review covered any outcomes, whether beneficial or adverse, reported in the included studies. This article focuses on describing the evidence for the 30 COS outcomes of the EGM (Dodd et al., 2018).

2.3.2.3. Eligible study designs. We considered SRs (including network meta-analyses) and RCTs with at least 100 participants. SRs were defined as a research process that identifies the research evidence on a specific question and synthesises this evidence according to rigorous and explicit methods. A review was eligible if it met, at least, the following criteria: a) It searched at least one bibliographic database (no need to report the search strategy), and b) It critically appraised the methodological quality of the included studies. RCTs were defined as a type of clinical study in which humans are assigned to the study groups following a random sequence. See non-eligible designs in Table 2.

2.3.3. Context (C)

Any setting and country were included. Complementary therapies could be self-administered or delivered by a healthcare professional. We included articles in English, French, German, Italian, Spanish, or

Table 1
Eligible complementary therapies.

Intervention group	Definition	Examples
1. Manual therapies	Interventions that are based on the manipulation of parts of the body	▪ Acupuncture ▪ Massage ▪ Osteopathy ▪ Reflexology
2. Mind-body therapies	Techniques to strengthen the mind or to bridge between mind and body to reduce disease symptoms and improve quality of life	▪ Self-care (such as meditation, mindfulness, and relaxation) ▪ Movement therapies (such as yoga, qigong, tai chi) ▪ Sensory-art therapies (such as music, painting)
3. Natural products-based therapies	The use of components found in nature. Natural substances can be taken into or applied to the body in any form, such as orally, topical, inhaled or injected	▪ Cannabis ▪ Supplements, e.g., vitamins, minerals, and probiotics ▪ Aromatherapy
4. Specific diets	Usually imply specific diet changes without the intake of supplements/vitamins	▪ Ketogenic diet (avoidance of carbohydrates) ▪ Gluten-free or vegan diets
5. Whole systems	Complete systems of theory and practice outside the conventional allopathic model	▪Homeopathy ▪Ayurvedic medicine ▪Traditional Chinese Medicine

Interventions based on exercise and movement of body parts to improve strength, endurance, and coordination were not considered complementary therapies in our study. Examples are sports, physiotherapeutic exercises or Pilates.

Portuguese. RCTs had no publication date limits, while SRs published since 2017 were eligible.

2.3.4. Managing overlapping studies

Overlapping RCTs (included also in an eligible SR) and overlapping SRs (examining the same intervention with common RCTs) were eligible.

2.4. Information sources

An information specialist (Noelia Álvarez-Díaz (NAD)) designed and executed the searches. A pilot search was conducted in PubMed to assess feasibility. We searched the following electronic databases (till October 4th, 2023) without publication language restrictions (Appendix II): MEDLINE (PubMed); EMBASE; CENTRAL (Cochrane Library); and Epistemonikos (which covers SRs indexed in CINAHL (The Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and LILACS (Literatura Latinoamericana y del Caribe en Ciencias de la Salud), among others. We used controlled vocabulary thesaurus, free text terms and methodological filters for SRs and RCTs. Search strategies were checked with the PRESS (Peer Review of Electronic Search Strategies) checklist (McGowan et al., 2016). We did not consider complementary therapies terms in the search strategies. We also consulted relevant institutions' websites (*NCCIH, 2019*) and asked the project stakeholders advisory board and other experts for additional sources. Manual screening of reference lists of the included studies was not conducted.

We looked for retraction notices on the articles' pages and in specialised retraction databases (PubPeer (PubPeer, 2025) and Retraction Watch (Retraction Watch, 2025)).

2.5. Study selection

We managed citations in Endnote X21 (EndNote X21, 2023) and removed duplicates, then imported unique records into Eppi-Reviewer (Thomas et al., 2022) for a second deduplication and study selection. Selection included title/abstract screening and full-text review. One reviewer (JL or YY) assessed records, cross-checked by another (YY or JL) using predefined criteria. Disagreements were resolved through discussion or senior researcher input (JB or CW). Authors were contacted if needed. Selection was piloted with 300 records. Results, including exclusion reasons, are detailed in Fig. 1 (PRISMA 2020 flow diagram (Page et al., 2021)) and Appendix III.

2.6. Data extraction

We extracted data using a pre-designed template in Eppi-Reviewer (Thomas et al., 2022). We considered a predefined list of potential complementary therapies based the operational definition of complementary and alternative medicine for the Cochrane collaboration (Wieland et al., 2011). JL and YY piloted and refined the form for consistency. One reviewer (YY or JL) extracted data, and the other cross-checked it. Disagreements were resolved through discussion. Missing or unclear information was requested from authors. We piloted extraction on 50 studies, revising the form during extraction. At the full-text stage, we merged records from the same study. Extracted data included citation details, methods, population, complementary therapy, and outcomes. Risk of bias was not assessed (Peters et al., 2022). The extraction template is available on the Open Science Framework (López-Alcalde et al., 2025).

Outcome extraction followed a multi-phase process. The development of the COS was informed by this scoping review and additional sources, such as surveys on MS symptoms (Gotta et al., 2018; Kim et al., 2018; Arji et al., 2022; Barin et al., 2018; Skovgaard, 2016) and direct consultation of stakeholders. Outcomes were categorized using the COMET taxonomy (Dodd et al., 2018), refined into a candidate list, and finalized through a survey and consensus process, generating a 30-outcome COS (submitted for publication elsewhere). See full details in COS protocol (López-Alcalde et al., 2024).

2.7. Data analysis, presentation, and mapping

We summarized included studies in tables, detailing study design, complementary therapies, and COS outcomes. Descriptive statistics (counts, percentages) were generated using EPPI-Reviewer (Thomas et al., 2022). A narrative summary accompanies the tables. Participant age and sex were summarized only for RCTs. We displayed the data in a publicly available online EGM (Digital Health Space, 2025), created using EPPI-Reviewer and EPPI-Mapper software (EPPI-Centre, 2025). Study IDs were used to link all components of the evidence map, enabling cross-filtering.

3. Results

3.1. Results of the search

Searches in electronic databases returned 35,776 records. After duplicates removal, 18,558 unique records were screened. After screening their titles and abstracts, we excluded 18,018 references. The most frequent reason for exclusion at this stage was that the intervention evaluated was a pharmacological treatment (n = 14,750; 81.9%). We retrieved 540 reports for full-text assessment. In the end, we included 83 studies (Abo et al., 2017; Agland et al., 2018; AlAmmar et al., 2021; Amatya et al., 2018; Azimi et al., 2019; Barnes et al., 1987; Bastani et al., 2015; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Behm and Morgan, 2018; Berezowska et al., 2019; Bitarafan et al., 2016; Bohlouli et al., 2022; Camu et al., 2019; Carletto et al., 2020; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Doosti-Irani et al., 2019; Dykukha et al., 2022; Ergul et al., 2022; Filippini et al., 2022; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Głąbska et al., 2021; Guerrero et al., 2022; Gusev et al., 2008; Hadoush et al., 2022; Hanaei et al., 2021; Hansen

Table 2
Non-eligible interventions and non-eligible study designs.

