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Review article

Digital psychosocial tools and interventions for supporting informal caregivers of people with multiple sclerosis: a systematic review

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ABSTRACT

Objective: Caring for a person affected by a neurodegenerative disease like multiple sclerosis (MS), which begins in early adulthood and leads to premature disability, can be perceived as a very challenging task. Patients' informal caregivers (ICs), play a crucial role in assisting people with MS, but frequently may experience burden and emotional distress. This systematic review aims to analyze digital tools promoting psychosocial wellbeing and resources in ICs of people with MS, focusing on intervention, ICs and MS characteristics, and outcomes such as effectiveness, and feasibility.
Methods: A systematic literature search was conducted across four databases, covering studies published from January 2000 to May 2024 to identify psychosocial interventions dedicated to ICs delivered through digital technology. The Mixed Methods Appraisal Tool (MMAT) was used to assess the quality of the studies included. Extracted results were synthesized and presented in a narrative text and a structured tabulation.
Results: Starting from 2749 records, a total of 8 studies met the inclusion criteria with half conducted as RCTs. Most of the interventions focused only on ICs, aiming to improve quality of life and reduce emotional burden. Web-based, mobile-health and most commonly tele-consulting modalities were used to deliver the interventions, generally showing signal of efficacy in improve psychological and performance parameters.
Conclusions: The diverse range of interventions offer flexibility and accessibility and appear to be promising solutions in addressing the diverse needs of ICs. However, the studies are few, recent, and varied, complicating synthesis and generalization and further research is necessary to strengthen evidence and optimize intervention strategies.

1. Introduction

Multiple sclerosis (MS) is the most common autoimmune inflammatory and neurodegenerative disease that causes disability in youth (Koch-Henriksen and Sørensen, 2010; Dimitrov and Turner, 2014). As the disease progresses, people often develop an accrual of symptoms and worsened disability (Harding-Forrester et al., 2023), leading to the need for external support. Informal caregivers (ICs) - individuals who provide direct unpaid care - (Buchanan et al., 2010) play a vital role in assisting People with MS (PwMS) in coping with their condition, offering emotional and practical assistance, significantly contributing to their well-being and day-to-day MS management (Maguire and Maguire, 2020; Bassi et al., 2020). Informal caregiving is considered multidimensional and not homogeneous (Nolan et al., 1995; Talley and Crews, 2012), since tasks may vary depending on the PwMS needs and severity, and ICs in different roles may find themselves taking on this position.

ICs may experience burden (Buchanan et al., 2009), feelings of helplessness, and loss of control linked to adverse psychological and physical changes, such as anxiety, depression, and decreased quality of life (Pakenham, 1998; Ponzio et al., 2024; Figved et al., 2007; Smith et al., 2011; Hoseinpur et al., 2023; Rajachandrakumar et al., 2022). While some studies have also highlighted that some caregivers report subjective positive outcomes, such as enhanced personal growth, strengthened relational closeness, or a renewed sense of meaning in life (Wang et al., 2024), frequently ICs face frustration as they grapple with the evolving needs of PwMS, indeed they are usually untrained and unprepared for this role (Bogosian et al., 2009; Strickland et al., 2015). Providing them with education, coping skills, problem solving, and support can increase quality of life for both the ICs and person with MS (Buchanan, 2010). Given the practical barriers caregivers face in

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Data sharing statement: The data and materials used during the current study are available from the corresponding author (MR) on reasonable request.

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accessing traditional support services – such as limited time due to intensive caregiving responsibilities, reduced financial resources, and difficulties in balancing employment and personal life – it becomes essential to make more flexible and accessible solutions available. Digital technologies can help overcome these barriers by providing timely, location-independent, and often cost-effective forms of support, thereby enabling caregivers to receive guidance and resources without the constraints typically associated with in-person services (Zhai et al., 2023).

In the last decades, digital technology has been increasingly used to improve healthcare delivery and health management, making treatments available to a wider population (Stoumpos et al., 2023; van der Vijver et al., 2023). The term “e-Health" (or “digital health”) is defined as “the use of information and communications technology in support of health and health-related fields” (Guideline WHO, 2019). The use of digital technologies could also allow for advantages in caregiver management, facilitating their involvement in patient care and providing them with an easily accessible space for sharing experiences, receiving support, and taking care of their wellbeing (Soares et al., 2024). The effectiveness of e-health interventions for ICs has been demonstrated in the context of different disease conditions (Li et al., 2022; Madara Marasinghe, 2016).

However, to the best of our knowledge, no previous review has specifically focused on studies describing digital interventions developed to provide support, to promote psychosocial wellbeing and to empower ICs of PwMS.

Existing systematic reviews highlight the importance of supportive interventions for caregivers of individuals with multiple sclerosis (MS) or other chronic conditions yet reveal significant limitations. Hoseinpour et al. (2023) provide a broad overview of “supportive interventions” without detailing psychological components or delivery methods. Rouch et al. (2021) examine intervention effectiveness for caregivers of patients with chronic conditions in general, without focusing on MS or digital modalities. Reviews on Acceptance and Commitment Therapy (ACT) for caregivers (Ye et al., 2023; Han et al., 2021) further suggest benefits for informal caregivers of chronic patients but are not specific to MS and highlight the need for further research across different caregiver populations and outcomes. Taken together, these gaps indicate a lack of systematic evidence on innovative, remotely accessible, technology-based interventions for caregivers of people with MS. The present review aims to address this gap by providing updated evidence on the effectiveness of e-health interventions specifically designed for MS caregivers, guiding the development of more targeted, sustainable, and accessible support strategies.

Thus, this review aims to systematically analyze studies focusing on digital tools and interventions to promote psychosocial wellbeing and resources (such as resilience, adaptation, health literacy, and empowerment) in ICs of PwMS, answering the following research questions: (a) What are the main characteristics of available digital solutions targeting to psychological outcomes of ICs of PwMS? (b) Which ICs and MS type have been considered? (c) What are the main results of those interventions in terms of effectiveness, feasibility, acceptability and engagement?

2. Methods

2.1. Overview

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The corresponding protocol was previously registered on the PROSPERO (ID: CRD42024530236).