Interventions	Definition	Examples
1. Exercise	Interventions based on exercise and movement of parts of the body to improve strength, endurance, and coordination. Exercise is not a complementary therapy but is often used within an integrative approach	■ Sports ■ Physiotherapeutic exercises ■ Pilates
2. Physiotherapy		■ Trigger point therapy ■ Other
3. Motor imagery	A cognitive process in which the patient imagines that s/he performs a movement without actually performing it (without even tensing the muscles)	■ Mirror therapy ■ Action observation therapy
4. Energy therapies	The use of energy fields, either the unconventional use of electromagnetic fields or the manipulation of energy fields that purportedly surround and penetrate the human body	■ Reiki ■ Phototherapy ■ Thermotherapy ■ Magnetic therapy, e.g., transcranial magnetic stimulation
5. Psychotherapy		■ Conventional psychotherapy (delivered face-to-face or online) ■ Mindfulness-Based Cognitive Therapy ■ Unconventional psychotherapy (such as Eye Movement Desensitization and Reprocessing) ■ Morita ■ Third-wave psychotherapy
6. Virtual reality	Virtual reality enables individuals to move through computer-generated environments, allowing them to learn new movement strategies for situations in the real world.	
Study designs		
RCTs defined as pilot or feasibility studies		
RCTs with <100 participants		
Ongoing trials or SRs		
Non-randomised intervention studies		■ Non-randomised trials ■ Observational studies
Subgroup analyses from RCTs		
Other evidence synthesis products		■ Overviews of systematic reviews ■ Scoping reviews ■ Narrative reviews ■ Clinical practice guidelines
Withdrawn or retracted articles or articles with expression of concern		
Studies not published as an article		■ Master or doctoral dissertations ■ Conference abstracts ■ Preprints
Ongoing systematic reviews		

et al., 2023; Heidari et al., 2022; Herzog et al., 2018; Hupperts et al., 2019; Jagannath et al., 2018; Jiang et al., 2021; Kavia et al., 2010; Kleiner et al., 2023; Kneebone et al., 2022; Kong et al., 2023; Langford et al., 2013; Langlois and Denimal, 2023; Longoria et al., 2022; Lopes and Keppers, 2021; López-Muñoz et al., 2023; Ma et al., 2023; Markovà et al., 2019; Marx et al., 2020; McClurg et al., 2018; McGuinness Sandra et al., 2002; McLaughlin et al., 2018; Mirashrafi et al., 2021; Morsali et al., 2023; Morshedi et al., 2019; Mousavi-Shirazi-Fard et al., 2021; Nabizadeh, 2023; Novotna et al., 2011; Parks et al., 2020; Phyo et al., 2018; Pommerich et al., 2018; Rawal et al., 2022; Rezapour-Firouzi et al., 2013; Salarvand et al., 2021; Schimrigk et al., 2017; Sedighian et al., 2019; Shohani et al., 2020; Snetselaar et al., 2023; Stuifbergen et al., 2003; Torres-Moreno et al., 2018; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yeni et al., 2022; Yuan et al., 2021; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022; Zheng et al., 2020; Zou et al., 2017) (described in 108 reports) and found four ongoing trials (German Clinical Trials Register, 2021; EU Clinical Trials Register, 2012; German Clinical Trials Register, 2020; Bruce et al., 2021). There are no studies awaiting classification or full-texts that we were unable to access. Fig. 1 documents the selection process.

3.2. Characteristics of the studies included in the EGM

The characteristics of the 83 included studies (Abo et al., 2017; Agland et al., 2018; AlAmmar et al., 2021; Amatya et al., 2018; Azimi et al., 2019; Barnes et al., 1987; Bastani et al., 2015; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Behm and Morgan, 2018; Berezowska et al., 2019; Bitarafan et al., 2016; Bohlouli et al., 2022; Camu et al., 2019; Carletto et al., 2020; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Doosti-Irani et al., 2019; Dykukha et al., 2022; Ergul et al., 2022; Filippini et al., 2022; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Głąbska et al., 2021; Guerrero et al., 2022; Gusev et al., 2008; Hadoush et al., 2022; Hanaei et al., 2021; Hansen et al., 2023; Heidari et al., 2022; Herzog et al., 2018; Hupperts et al., 2019; Jagannath et al., 2018; Jiang et al., 2021; Kavia et al., 2010; Kleiner et al., 2023; Kneebone et al., 2022; Kong et al., 2023; Langford et al., 2013; Langlois and Denimal, 2023; Longoria et al., 2022; Lopes and Keppers, 2021; López-Muñoz et al., 2023; Ma et al., 2023; Markovà et al., 2019; Marx et al., 2020; McClurg et al., 2018; McGuinness Sandra et al., 2002; McLaughlin et al., 2018; Mirashrafi et al., 2021; Morsali et al., 2023; Morshedi et al., 2019; Mousavi-Shirazi-Fard et al., 2021; Nabizadeh, 2023; Novotna et al., 2011; Parks et al., 2020; Phyo et al., 2018; Pommerich et al., 2018; Rawal et al., 2022; Rezapour-Firouzi et al., 2013; Salarvand et al., 2021; Schimrigk et al., 2017; Sedighian et al., 2019; Shohani et al., 2020; Snetselaar et al., 2023; Stuifbergen et al., 2003; Torres-Moreno et al., 2018; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yeni et al., 2022; Yuan et al., 2021; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022; Zheng et al., 2020; Zou et al., 2017) are detailed in Appendix IV and displayed in an EGM available in English, German, French and Italian (Digital Health Space, 2025). Fig. 2 provides a snapshot of the map.