2.2. Search strategy and screening procedure

A systematic search of four electronic databases (i.e., PubMed, Scopus, PsycINFO, Web of Science) was conducted up to May 2024, restricting the search to peer-reviewed articles published in English and Italian after the 1st of January 2000 up until the day of the search. We limited our search to studies published from 2000 onward, targeting a period that is both broadbut also relevant, as the use of digital health technologies in clinical research, particularly in neurology, increased significantly since then (Masanneck et al., 2023). Unpublished studies and grey literature were not included to maintain the methodological rigor and reliability of the findings. This decision reflects the challenges posed by the non-indexed and heterogeneous nature of grey literature, which increases the risk of selection bias. A combination of key terms related to the following three main topics was used as search strategy linked with the Boolean operator “AND”: (i) caregiver (e.g., carer, partner, family); (ii) multiple sclerosis and (iii) e-health (e.g., telemedicine, telehealth, m-health) (see Appendix A for a detailed description of the search string). Moreover, to identify recently published articles, automatic monthly e-mail search alerts were set up until 10th June 2024. An additional manual search of the relevant references was done through the screening of reviews that emerged from the search strategy.

Articles were exported into the Systematic Reviews Web application Rayyan (Ouzzani et al., 2016), and duplicates were removed. Two reviewers (GG and AF) independently assessed titles and abstracts for eligibility and, subsequently, retrieved and assessed full texts of the potentially eligible articles against eligibility criteria. Doubts were discussed and, if necessary, a third reviewer (VD) was consulted.

2.3. Inclusion and exclusion criteria

All the studies describing the development and/or the implementation and/or evaluation of digitally delivered psychosocial interventions or digital tools promoting well-being and resources in ICs of PwMS were included. Although several conceptualizations exist, in the present work we define psychosocial interventions/tools as interpersonal or informational activities, techniques, or strategies that target different factors with the aim of improving health, functioning, and well-being (England et al., 2015). In particular, we focus on psychosocial interventions designed to influence at least one psychosocial outcome, assessed either qualitatively or quantitatively. Outcomes were broadly defined to capture the diverse effects addressed by these interventions. This approach is reflected in our PICO framework: Population (informal caregivers of PwMS, without restrictions on specific characteristics), Intervention (psychosocial eHealth interventions), Comparison (any or none), Outcomes (a broad range relevant to psychosocial functioning and well-being) (see Table 1). Interventions were included if they utilized a digital or blended approach (i.e., combining digital and face-to-face components), while they were excluded if the intervention was conducted exclusively face-to-face, with no digital component. The inclusion criteria are broad and not restricted to specific psychosocial aims or digital methods of interventions so that all possible digital-delivery psychosocial interventions dedicated to caregivers can be captured and the potential different purposes and content of interventions can be described. Table 1 summarizes the inclusion and exclusion criteria according to the PICO format.

Reviews of any type, meta-analyses, bibliometric analyses, letters, case-studies, books/book chapters, comments, editorials, congress abstracts, poster presentations, and dissertations were excluded. Secondary studies were excluded if they focused on the same intervention for which the primary study had already been included but not further relevant outcomes were evaluated. Study protocols were included only when no corresponding original article specific to caregiver interventions was available.

2.4. Data extraction and synthesis

All eligible full texts were considered for data extraction. In a first step, data extraction was undertaken by two independent reviewers –

Table 1
PICO (Population, Intervention, Comparison, Outcome) inclusion and exclusion criteria.

	Inclusion criteria	Exclusion criteria
Population	Informal caregivers (ICs) of persons with multiple sclerosis, with no restriction regarding gender, age, type of MS, social/familial role of caregiver.	Studies regarding formal caregivers (e.g., healthcare professionals). Studies that included diseases other than MS, if results are not presented separately for ICs of PwMS. Studies targeting both persons with MS and their ICs, or targeting both formal and informal caregivers, if part of the intervention or tool, or the results that are described, are not directly referred to the informal caregiver.
Intervention	Any type of digital-delivered psychosocial tool or intervention, such as supportive, psycho-educational, self-management and behavioral interventions. Any type of digital component and mode of delivery, including blended (i.e., where the digital component is part of a mixed mode of participation) and intervention delivered by any individual (e.g., peers, healthcare professionals).	Face-to-face interventions. Digital-delivered interventions that do not have the aim of promoting psychosocial wellbeing and/or psychosocial resources or interventions that have these aims but do not include at least a partial digital component.
Comparison	Any comparison, if available.	None.
Outcome	Any psychosocial outcome (e.g., quality of life, mental health, adaptation, self-esteem, self-efficacy, psychosocial competence, resilience, mental health, health literacy, empowerment, emotional distress, burden) measured with quantitative or qualitative measures.	None.

clinical psychologists and researchers expert in the field (GG, AF) –, who independently read the full text of the included articles, manually extracted the data in an excel spreadsheet categorizing the information according to the categories detailed below. In a second step, reviewers discussed data extraction and when discrepancies and/or doubts emerged they were resolved with consultation by the wider team (VD, SP, MR). The following information have been collected in an Excel spreadsheet: authors, publication year, country, type of study and study design, overall type/strategy of intervention, sample size, inclusion and exclusion criteria, gender distribution, mean age, caregiver role, MS type/disability level/time since diagnosis, control group, aim of the intervention/tool, intervention main contents, intervention structure, target group, intervention duration, delivery modality, provider of the intervention, and follow-up. To improve consistency, at the beginning of the data extraction process, the two reviewers familiarized themselves with the Excel spreadsheet running a pilot extraction followed by a discussion with the wider team to anticipate potential issues in data extraction.

2.5. *Methodological quality assessment*

The extracted information was presented in tabular form (i.e., Table 2 presents the main characteristics of the study and of the target population; Table 3 presents the main characteristics of the interventions and the delivery methods; Table 4 presents the primary and secondary outcomes) along with a narrative summary. Moreover, to make the narrative synthesis more structured, the interventions have been categorized according to their general purpose and the digital method of delivery.

The quality of the included studies was evaluated by the two independent reviewers (GG, AF) with the involvement of a third rater to adjudicate disagreements and doubts (SP), using the latest version of Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018). This tool is specifically designed to evaluate methodological quality across a wide range of study designs, including qualitative research, randomized controlled trials, non-randomized quantitative studies, and mixed-methods studies. The MMAT evaluates five core methodological criteria tailored to each study design (i.e., clarity of the research questions, the relevance of the data sources, the appropriateness of the methods used, the integrity of the results, and the coherence of the conclusions). Each criterion is scored as ’Yes,’ ’No,’ or ’Cannot Tell’ based on the information provided in the study. This structured approach allows for a standardized and transparent appraisal of methodological rigor, facilitating comparisons across diverse types of research. Only the criteria relevant to the specific design of each study were assessed, ensuring accuracy and applicability in the evaluation process.

3. Results

The electronic database search initially yielded 2749 records. After duplicate removal and titles and abstracts screening, seventeen records were evaluated for full-text screening and seven were excluded according to inclusion and exclusion criteria (see PRISMA flowchart, Fig. 1). Of the 10 papers meeting the eligibility criteria, one study was excluded from the final data extraction as it was a protocol for a RCT of an e-Health intervention, that was already included (Douglas et al., 2023), while another was excluded for being a secondary analysis of this same RCT. Thus, eight papers were ultimately included in this review. No additional records emerged from the search alerts (deactivated on June 10, 2024).

3.1. *Characteristics of the included studies*

All studies have been published within the last eight years. Three studies took place in the United States (Kalb et al., 2023; Douglas et al., 2023; Halstead et al., 2020); two in Iran (Motaharinezhad et al., 2024; Khazaeili et al., 2019), one in Italy (Cavalera et al., 2016), one in the United Kingdom (Potter et al., 2021), and one in Germany (Strupp et al., 2017). Half of the studies were randomized control trials (RCT) (Douglas et al., 2023; Motaharinezhad et al., 2024; Potter et al., 2021; Khazaeili et al., 2019). The remaining four are two study protocols - one of a RCT (Cavalera et al., 2016) and one of a feasibility study (Kalb et al., 2023) -, and two pilot feasibility studies (Halstead et al., 2020; Strupp et al., 2017).

3.2. *Quality of the included studies*

MMAT results are reported in Appendix B, with a description of the methodological flaws and strengths of each included study. The instrument was not fully applicable to the two protocols; however, for the other six studies, the screening results indicated variability in quality, with an overall medium rating.

Regarding randomized controlled trials, they presented some incomplete or unreported information on outcome data (Douglas et al., 2023), adherence and dropout rates (Douglas et al., 2023; Motaharinezhad et al., 2024; Khazaeili et al., 2019) and randomization procedures (Khazaeili et al., 2019). Moreover, due to the reliance of patient-reported outcome, blinding was not always feasible (Douglas et al., 2023; Potter et al., 2021; Khazaeili et al., 2019).

The mixed-method study by Potter et al. (2021) demonstrated good methodological rigor overall, with good reporting and adequate integration of qualitative and quantitative results.

Concerning quantitative non-randomized designs, Halstead et al. (2020) lacked information on representativeness of participants and

Table 2
Included studies main characteristics.

Authors, publication year	**Country**	**Type of study and study design**	**Overall type/ strategy of intervention**	**Sample size (n)**	**Inclusion criteria**	**Exclusion criteria**	**Gender: Female, sample size [percentage or n (%)]**	**Age, years [mean (SD)]**	**Caregiver role (partner/ close friend/ family member) [n (%)]**	**MS type, disability level and time since diagnosis [M, SD]**	**Control group**	**Follow-up**
Douglas et al., 2023	USA	RCT. Piloting and evaluation of the feasibility with 2 arms	website and telecoaching personalized sessions to reduce negative emotional outcomes.	142	(1) Self-identified as an adult informal caregiver for a person with MS. (2) Capable of providing informed consent. (3) Identified English as primary language. (4) Able to access the internet.	No exclusion criteria.	Intervention group (Arm 1): 40 (52.6) Control group (Arm 2): 40 (53.3)	Arm 1: 53.2 (14.1) Arm 2: 51.9 (13.8)	Informal caregivers, spouse/ partner to individual with MS Arm 1: 62 (81.6) Arm 2: 58 (77.3)	Time since MS diagnosis, years Arm 1: 13.1 (10.6) Arm 2: 12.1 (9.7) MS Type: Relapse (other group Progressive) [%] Arm 1: 39 (53.4) Arm 2: 48 (65.7)	The control group accessed to: (1) information about MS, (2) obtaining MS information on the web, (3) practical strategies for caring for PwMS, (4) COVID-19 concerns, (5) self-care strategies, (6) planning and decision-making.	6 weeks after the intervention.
Kalb et al., 2023	USA	Study protocol for the co-creation and the piloting of the intervention	Emotional support and information to mitigate the overwhelming stress and anxiety and enhance wellbeing.	N/A	Being an ICs of PwMS.	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Motaharinezhad et al., 2024	Iran	Single blind RCT	Online group, educational and client-centered program to improve the mastery, performance, and satisfaction through occupational therapy.	24	(1) Family members of people with MS. (2) Aged 18–60 years old. (3) Not had a disease that affects their ability. (4) Could communicate in Persian. (5) Access and the ability to use smartphones and communication software.	In cases of a patient’s relapsing or worsening MS attack, their caregivers were excluded from the study.	Intervention group: 6 (50) Control group: 7 (58.3)	Intervention group: 38.6 (13.39) Control group: 36.6 (12.05)	Intervention group Wife: 3 (25) Husband: 0 Mother: 2 (16.6) Daughter: 5 (41.6) Son: 1 (8.3) Sister: 1 (8.3) Control group Wife: 3 (25) Husband: 3 (25) Mother: 0 Daughter: 2	EDSS* Intervention group: 6.58 (1.06) Control group: 6.6 (1.28) Duration of MS Intervention group: 14.08 (4.64) Control group: 10.2 (7.33)	The control group received educational materials related to the intervention group in an online booklet and were followed up during four online voice calls.	1-month follow-up

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Table 2 (*continued*)