46 studies were SRs (Abo et al., 2017; AlAmmar et al., 2021; Amatya et al., 2018; Azimi et al., 2019; Behm and Morgan, 2018; Berezowska et al., 2019; Carletto et al., 2020; Doosti-Irani et al., 2019; Dykukha

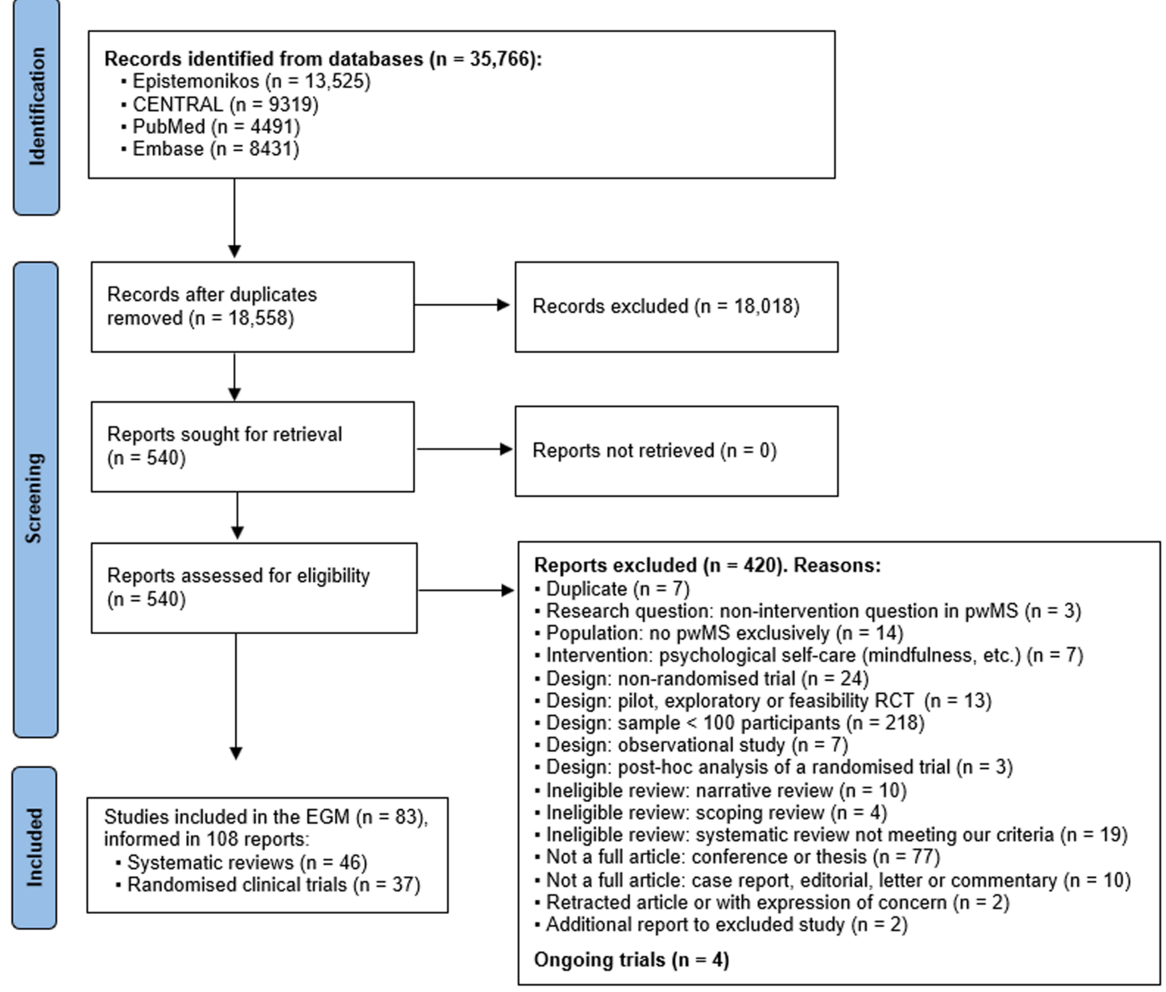

Fig. 1. Flow chart.

et al., 2022; Ergul et al., 2022; Filippini et al., 2022; Głąbska et al., 2021; Guerrero et al., 2022; Hadoush et al., 2022; Hanaei et al., 2021; Heidari et al., 2022; Herzog et al., 2018; Jagannath et al., 2018; Jiang et al., 2021; Kleiner et al., 2023; Kneebone et al., 2022; Kong et al., 2023; Langlois and Denimal, 2023; Longoria et al., 2022; Lopes and Keppers, 2021; López-Muñoz et al., 2023; Ma et al., 2023; Marx et al., 2020; McLaughlin et al., 2018; Mirashrafi et al., 2021; Morsali et al., 2023; Morshedi et al., 2019; Nabizadeh, 2023; Parks et al., 2020; Phyo et al., 2018; Pommerich et al., 2018; Rawal et al., 2022; Salarvand et al., 2021; Sedighian et al., 2019; Shohani et al., 2020; Snetselaar et al., 2023; Torres-Moreno et al., 2018; Yuan et al., 2021; Zhang et al., 2022; Zheng et al., 2020; Zou et al., 2017) (one of them a network meta-analysis) (Snetselaar et al., 2023) and 37 were RCTs (Agland et al., 2018; Barnes et al., 1987; Bastani et al., 2015; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Bitarafan et al., 2016; Bohlouli et al., 2022; Camu et al., 2019; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Gusev et al., 2008; Hansen et al., 2023; Hupperts et al., 2019; Kavia et al., 2010; Langford et al., 2013; Markovà et al., 2019; McClurg et al., 2018; McGuinness Sandra et al., 2002; Mousavi-Shirazi-Fard et al., 2021; Novotna et al., 2011; Rezapour-Firouzi et al., 2013; Schimrigk et al., 2017; Stuifbergen et al., 2003; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yeni et al., 2022; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012). All the studies were published between 1977 and 2023. Of the 46 SRs, most (n = 31; 67.4%) were published after 2019. The RCTs were published between 1977 and 2023, with more than half (n = 21; 56.8%) published after 2012. Most of the 37 trials were conducted in Europe (n = 28; 75.7%) (Barnes et al., 1987; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Camu et al., 2019; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Gusev et al., 2008; Hansen et al., 2023; Hupperts et al., 2019; Kavia et al., 2010; Langford et al., 2013; Markovà et al., 2019; McClurg et al., 2018; McGuinness Sandra et al., 2002; Novotna et al., 2011; Schimrigk et al., 2017; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012), followed by the Middle East/North Africa (n = 6; 16.2%) (Bastani et al., 2015; Bitarafan et al., 2016; Bohlouli et al., 2022; Mousavi-Shirazi-Fard et al., 2021; Rezapour-Firouzi et al., 2013; Yeni et al., 2022), North America (n = 3; 8.1%) (Cassard et al., 2023; Langford et al., 2013; Stuifbergen et al., 2003), and the Pacific region (n = 1; 2.7%) (Agland et al., 2018). One trial was multinational, conducted in Europe and North America (Langford et al., 2013). No RCTs were identified from Asia, Sub-Saharan Africa, Central America, Caribbean region, or South America.