Authors, publication year	Country	Type of study and study design	Overall type/ strategy of intervention	Sample size (n)	Inclusion criteria	Exclusion criteria	Gender: Female, sample size [percentage or n (%)]	Age, years [mean (SD)]	Caregiver role (partner/ close friend/ family member) [n (%)]	MS type, disability level and time since diagnosis [M, SD]	Control group	Follow-up
									(16.6) Son: 3 (25) Sister: 3 (25)			
Potter et al., 2021	UK	Feasibility RCT	Acceptance and commitment therapy self-help program integrated with telephone-supported call to reduce strain.	24	(1) Over 18 years old. (2) The primary carer for a person with MS. (3) English speaking. (4) Informed consent. (5) To score at least 21 on the Zarit Burden Interview (Zarit, Orr, & Zarit, 1985), demonstrating a minimum level of “mild distress”.	(1) Having a diagnosis of MS. (2) Reporting a psychiatric diagnosis.	SH+ (Enhanced self-help): 4 (57.1) SH (Self-help): 7 (77.8) UC (Usual care): 8 (100)	SH+: 50.23 (7.0) SH: 53.52 (12.6) UC: 58.4 (9.4)	Partner: SH+ = 6 (85.7 %); SH = 7 (77.8 %); UC: 8 (100 %). Parent: SH+ = 1 (14.3 %); SH = 1 (11.1 %); UC: 0. Other: SH+ = 0; SH = 1 (11.1 %); UC: 0.	MS type Relapsing-remitting SH+: 4 (57.1 %); SH: 4 (44.4 %); UC: 3 (37.5 %). Primary progressive SH+: 1 (14.3 %); UC: 3 (37.5 %); SH: 3 (33.3 %). Secondary progressive SH+: 2 (28.6 %); SH: 2 (22.2 %); UC: 2 (25 %). Years since diagnosis SH+: 14.4 (9.0) SH: 14.3 (6.0) UC: 14.0 (8.7)	Participants allocated to the SH group did not receive any additional support associated with reading the chapters.	3- and 6-month post-randomisation.
Halstead et al., 2020	USA	Pilot Feasibility study	Resilience-based skills program including education and practical skills	31	(1) Both partners (PwMS and their close family member) had to live together in the US. (2) Aged 18–65 years old. (3) Have access to a computer with a stable internet connection in a private setting.	N/A	*n* = 10 (38,4 %)	N/A	Spouses: 26 Cohabiting partners: 2 Parent–child dyads: 3	MS Type Relapsing–remitting 29 Secondary progressive: 1 Progressive relapsing: 1 Mean time since diagnosis: 13.2	No control group.	3-month follow-up.
Khazaeili et al., 2019	Iran	Randomized quasi-experimental study with control group.	Mindfulness-based skills to reduce burden, anxiety and depression	30	(1) Living with the patient. (2) Having ability to communicate and understand tasks. (3) Having relatively high-speed Internet access with a	(1) Severe physical problems. (2) Mental illness and addiction. (3) Failure to communicate. (4) Lacking access to the Internet. (5) Unwilling to participate.	N/A	N/A	N/A	Relapsing-remitting MS (RRMS)	The control group received no intervention.	1-month follow-up.

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Table 2 (*continued*)

Authors, publication year	Country	Type of study and study design	Overall type/ strategy of intervention	Sample size (n)	Inclusion criteria	Exclusion criteria	Gender: Female, sample size [percentage or n (%)]	Age, years [mean (SD)]	Caregiver role (partner/ close friend/ family member) [n (%)]	MS type, disability level and time since diagnosis [M, SD]	Control group	Follow-up
					personal computer or mobile phone. (4) Having enough literacy. (5) Being 20–70 years old.							
Strupp et al., 2017	Germany	Pilot Feasibility study	Hotline that provides information about PHC and local available PHC services.	61	Being an MS caregiver/ family member/ close friend.	N/A	62.3 %	N/A	Spouses: 26.2 % Friends and neighbors: 16.4 % Children: 14.8 % Parents: 9.8 % Siblings: 6.6 %	N/A	No control group.	N/A
Cavalera et al., 2016	Italy	Study protocol for an RCT with 2 arms		N/A	(1) Living with the MS patient and providing him or her with the most care and assistance; (2) Ability to communicate and to understand tasks; (3) Availability of a computer, smartphone, or tablet; (4) Informed consent; (5) Age >18 years.	(1) Severe co-morbidity. (2) Severe neuropsychological impairment. (3) Psychosis or dissociative disorders. (4) Pregnancy.	N/A	N/A	N/A	N/A	The control intervention includes a psycho-education online program about MS, characterized by interviews, practical advice, and exercises.	27 weeks after the intervention.

[*] Expanded Disability Status Scale.

Table 3
Main characteristics of the included digital interventions and tools.

Authors, publication year	**Aim of the intervention/tool**	**Intervention Main contents**	**Intervention Structure**	**Target group**	**Intervention Duration**	**Delivery of the intervention**	**Who delivered the intervention**
Cavalera et al., 2016	To test MBSR protocol adapted to MS requirements and clinical peculiarities.	An online meditation treatment, provided with audio and video stimulations, with multiple interactions with the trainer.	2 h/week of online meditation in a group setting, plus 1 hour/week of individual exercises.	Patient-caregiver couples	8 weeks	The intervention is designed to be delivered in an e-Health modality through a specifically developed software.	Trainer
Kalb et al., 2023	(1) To mitigate the overwhelming stress and anxiety experienced by MS ICs by connecting them to available information, support, resources, and services. (2) To increase ICs health and well-being.	Emotional support and information about financial assistance, long-term care planning, and community resources training for specialized tasks, communication strategies and conversation-starters for difficult conversations, coaching by other support partners, information for children about MS.	The CPT recruited an 8-member Caregiver Advisory Board (CAB). The needs and priorities identified were expanded and validated through an online survey distributed to additional MS caregivers via the Accelerated Cure Project, iConquer MS, Can Do MS mailings, and RealTalk MS podcasts.	Only ICs	Open	86.4 % of survey responders chose a web portal with materials they could access at any time; 70.9 % opted for online support groups and/or coaching; 42.7 % preferred in-person support groups and/or coaching; and 34.5 % selected print materials.	N/A
Douglas et al., 2023	To reduce MS ICs negative emotional outcomes.	Participants in arm 1 received 2 components: (a) 4 personalized coaching sessions, and (b) access to the study-designed website. The key components of the coaching sessions were session 1. identifying informal caregivers' needs for information and support; session 2. strategies for caring for a loved one with MS; session 3. caring for yourself; and session 4. planning and decision-making.	Arm 1: study-designed website access and telecoaching personalized sessions. Arm 2: study-designed website access.	Only ICs	N/A	Coaching sessions were delivered via videoconference or telephone, while the website was always available through a personal password that allowed for website usage tracking.	Two independent social workers.
Motaharinezhad et al., 2024	To improve the mastery, performance, and satisfaction of ICs through an online occupational therapy program.	The intervention group received the AOCCMS which was an online group, educational and client-centered program. Each session of the program was followed with a specific goal.	Intervention group: five two-hours sessions, once a week, and access to educational materials, videos, and shared photos.	Only ICs	5 weeks	Group sessions were held online through the Sky-room program in two small groups during five two-hour sessions spread over five weeks.	An experienced and trained occupational therapist.
Halstead et al., 2020	(1) To increase resilience focusing on building individual resilience and associated factors (2) To increase family support and cohesion to facilitate positive psychological adjustment and overall well-being through teaching communication skills.	The resilience-based skills program included both education and practical skills. Sessions: (a) Positive adjustment to MS, (b) Acceptance, and (c) Education about resilience in MS; (d) Information: Symptoms of MS; (e) Communication skills; (f) Healthy coping strategies, (g) Seeking support, and social connection; (h) Advocacy skills, and (i) Self-care for the support	Six sessions of 45 min. Two of the six modules were designed to be attended by both participants, the four intermediate sessions were designed for the support partner only. Each session included Q&A/ videos; role play/ vignettes; connect the dots (How does this	Patient-caregiver couples	6 weeks (six 45-min weekly sessions)	The study was delivered through the web-based portal "MS Hub", developed for this study. The MS Hub enabled participants to access related program software, including an HTML-based linear presentation, Adobe Connect (video tele-conferencing), and Adobe Sign (completion of electronic consent forms).	A "resilience coach," who was an experienced licensed social worker, with prior experience working closely with caregivers.

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Table 3 (*continued*)

Authors, publication year	**Aim of the intervention/tool**	**Intervention Main contents**	**Intervention Structure**	**Target group**	**Intervention Duration**	**Delivery of the intervention**	**Who delivered the intervention**
		partner; (j) Identifying and accessing resources.	relate to me?); and selecting activities to practice at home.				
Potter et al., 2021	To reduce carer strain in ICs of people with MS.	Participants in the intervention arm received chapters weekly from the ACT self-help text "Get out of your mind and into your life: The new Acceptance and Commitment Therapy" (Hayes and Smith, 2005). Those allocated to the enhanced self-help group received also a weekly telephone-supported call.	Week 1: Human Suffering and Language Week 2: Avoidance and Letting Go Week 3: Introduction to Thoughts Week 4: Defusion and the Observing-Self Week 5: Mindfulness Week 6: Willingness Week 7: Values Week 8: Commitment	Only ICs	8 weeks	The intervention was delivered through an online platform. Those in the SH+ received telephone-supported call.	A psychology trainee with expertise in the provision of structured support.
Khazaeili et al., 2019	To reduce caregiver burden, anxiety and depression through an online program combining mindfulness-based cognitive therapy and mindfulness-based stress reduction.	The MBI program focused on developing mindfulness skills through various exercises, such as body scans, meditation, and staying present. Participants learned to manage daily challenges, recognize and accept their thoughts and emotions, and create coping strategies for depression. The program also emphasized self-care and applying mindfulness in future interactions.	The test group received eight 2-hour sessions of MBI via a web conferencing software.	Only ICs	8 weeks	Caregivers were told that they would be added to a group in the Telegram application to receive educational notes and audio files. Library method was used and data from the participants gathered online via Telegram. Adobe Connect V. 9.6 was used as web conferencing application.	N/A
Strupp et al., 2017	To answer the needs and problems of patients severely affected by MS and their caregivers, trying to be a first contact point for information about PHC and its structures.	The hotline provided information about PHC and local available PHC services, according to the needs of the callers.	Hotline office hours were 9.00 to 11.00 h on Wednesdays.	Both PwMS and their ICs	2 years	The intervention (hotline) was fully delivered via telephone.	An experienced social worker and coordinator of an outpatient hospice service.
Cavalera et al., 2016	Italy	Study protocol for an RCT with 2 arms	Online mindfulness-based treatment	N/A	(1) Living with the MS patient and providing him or her with the most care and assistance (2) Ability to communicate and to understand tasks (3) Availability of a computer, smartphone, or tablet; (4) Informed consent (5) Age >18 years.	(1) Severe co-morbidity. (2) Severe neuropsychological impairment. (3) Psychosis or dissociative disorders. (4) Pregnancy.	N/A

Table 4
Outcomes.