The sample sizes of the RCTs were generally small. 26 trials (70.3%) enrolled 100–200 participants (Agland et al., 2018; Barnes et al., 1987; Bastani et al., 2015; Bates et al., 1977; Bates et al., 1978; Bitarafan et al., 2016; Bohlouli et al., 2022; Camu et al., 2019; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2007; Fiorella et al., 2022; Gallien et al., 2014; Gusev et al., 2008; Hansen et al., 2023; Kavia et al., 2010; Markovà et al., 2019; McClurg et al., 2018; McGuinness Sandra et al., 2002; Mousavi-Shirazi-Fard et al., 2021; Rezapour-Firouzi et al., 2013; Stuifbergen et al., 2003; Tourbah et al., 2016; Vachová et al., 2014;

Evidence and Gap Map of complementary therapies for people in Multiple Sclerosis (v1)

Developed by the Institute for Complementary and Integrative Medicine (University Hospital Zurich) in collaboration with the Swiss MS Registry.

https://digital-health-space.ch/en/multiple-sclerosis

Fig. 2. Evidence and gap map of complementary therapies for people with MS.

Wade et al., 2004; Yeni et al., 2022), eight trials (21.6%) enrolled 201–500 participants (Bates et al., 1989; Baumhackl et al., 2005; Collin et al., 2010; Hupperts et al., 2019; Langford et al., 2013; Schimrigk et al., 2017; Zajicek et al., 2013; Zajicek et al., 2012), and three trials (8%) enrolled >500 (Freeman et al., 2006; Novotna et al., 2011; Zajicek et al., 2003). 218 trials with fewer than 100 participants were excluded at the full-text assessment stage. Most RCTs included participants of both sexes (n = 31; 83.8%) (Barnes et al., 1987; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Bitarafan et al., 2016; Camu et al., 2019; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Gusev et al., 2008; Hansen et al., 2023; Hupperts et al., 2019; Kavia et al., 2010; Langford et al., 2013; Markovà et al., 2019; Mousavi-Shirazi-Fard et al., 2021; Novotna et al., 2011; Rezapour-Firouzi et al., 2013; Schimrigk et al., 2017; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yeni et al., 2022; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012). The remaining six trials (16.2%) (Agland et al., 2018; Bastani et al., 2015; Bohlouli et al., 2022; McClurg et al., 2018; McGuinness Sandra et al., 2002; Stuifbergen et al., 2003) predominantly included female participants (>80% were female). Regarding the participants age, the majority of trials (n = 25; 67.6%) (Agland et al., 2018; Barnes et al., 1987; Cavalera et al., 2019; Collin et al., 2007; Collin et al., 2010; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Gusev et al., 2008; Hansen et al., 2023; Kavia et al., 2010; Langford et al., 2013; Markovà et al., 2019; McClurg et al., 2018; McGuinness Sandra et al., 2002; Novotna et al., 2011; Schimrigk et al., 2017; Stuifbergen et al., 2003; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yeni et al., 2022; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012) enrolled predominantly middle-aged adults, with a mean or median age of 40–60 years. The remaining 12 trials (32.4%) predominantly enrolled younger adults, with a mean or median age of 18–39 years (Bastani et al., 2015; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Bitarafan et al., 2016; Bohlouli et al., 2022; Camu et al., 2019; Cassard et al., 2023; Hupperts et al., 2019; Mousavi-Shirazi-Fard et al., 2021; Rezapour-Firouzi et al., 2013).

Table 3 lists the complementary therapies evaluated in the included studies. Natural product therapies were the most frequently assessed group (n = 57; 68.7%) (Abo et al., 2017; AlAmmar et al., 2021; Azimi et al., 2019; Barnes et al., 1987; Bates et al., 1989; Bates et al., 1977; Bates et al., 1978; Baumhackl et al., 2005; Behm and Morgan, 2018; Berezowska et al., 2019; Bitarafan et al., 2016; Camu et al., 2019; Cassard et al., 2023; Collin et al., 2007; Collin et al., 2010; Doosti-Irani et al., 2019; Dykukha et al., 2022; Ergul et al., 2022; Filippini et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Głąbska et al., 2021; Gusev et al., 2008; Hanaei et al., 2021; Hansen et al., 2023; Herzog et al., 2018; Hupperts et al., 2019; Jagannath et al., 2018; Jiang et al., 2021; Kavia et al., 2010; Kleiner et al., 2023; Langford et al., 2013; Langlois and Denimal, 2023; Longoria et al., 2022; López-Muñoz et al., 2023; Markovà et al., 2019; Marx et al., 2020; McGuinness Sandra et al., 2002; McLaughlin et al., 2018; Mirashrafi et al., 2021; Morsali et al., 2023; Morshedi et al., 2019; Nabizadeh, 2023; Novotna et al., 2011; Parks et al., 2020; Rezapour-Firouzi et al., 2013; Schimrigk et al., 2017; Sedighian et al., 2019; Torres-Moreno et al., 2018; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yuan et al., 2021; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zheng et al., 2020), followed by mind-body therapies (n = 12; 14.5%) (Agland et al., 2018; Amatya et al., 2018; Carletto et al., 2020; Cavalera et al., 2019; Hadoush

Table 3
Complementary therapies for pwMS evaluated in the included studies.

Complementary therapy	Number of studies (%)
Any complementary therapy	83 (100)
I. Manual therapies	8 (9.6)
Acupressure	2 (2.4)
Massage therapy	4 (4.8)
Reflexology	2 (2.4)
II. Mind-body therapies	12 (14.5)
Hypnosis	3 (3.6)
Meditation & Relaxation	5 (6.0)
Mind-body movement therapies	2 (2.4)
Yoga	1 (1.2)
Tai chi	1 (1.2)
Sensory-based interventions	2 (2.4)
Miscellaneous mind-body therapies	1 (1.2)
III. Natural products-based therapies	57 (68.7)
Botanicals	4 (4.8)
Cranberry	2 (2.4)
Curcumin	1 (1.2)
Evening primrose	1 (1.2)
Ginseng	1 (1.2)
Ginkgo biloba	1 (1.2)
Lemon verbena	1 (1.2)
Green tea	1 (1.2)
Botulinum toxin	2 (2.4)
Cannabis-based medicine	24 (28.9)
Melatonin or phytoestrogens	1 (1.2)
Oxygen therapy	1 (1.2)
Supplements	26 (31.0)
Antioxidants	2 (2.4)
Enzymes and co-enzymes	1 (1.2)
Fatty acids	5 (6.0%)
Vitamins	15 (18.1)
Probiotics and prebiotics	3 (3.6)
IV. Specific diets	7 (8.4)
Anti-inflammatory diet	1 (1.2)
High-calcium diet	1 (1.2)
Iranian diet	1 (1.2)
Hot nature diet	1 (1.2)
Low-fat diet	1 (1.2)
Mediterranean diet	1 (1.2)
Paleo diet	1 (1.2)
Unspecified diet	1 (1.2)
V. Whole systems, such as TCM or Homeopathy	0 (0)