Authors, publication year	Outcomes (variables, questionnaires)
Cavalera et al., 2016	**Main outcomes** (1) Medical Outcomes Study short form (MOS; Ware and Sherbourne, 1992) to assess ICs' quality of life. (2) Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983) to evaluate anxiety and depression levels. **Secondary/other outcomes** (1) Langer Mindfulness/Mindlessness Scale (MMS, Haigh et al., 2011). (2) Medical Outcomes Study sleep measure (Hays et al., 2005). (3) actigraphy, a non-invasive method of monitoring cycles of rest and activity.
Kalb et al., 2023	**Main outcomes** The study focuses on the development of a comprehensive online caregiver intervention (no specifical outcomes indicated). **Secondary/other outcomes** N/A
Douglas et al., 2023	**Main outcomes** An overall index of negative emotion that included depression, anxiety and stress, measured with the composite score of the Depression Anxiety Stress Scale (DASS; Lovibond and Lovibond, 1995). **Secondary/other outcomes** (1) Depression, anxiety, and stress scores as measured by the subscales of the DASS (Lovibond and Lovibond, 1995). (2) Distress Thermometer (DT), a single-item, self-report measure (Cutillo et al., 2017).
Motaharinezhad et al., 2024	**Main outcomes** (1) Canadian Occupational Performance Measure (COPM; Carswell et al., 2004) to measure occupational performance. (2) Relative Mastery scale (RMS; Krusen et al., 2018), to measure the adaptive response (mastery) of ICs in the face of occupational challenges and the effect of occupational therapy interventions. **Secondary/other outcomes** N/A
Halstead et al., 2020	**Outcomes** (1) Resilience (10-item Connor–Davidson Resilience Scale; Connor and Davidson, 2003). (2) Knowledge of MS (10-item questionnaire created by the authors). (3) General Life Satisfaction Survey (Salsman et al., 2013). (4) Positive and Negative Affect Schedule (valid within the last week; Watson et al., 1988). (5) Burns Relationship Satisfaction Scale (Burns D., & Sayers, S., 1988). (6) Hospital Anxiety and Depression Scale (HADS; Zigmond et al., 1983). (7) Perceived Stress Survey (Cohen et al., 1994). (8) General Self-Efficacy Scale (Salsman et al., 2013). (9) Sense of Competence Questionnaire (SCQ; Vernooij-Dassen et al., 1986). (10) Zarit Burden Interview (ZBI; Zarit et al., 1980).
Potter et al., 2021	**Outcomes** (1) The Modified Carer Strain Index (MCSI; Robinson, 1983; Thornton and Travis, 2003) to assess aspects of caring and the impact that caring has on various life domains. (2) The CAREQOL-MS (Benito-Leon et al., 2011) to assess HRQoL and was designed and validated specifically for carers of PwMS. Process measures: (1) Acceptance and Action Questionnaire (Bond et al., 2011). (2) Comprehensive Assessment of Acceptance and Commitment Therapy (CompACT; Francis et al., 2016). Semi-structured feedback interview after their 3-month follow-up about the acceptability of the intervention
Khazaeili et al., 2019	**Main outcomes** N/A**Secondary/other outcomes** Anxiety, depression, and burden of the caregivers. (1) Beck anxiety inventory (BAI; Beck et al., 1988). (2) Beck depression inventory, Second Edition (BDI-II; Beck et al., 1996). (3) Caregiver burden inventory (CBI; Novack & Guest, 1989) (4) Five-facet mindfulness questionnaire (FFMQ; Baer et al., 2006).
Strupp et al., 2017	**Outcomes** The study focuses on retrospective analysis of helpline interactions.

administration of the intervention. Moreover, issues about outcome completeness, and consideration of confounders where highlighted. For the qualitative study, Strupp et al. (2017) had appropriate design, data collection, and interpretation of findings.

Although not directly evaluated by the MMAT, follow-up evaluation was performed by five studies (Douglas et al., 2023; Potter et al., 2021; Khazaeili et al., 2019; Halstead et al., 2020; Motaharinezhad et al., 2024) and planned by one protocol (Cavalera et al., 2016). However, follow-up evaluations were usually brief, ranging from 1 month to three months in four studies (Douglas et al., 2023; Khazaeili et al., 2019; Halstead et al., 2020; Motaharinezhad et al., 2024) and being up to six or seven months in the other two (Potter et al., 2021; Cavalera et al., 2016).

3.3. *Population characteristics of the included studies*

The majority of interventions were designed exclusively for ICs (Kalb et al., 2023; Douglas et al., 2023; Motaharinezhad et al., 2024; Potter et al., 2021; Khazaeili et al., 2019). Two studies involved PwMS-caregiver couples (Cavalera et al., 2016; Halstead et al., 2020), and only one was open to both PwMS and their ICs, separately (Strupp et al., 2017).

All studies included only adults, except for the study by Strupp (2017), which was open to a broader age range (including also children). Where the age was reported, the average age of ICs was between 49.5 and 58.4 years. In Motaharinezhad et al. (2024), a younger population

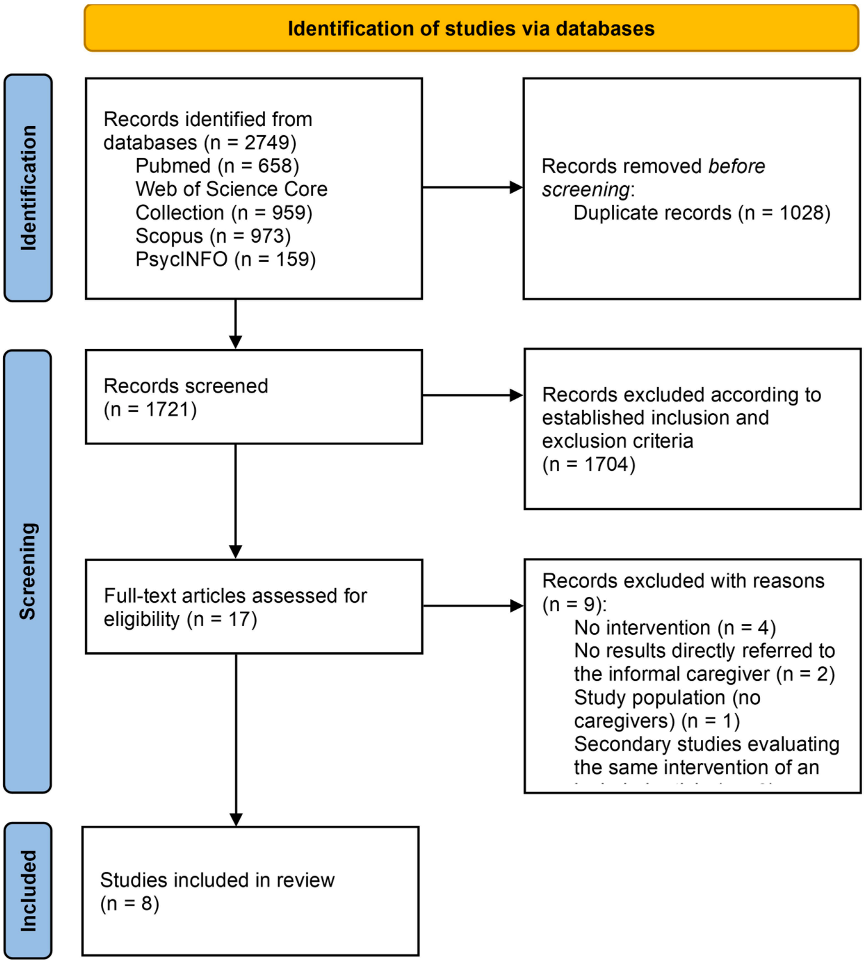

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

was recruited (mean age 38.6). Four studies reported the gender of the ICs involved, and in three out of them the proportion of female is higher than that of male (Douglas et al., 2023; Motaharinezhad et al., 2024; Potter et al., 2021).

There are no specific criteria restricting the role of ICs, although in many cases, only family members or people living with the PwMS participated in the study (Cavalera et al., 2016; Motaharinezhad et al., 2024; Halstead et al., 2020; Khazaeili et al., 2019). Most of the ICs involved are spouses or partners of PwMS, with a percentage that spans from 26.2 % (Strupp et al., 2017) to 90.3 % (Halstead et al., 2020). In the telephone hotline for palliative and hospice care also friends and neighbors are mentioned (Strupp et al., 2017). In a specific study (Potter et al., 2021), it was established as an inclusion criterion that ICs participants had to exhibit a minimum level of mild distress, scoring at least 21 on the Zarit Burden Interview (Zarit, Orr, & Zarit, 1985).

The MS diagnosis and level of disability of the patients is not considered as an inclusion/exclusion criterion. In the five studies where the patients' MS type was indicated, mainly ICs of people with relapsing-remitting MS participated (Cavalera et al., 2016; Douglas et al., 2023; Halstead et al., 2020; Potter et al., 2021; Khazaeili et al., 2019), and three of these included also ICs of those with secondary-progressive MS (Cavalera et al., 2016; Halstead et al., 2020; Potter et al., 2021), and only one study (Potter et al., 2021) included ICs of people with primary-progressive MS.

3.4. Interventions main characteristics

Interventions and tools in the included papers were different in terms of goals, structure, contents, specific outcomes, and duration (see Table 2), with some similarities summarized below. Looking at the goals of the interventions five interventions primarily focused on promoting psychological strategies through structured sessions to reduce burden and emotional distress (Cavalera et al., 2016; Khazaeili et al., 2019; Potter et al., 2021; Halstead et al., 2020; Motaharinezhad et al., 2024), while three emphasize more general informative and supportive aims (Kalb et al., 2023; Douglas et al., 2023; Strupp et al., 2017). Below we map the characteristics of these interventions according to these two groups, in order to facilitate synthesis of common interventions components.

Regarding the first group, in the intervention by Cavalera et al. (2016), PwMS-caregiver pairs participated in a weekly two-hour online group mindfulness course, along with one hour of individual exercises, over an 8-week period. Similarly, Khazaeili et al. (2019) offered a weekly two-hour online mindfulness-based intervention (MBI), combining mindfulness-based cognitive therapy and mindfulness-based stress reduction, exclusively for ICs. Both these interventions aimed to reduce anxiety and depression and improve the quality of life by lowering the burden levels of ICs of PwMS. The intervention by Potter and collaborators was a self-help intervention based on an Acceptance and Commitment Therapy (ACT) approach and designed exclusively for ICs, in which participants received a chapter from a self-help workbook once a week, for 8 consecutive weeks. Additionally, members of the enhanced self-help group (the experimental arm) received weekly telephone calls from an expert psychology trainee to provide supplementary support.

The resilience-based skills program by Halstead and colleagues

(2020) - conducted by an experienced licensed social worker - included both informative and practical skills on topics such as positive adjustment, acceptance, communication skills, and self-care for the ICs. This intervention was also targeted for PwMS, and it was divided into six online modules: two were designed to be attended by both participants, while the four intermediate sessions were designed for the support partners only.

Occupational therapy was employed in Motaharinezhad et al. (2024) to enhance the proficiency, effectiveness, and satisfaction of ICs of PwMS. In each of the five weekly two-hours online sessions, an experienced occupational therapist guided ICs in the management of challenges at the personal and environmental subsystem levels, including techniques on stress management, coping with emotions, communication, use of resources and support services, problem-solving for occupational challenges.

The second group of interventions comprises three studies. The study of Kalb and collaborators (2023) describes the co-creation phase of an online tool designed to mitigate stress and anxiety in ICs of PwMS, connecting them to available information, support, resources, and services at the time of the MS diagnosis and throughout the disease course. The aim of the tele-coaching intervention by Douglas and colleagues (2023) is to reduce ICs negative emotional outcome through the combination of a website plus personalized coaching sessions conducted by two independent social workers: the website gathers informational materials, including practical advice on how to support and care for PwMS; participants in the experimental group also received four telematic personalized coaching sessions on topics as caring for both the caregiver and the care recipient, as well as planning and decision-making for the future. Lastly, the telephone support service (Strupp et al., 2017) is designed to address the challenges of an advanced stage of the disease, offering a contact point for information about Palliative Hospice Care and recommending local services according to individual's needs.

3.5. *e-Health modalities adopted for interventions*

The digital tools used by the studies fell into three main categories: web-based interventions (i.e., psychological interventions and wellbeing programs accessible through websites), m-health (mobile-health) modalities; Tele-health, such as telephone-consulting or video-consulting. Tele-consulting might be considered a subset of telehealth, involving digital consultations between healthcare professionals and caregivers or patients to provide guidance, support, or problem-solving, whereas telehealth more broadly encompasses a wide range of remote healthcare services (Dawson et al., 2022). Most studies (5 out of 8) used a combination of these approaches to deliver interventions. The most used modality to deliver the intervention is tele-consulting. The only study that did not use this modality is that of Cavalera and colleagues (2016) whose intervention is exclusively web-based. In three interventions the core contents (such as book chapters or access to websites) were sent directly to participants via email or through a mobile messaging application.

Although these interventions do not include an in-person component two of these interventions explicitly enable ICs to connect remotely with healthcare professionals, support groups, and other services, offering integrated and personalized support (Potter et al., 2021; Strupp et al., 2019).