et al., 2022; Kneebone et al., 2022; Kong et al., 2023; Lopes and Keppers, 2021; Phyo et al., 2018; Shohani et al., 2020; Stuifbergen et al., 2003; Zou et al., 2017), manual therapies (n = 8; 9.6%) (Bastani et al., 2015; Heidari et al., 2022; Ma et al., 2023; McClurg et al., 2018; Rawal et al., 2022; Salarvand et al., 2021; Yeni et al., 2022; Zhang et al., 2022), and specific diets (n = 7; 8.4%) (Bohlouli et al., 2022; Fiorella et al., 2022; Guerrero et al., 2022; Mousavi-Shirazi-Fard et al., 2021; Pommerich et al., 2018; Rezapour-Firouzi et al., 2013; Snetselaar et al., 2023). However, no study was found for the group whole systems with interventions, such as TCM or homeopathy.

Among individual therapies, cannabis-based products were the most evaluated (n = 24; 28.9%) (Abo et al., 2017; Behm and Morgan, 2018; Collin et al., 2007; Collin et al., 2010; Dykukha et al., 2022; Ergul et al., 2022; Filippini et al., 2022; Freeman et al., 2006; Hansen et al., 2023; Herzog et al., 2018; Kavia et al., 2010; Kleiner et al., 2023; Langford et al., 2013; Longoria et al., 2022; Markovà et al., 2019; Novotna et al., 2011; Rezapour-Firouzi et al., 2013; Schimrigk et al., 2017; Torres-Moreno et al., 2018; Vachová et al., 2014; Wade et al., 2004; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012), followed by vitamins (n = 15; 18.1%) (Azimi et al., 2019; Berezowska et al., 2019; Bitarafan et al., 2016; Camu et al., 2019; Cassard et al., 2023; Doosti-Irani et al., 2019; Głąbska et al., 2021; Hanaei et al., 2021; Hupperts et al., 2019; Jagannath et al., 2018; Langlois and Denimal, 2023; López-Muñoz et al., 2023; McLaughlin et al., 2018; Tourbah et al., 2016; Yuan et al., 2021). Among the 63 complementary therapies listed in the map, no evidence was found for 41 interventions (65.1%). Of the 22 interventions with at least one study, 12 (54.5%) were supported by only one (either an RCT or an SR).

The map planned to display the evidence for a COS of 30 outcomes. Fig. 3 presents the outcomes domains informed in the included studies. The most frequent were overall wellbeing (n = 57, 68.7%) (Agland et al., 2018; AlAmmar et al., 2021; Barnes et al., 1987; Bates et al., 1977; Bates et al., 1978; Berezowska et al., 2019; Bohlouli et al., 2022; Camu et al., 2019; Carletto et al., 2020; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2010; Doosti-Irani et al., 2019; Filippini et al., 2022; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Głąbska et al., 2021; Guerrero et al., 2022; Gusev et al., 2008; Hanaei et al., 2021; Hansen et al., 2023; Herzog et al., 2018; Hupperts et al., 2019; Jagannath et al., 2018; Jiang et al., 2021; Kavia et al., 2010; Kleiner et al., 2023; Kneebone et al., 2022; Langford et al., 2013; Langlois and Denimal, 2023; Lopes and Keppers, 2021; Ma et al., 2023; Markovà et al., 2019; Marx et al., 2020; McClurg et al., 2018; McLaughlin et al., 2018; Mirashrafi et al., 2021; Mousavi-Shirazi-Fard et al., 2021; Novotna et al., 2011; Parks et al., 2020; Rawal et al., 2022; Rezapour-Firouzi et al., 2013; Schimrigk et al., 2017; Sedighian et al., 2019; Shohani et al., 2020; Snetselaar et al., 2023; Stuifbergen et al., 2003; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yuan et al., 2021; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022; Zou et al., 2017) and general issues (n = 38, 45.8%) (Bastani et al., 2015; Bitarafan et al., 2016; Bohlouli et al., 2022; Carletto et al., 2020; Cavalera et al., 2019; Collin et al., 2010; Głąbska et al., 2021; Guerrero et al., 2022; Hansen et al., 2023; Heidari et al., 2022; Herzog et al., 2018; Jagannath et al., 2018; Kleiner et al., 2023; Kneebone et al., 2022; Langford et al., 2013; Longoria et al., 2022; Lopes and Keppers, 2021; López-Muñoz et al., 2023; Ma et al., 2023; Markovà et al., 2019; Marx et al., 2020; Morsali et al., 2023; Mousavi-Shirazi-Fard et al., 2021; Novotna et al., 2011; Parks et al., 2020; Phyo et al., 2018; Pommerich et al., 2018; Rawal et al., 2022; Salarvand et al., 2021; Shohani et al., 2020; Snetselaar et al., 2023; Tourbah et al., 2016; Wade et al., 2004; Yeni et al., 2022; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022; Zou et al., 2017). The least frequent were the cognition (n = 13, 15.7%) (Dykukha et al., 2022; Fiorella et al., 2022; Guerrero et al., 2022; Hansen et al., 2023; Marx et al., 2020; Morsali et al., 2023; Mousavi-Shirazi-Fard et al., 2021; Nabizadeh, 2023; Parks et al., 2020; Shohani et al., 2020; Vachová et al., 2014; Wade et al., 2004; Zajicek et al., 2013) and gastrointestinal (n = 2, 2.4%) (Barnes et al., 1987; McClurg et al., 2018) domains.

The number of studies evaluating each outcome of the COS was generally low. Thirteen of the thirty COS outcomes (43.3%) were evaluated in at least five studies. However, seventeen outcomes (56.7%) were evaluated in fewer than five studies. Notably, seven outcomes—dizziness or vertigo, sexual problems, emotional lability, sensory problems, speech problems, paralysis, and dysphagia—were not evaluated in any study. See Table 4 for further details.

The most frequently assessed outcome was the ability to work or perform daily activities (n = 40, 48.2%) (AlAmmar et al., 2021; Barnes et al., 1987; Bates et al., 1989; Bates et al., 1978; Berezowska et al., 2019; Bohlouli et al., 2022; Camu et al., 2019; Cassard et al., 2023; Collin et al., 2010; Doosti-Irani et al., 2019; Filippini et al., 2022; Fiorella et al., 2022; Gallien et al., 2014; Guerrero et al., 2022; Gusev et al., 2008; Hanaei et al., 2021; Hansen et al., 2023; Hupperts et al., 2019; Jagannath et al., 2018; Jiang et al., 2021; Kleiner et al., 2023; Langford et al., 2013; Markovà et al., 2019; Marx et al., 2020; McLaughlin et al., 2018; Mirashrafi et al., 2021; Mousavi-Shirazi-Fard et al., 2021; Novotna et al., 2011; Parks et al., 2020; Rezapour-Firouzi et al., 2013; Sedighian et al., 2019; Stuifbergen et al., 2003; Tourbah et al., 2016; Vachová et al., 2014; Wade et al., 2004; Yuan et al., 2021; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022), followed by the safety of complementary therapies (n = 37, 44.6%) (Abo et al., 2017; Berezowska et al., 2019; Bitarafan et al., 2016; Camu et al., 2019; Cassard et al., 2023; Collin et al., 2007; Collin et al., 2010; Dykukha et al., 2022; Filippini et al., 2022; Freeman et al., 2006; Gallien

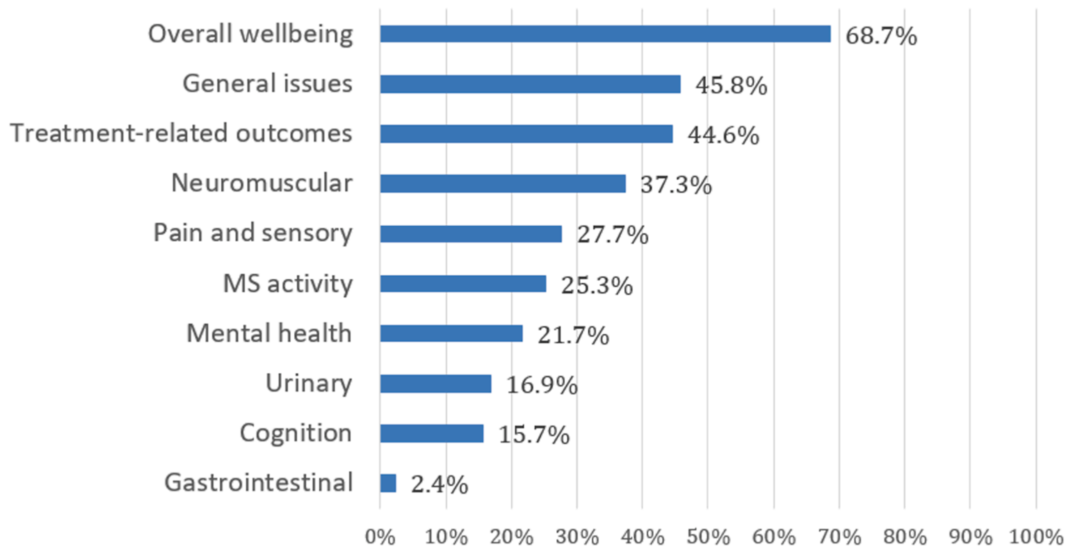

Fig. 3. Percentage of studies informing each outcome domain.

Table 4
. Outcomes informed in the included studies.

Outcome	Count	%
I. MS activity	**21**	**25.3%**
1. MS Clinical relapses	21	25.3%
II. General issues	**38**	**45.8%**
2. Fatigue	31	37.3%
3. Sleep problems	13	15.7%
4. Dizziness or vertigo	0	0%
5. Sexual problems	0	0%
III. Mental health	**18**	**21.7%**
6. Anxiety	11	13.3%
7. Depressive mood	16	19.3%
8. Emotional lability	0	0%
IV. Cognition	**13**	**15.7%**
9. Attention and concentration problems	13	15.7%
10. Memory problems	3	3.6%
V. Pain and sensory	**23**	**27.7%**
11. Pain	22	26.5%
12. Visual problems	1	1.2%
13. Sensory problems	0	0%
VI. Neuromuscular	**31**	**37.3%**
14. Muscular weakness	1	1.2%
15. Spasticity, tremors, or spams	21	25.3%
16. Gait and mobility problems	18	21.7%
17. Balance problems	3	3.6%
18. Dexterity problems	4	4.8%
19. Speech problems	0	0%
20. Paralysis	0	0%
VII. Gastrointestinal	**2**	**2.4%**
21. Dysphagia	0	0%
22. Bowel problems	2	2.4%
VIII. Urinary	**14**	**16.9%**
23. Bladder and prostate problems	13	15.7%
24. Urinary tract infections	3	3.6%
IX. Overall wellbeing	**57**	**68.7%**
25. General quality of life	2	2.4%
26. Health-related quality of life	32	38.6%
27. Emotional wellbeing	3	3.6%
28. Ability to work or perform daily activities	40	48.2%
29. Social wellbeing	4	4.8%
X. Treatment-related outcomes	**37**	**44.6%**
30. Safety of complementary therapies	37	44.6%

et al., 2014; Guerrero et al., 2022; Gusev et al., 2008; Hansen et al., 2023; Hupperts et al., 2019; Jagannath et al., 2018; Kavia et al., 2010; Kong et al., 2023; Langford et al., 2013; Markovà et al., 2019; McClurg et al., 2018; McLaughlin et al., 2018; Morsali et al., 2023; Novotna et al., 2011; Parks et al., 2020; Rezapour-Firouzi et al., 2013; Salarvand et al., 2021; Schimrigk et al., 2017; Torres-Moreno et al., 2018; Tourbah et al., 2016; Wade et al., 2004; Zajicek et al., 2013; Zajicek et al., 2003; Zajicek et al., 2012; Zhang et al., 2022; Zheng et al., 2020; Zou et al., 2017), health-related quality of life (n = 32, 38.6%) (AlAmmar et al., 2021; Berezowska et al., 2019; Camu et al., 2019; Carletto et al., 2020; Cassard et al., 2023; Cavalera et al., 2019; Collin et al., 2010; Filippini et al., 2022; Fiorella et al., 2022; Freeman et al., 2006; Gallien et al., 2014; Hansen et al., 2023; Herzog et al., 2018; Jagannath et al., 2018; Kavia et al., 2010; Kneebone et al., 2022; Langford et al., 2013; Langlois and Denimal, 2023; Lopes and Keppers, 2021; Ma et al., 2023; Markovà et al., 2019; Marx et al., 2020; McClurg et al., 2018; Mousavi-Shirazi-Fard et al., 2021; Parks et al., 2020; Rawal et al., 2022; Schimrigk et al., 2017; Shohani et al., 2020; Snetselaar et al., 2023; Stuifbergen et al., 2003; Tourbah et al., 2016; Zou et al., 2017), and fatigue (n = 31, 37.3%) (Bastani et al., 2015; Bitarafan et al., 2016; Bohlouli et al., 2022; Carletto et al., 2020; Cavalera et al., 2019; Collin et al., 2010; Głąbska et al., 2021; Guerrero et al., 2022; Heidari et al., 2022; Jagannath et al., 2018; Kneebone et al., 2022; Langford et al., 2013; Lopes and Keppers, 2021; López-Muñoz et al., 2023; Ma et al., 2023; Marx et al., 2020; Morsali et al., 2023; Mousavi-Shirazi-Fard et al., 2021; Parks et al., 2020; Phyo et al., 2018; Pommerich et al., 2018; Rawal et al., 2022; Salarvand et al., 2021; Shohani et al., 2020; Snetselaar et al., 2023; Tourbah et al., 2016; Wade et al., 2004; Yeni et al., 2022; Zajicek et al., 2003; Zhang et al., 2022; Zou et al., 2017).

3.3. *Knowledge gaps*

Table 5 presents the complementary therapies without studies. Moreover, among those therapies with at least one study, the number of studies was generally low. Except for cannabis-based medicine and vitamins, no therapy had more than five studies, and 18 of the 40 map interventions (45%) were supported by a single study (RCT or SR).

Seven out of the 30 COS outcomes (23.3%) had no study: dizziness/vertigo, sexual problems, emotional lability, sensory problems, speech problems, paralysis, and dysphagia. An additional 10 outcomes (33.3%) were each reported in no more than four studies (visual problems, muscular weakness, balance problems, dexterity problems, bowel problems, memory problems, urinary tract infections, general quality of life, emotional well-being, and social well-being).

3.4. *Excluded studies and ongoing studies*

We excluded 420 reports at full-text assessment, mostly due to

Table 5
Knowledge gaps: complementary therapies with no studies.

Complementary therapy group	Complementary therapy
I. Manual therapies	Acupuncture
	Bowen therapy [a]
	Chiropractic manipulation [b]
	Craniosacral therapy [c]
	Cupping therapy [d]
	Neuro-reflexotherapy [e]
	Kinesiology [f]
	Osteopathy [g]
	Prolotherapy [h]
II. Mind-body therapies	Feldenkrais method [i]
	Hippotherapy [j]
	Inpatient energy management education [k]
	Laughter therapy [l]
	Natural environments therapies [m]
III. Natural products-based therapies	Bach flowers [n]
	Helminthic therapy [o]
	Hydrotherapy [p]
IV. Specific diets	Calorie-restricted diet
	Carbohydrate-restricted diet
	Casein-free diet
	Fasting diet
	Gluten-free diet
	High-fiber diet
	High-sodium diet
	Low-fat plant restricted diet
	Low glycemic-index diet
	Protein-restricted diet
	Sodium-restricted diet
	Vegan diet
	Vegetarian diet
V. Whole systems	Ayurvedic medicine [q]
	Folk medicine [r]
	Homeopathy [s]
	Naturopathy [t]
	Traditional Chinese Medicine
	Traditional European Medicine
	Traditional Indian Medicine
	Traditional Japanese Medicine

[a] Gentle muscle and tissue manipulation.
[b] Adjustments to the spine or joints.
[c] Gentle touch on the head and spine.
[d] Use of suction cups on the skin.
[e] Placing small metal implants on skin points to stimulate nerve pathways and block pain signals.
[f] Study of body movement to identify imbalances and improve health through exercises.
[g] Manipulation of muscles and bones to improve body function.
[h] Injections to stimulate tissue healing and relieve joint or tendon pain.
[i] Exercise therapy focusing on improving movement and function through gentle, mindful movement and self-awareness.
[j] Use of horse riding as a therapeutic or rehabilitative treatment.
[k] Teaching patients how to conserve energy, balance rest with activity, and pace themselves, aiding recovery and reducing fatigue, especially for chronic conditions or post-surgery.
[l] Use of voluntary laughter exercises to improve mental and physical health.
[m] Use of outdoor settings, like gardens, to reduce stress, improve mood, and promote healing by connecting individuals with nature.
[n] Use of flower essences to address emotional imbalances, like anxiety, and promote emotional well-being.
[o] Introduction of harmless worms into the body to modulate the immune system, potentially helping manage autoimmune diseases and allergies.
[p] Use of water in various forms (hot, cold, steam, or ice) to relieve pain, improve circulation, and promote relaxation, often used in physical therapy and rehabilitation.
[q] Holistic healing system, originated in India, that focuses on balancing the mind, body, and spirit to promote health and prevent disease.
[r] Healing practices and health-related beliefs that originate within a specific culture or community and are often passed down through generations—usually via oral tradition rather than formal education.
[s] Therapy using extremely diluted substances that mimic symptoms, aiming to stimulate the body's self-healing processes.
[t] Use of natural methods—like herbs, nutrition, and lifestyle changes—to support the body's self-healing and prevent disease.

sample sizes under 100 (n = 218). Two studies were excluded following journal retractions: Kouchaki (data validity concerns) (Kouchaki et al., 2018; Erratum, 2021) and Ghasemi (authorship issues) (Ghasemi et al., 2022; Office NE, 2022). See Fig. 1 and Appendix III for all exclusion reasons and ongoing studies.

4. Discussion

4.1. Principal results

We performed a scoping review to identify the interventions and outcomes evaluated in SRs and RCTs of complementary therapies for pwMS. The review informed the development of a COS (López-Alcalde et al., 2024) and an EGM (Digital Health Space, 2025). The EGM displays 63 complementary therapies, 30 COS outcomes, and 83 studies (46 SRs, 37 RCTs) assessing the effects of complementary therapies on these core outcomes in pwMS. Most trials were conducted in Europe (75.7%) and were small (70.3% had 100–200 participants). Natural products, that is, the use of components found in nature, such as cannabis, vitamins or aromatherapy, was the most frequently assessed group of interventions (68.7%), followed by mind-body therapies (14.5%), manual therapies (9.6%), and specific diets (8.4%). No study evaluated whole systems interventions, such as Traditional Chinese Medicine or homeopathy. Among individual interventions, cannabis-based products were the most frequently evaluated (28.9%), followed by vitamins (18.1%). For most of the 63 complementary therapies displayed in the map, evidence was lacking or scarce: 65.1% of the interventions had no evidence, and 19.0% were supported by a single study (either a RCT or a SR). The number of studies evaluating each COS outcome was generally low. 56.7% of the 30 outcomes of the COS were evaluated in fewer than five studies. 23.3% of the outcomes were not evaluated in any study.

4.2. Strengths and limitations

Our scoping review has several strengths. First, it was prospectively registered and followed rigorous methods (Peters et al., 2020; López-Alcalde et al., 2024). Second, a participatory approach, engaging pwMS, likely enhanced its relevance (Pollock et al., 2022; Cottrell et al., 2014). Third, instead of searching for inconsistently used terms like "complementary" or "alternative" therapies (Ng et al., 2022), we screened all RCTs and SRs of pwMS for those evaluating our pre-defined eligible complementary therapies. This strategy probably increased sensitivity. Fourth, we used the COMET taxonomy to classify outcomes (Dodd et al., 2018), ensuring categorization with established relevance in COS development, systematic reviews, and clinical trials (Development of a core outcome set for gastric cancer treatment trials, 2022; Initiative CCOMiET, 2017; Core Health Outcomes in Childhood Epilepsy (CHOICE), 2019). Finally, our EGM displays the evidence for the COS defined by pwMS and other stakeholders as relevant for complementary therapy use (Lopez-Alcalde et al., 2025), clearly highlighting areas where gaps exist.

Our review also has limitations. First, language bias may exist, as we excluded studies not published in English, French, German, Italian, Spanish, or Portuguese, likely underrepresenting research from regions where complementary therapies are widely used (e.g., China, Japan, India). Second, we focused on studies of complementary therapies in pwMS, excluding research in other populations (e.g., yoga in cancer patients). While the excluded evidence may still be useful for pwMS, our decision is justified by our intention to provide a clear starting point for mapping evidence in MS. Third, we excluded studies with fewer than 100 participants, resulting in the exclusion of 218 trials during the full-text assessment stage. Although this criterion may disadvantage research fields with limited funding, such as traditional Asian medicine,

it is justified by evidence suggesting that studies with small sample sizes often report inflated effect sizes (Beets et al., 2023). Sixth, we did not cover ongoing systematic reviews or trials, limiting the map's ability to highlight areas where new evidence is forthcoming. Finally, one of the typical drawbacks of EGMs is that they usually indicate whether evidence exists, but they do not provide details on the direction of the effects (such as the presence of a benefit or harm) or the certainty of the evidence (White, 2021). In this line, we did not extract effect estimates or assess certainty, so a higher number of studies in a cell does not indicate stronger evidence. Seventh, the interpretability of the evidence and gap map may be constrained by the fact that the number of studies per cell does not inherently correspond to the strength or clinical effectiveness of the evidence presented. This discrepancy could lead to misinterpretations, particularly among non-specialist users of the map. To address this potential misunderstanding, we have explicitly highlighted this limitation in the instructions section of the map.

4.3. Comparison with prior work

Our scoping review builds on Arji's classification of complementary therapies for MS symptom management (31 trials till 2020) (Arji et al., 2022). While both reviews highlight the need for rigorous trials, our review differs in several key aspects. We followed Joanna Briggs Institute methods (Peters et al., 2020), included 83 studies (37 RCTs, 46 SRs), used a stakeholder-developed COS, assessed benefits and harms, and presented findings in an EGM for accessibility. This expands Arji's work by offering a broader, more accessible overview of evidence and gaps.

Our study has key clinical implications. First, limited evidence for most intervention-outcome pairs reflects a fragmented research base. Second, given the widespread use of complementary therapies among pwMS (Gotta et al., 2018; Kim et al., 2018; Silbermann et al., 2020; Lopez-Alcalde et al., 2025), healthcare professionals and pwMS probably need more and better information on the effects complementary therapies. Third, the scarcity of non-Western studies in our map underscores the need to find this evidence, assess its certainty, and, if appropriate, integrate their findings to inform decisions on complementary therapies in our context. Fourth, preventing the dissemination of fraudulent research is crucial to avoid misleading clinicians and patients about the efficacy and safety of treatments. This helps maintain trust in research and ensures that clinical decisions are based on reliable information (de Melo-Martín et al., 2018). We excluded two studies due to validity concerns (Kouchaki et al., 2018; Ghasemi et al., 2022). Tools like PubPeer, Retraction Watch, and Cochrane's retraction initiative help identify unreliable evidence (PubPeer, 2025; Retraction Watch, 2025; Cochrane, 2025).

Research implications include the need for more RCTs, as many COS-defined outcomes lack evidence. Many included RCTs had small sample sizes, and we excluded 218 trials with fewer than 100 participants. Adequately powered trials are needed to detect meaningful differences in pwMS-relevant outcomes. Finally, applications using artificial intelligence should be tested for maintaining a living EGM. Our team plans to develop a strategy for continuous updates using machine learning, though its effectiveness remains to be evaluated (Lorenc et al., 2020; Zhao et al., 2024; EPPI-Reviewer, 2024).

5. Conclusions

This scoping review and EGM provide an overview on RCTs and SRs of complementary therapies for pwMS. Evidence is scarce, with many interventions and outcomes unevaluated. Most trials had small sample sizes, which highlights the need for adequately powered RCTs. Future research should prioritize adequately powered RCTs that assess outcomes relevant to pwMS. Efforts should be made to integrate research from non-Western studies to inform decisions about complementary therapies. AI tools, including machine learning for literature surveillance and data extraction, have the potential to support continuous updates of the map and improve access to emerging evidence.

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During the preparation of this work the authors used Chat/GPT and Grammarly in order to improve readability. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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CRediT authorship contribution statement

Jesus Lopez-Alcalde: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Yuqian Yan:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Claudia Canella:** Writing – review & editing, Methodology, Data curation. **Jürgen Barth:** Writing – review & editing, Methodology. **Nina Steinemann:** Writing – review & editing. **Viktor von Wyl:** Writing – review & editing. **Claudia Baum:** Writing – review & editing. **Sarah Bolt:** Writing – review & editing. **Stefan Haegele-Link:** Writing – review & editing. **Gabriela Rettenmund Grob:** Writing – review & editing. **Anna Katharina Tietjen:** Writing – review & editing, Data curation. **Noelia Álvarez-Díaz:** Writing – review & editing, Methodology, Data curation. **Claudia M Witt:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Supplementary materials

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