3.6. *Effectiveness and feasibility results of the interventions*

Primary and secondary outcomes of the studies, including those specified in the protocols, are reported in Table 4. Below, we will describe the results of the main outcomes and feasibility, as well as follow-up results when reported (i.e., excluding the protocols studies).

Among the included articles, the four RCTs compared the e-Health interventions with other control conditions (see Table 1 for a description of the control groups characteristics). In Douglas et al. (2023), the group-by-time interaction was statistically significant for the Depression Anxiety Stress Scale (DASS) Total Composite score ($p = .037$) and the DASS Stress subscale (p=.047), indicating a greater effectiveness of the intervention in Arm 1 (website and telecoaching) compared to Arm 2 (website only). No differences were highlighted for DASS Depression subscale, DASS Anxiety subscale and for the Distress Thermometer score. Arm 1 significantly improved on the DASS Total Composite score ($p < .01$; small effect size, $d = 0.41$), and the DASS Stress subscale ($p < .01$; small effect size, $d = 0.41$) after the intervention and at the at the 6-week follow-up ($p < .01$; small effect size, $d = 0.34$ for DASS Total Composite score; small effect size, $d = 0.32$ for DASS Stress subscale), according to post hoc pairwise comparison analyses. In contrast, Arm 2 did not show significant improvements either post-intervention ($p = .41$) or at follow-up ($p = .12$) on DASS Total Composite score. An improvement for Arm 2 was found at the 6-week follow-up for the DASS Stress subscale ($p = .019$).

In Motaharinezhad et al. (2024), time*group analysis highlighted a significant difference in occupational performance and satisfaction scores between the intervention group (occupational therapy intervention) and the active control group ($p < .001$). Additionally, ICs mastery increased significantly post-intervention in the intervention group compared to pre-test ($p < .001$), although changes between the intervention and control groups were not significant ($p = .175$). The results were sustained up to one-month after the intervention.

The resilience-based telehealth program (Halstead et al., 2020) significantly improved satisfaction with own performance as an IC ($p = .007$), according to linear regression analysis. No significant changes were reported for satisfaction with care recipients, and the consequences of involvement in care for the personal life of the IC. Stress and anxiety levels decreased post intervention (respectively, $p = .030$ and $p = .024$). Furthermore, results indicate that relationship satisfaction (reported by spousal couples only) improved for support partners ($p = .022$), but not for people with MS. The intervention did not show statistically significant effects on knowledge of MS, resilience, life satisfaction, positive and negative affect, depression, self-efficacy and burden.

In Potter et al. (2021) significant allocation-by-time interaction effects were highlighted using intention-to-treat mixed linear model analysis; however, no differences between groups were found with contrast analyses. Significant within-group changes ($p < .05$) were reported for the enhanced self-help group on burden, carer strain, and on ACT-related process such as experiential avoidance, behavioral awareness, and the total score of the CompACT, between baseline and the three months follow-up. Additionally, at the six-month follow-up, the valued action subscale also improved ($p < .05$). The standard self-help group showed a significant change (p<.05) on the experiential avoidance subscale of CompACT at 3-month follow-up. On comparisons of baseline to 6-month follow-up, results showed significant improvement ($p < .05$) on the ZBI, the Acceptance and Action Questionnaire and the CompACT total score and its subscales, except for the valued action subscale (p=.248). No significant changes were reported for the usual care group.

In the mindfulness-based intervention proposed by Khazaeili and its group (2019) the group-by-time interaction revealed a significant difference between anxiety ($p < .05$) and burden scores ($p = .001$) in the intervention (mindfulness-based program) and control groups (no intervention) in the pre-test, post-test and follow-up. No significant differences were highlighted for depression ($p = .721$).

Only two studies reported results in terms of feasibility. The intervention implemented by Halstead and colleagues (2020) met its feasibility goals, defined as the willingness of eligible couples to participate and their level of engagement (i.e., 83.8 % completion rate). High levels of satisfaction were reported as highlighted by a mean overall satisfaction of the sessions of 4.76 (on a scale 0 to 5). In Potter and colleagues (2021), the overall attrition rate at the 3-month follow-up was 16 % (22 % in the self-help group and 29 % in the enhanced self-help group). By the 6-month follow-up, the overall attrition rate was 21 %. A higher attrition rate was reported for the two interventions compared to usual care. The enhanced self-help group reported reading higher percentages of the self-help text each week (50–75 %) compared to the self-help group (25–50 %). Semi-structured interviews with participants uncovered that ICs found the text not accessible, with consequent discouragement and less engagement. All participants felt that the weekly reading load was excessive given their caregiving duties, and they preferred shorter summaries or more relevant examples for carers. Additionally, some found basic ACT concepts hard to grasp and difficult to apply. The people in the enhanced self-help group positively evaluated the phone calls to improve motivation. The interviews investigated self-perceived changes, with participants in the self-help group not reporting any benefits, and participants in the enhanced intervention reporting positive changes, which they attributed to skills-based learning and the relational aspects of the telephone calls (Potter et al., 2021).

Lastly, Strupp's study focuses on retrospective analysis of helpline interactions rather than setting specific outcomes. Twenty-five ICs out of 61 expressed personal needs, for example having someone to talk to, about making decision and about death and dying; moreover, they also asked for emotional support.

4. Discussion

The current systematic review includes eight recent studies on the existent eHealth psychosocial interventions and tools dedicated to support ICs of individuals with MS: among them two protocol papers, suggesting the emerging interest and the scarcity of studies in this research field. Although this result is in line with the literature on ICs interventions, which consider how this is still a developing research area (Hoseinpur et al., 2023; Rajachandrakumar et al., 2021), the paucity of studies is in contrast with the substantial evidence of the essential role of informal caregiving in chronic diseases and the recognized ICs needs (Sorayyanezhad et al., 2022; Chow et al., 2023; Maguire and Maguire, 2020). Among the possible explanations, a prominent one is the frequent neglect of ICs' support, as caregiving models often prioritize patient care over the patient-caregiver dyad, despite the fact that the well-being of ICs directly influences the quality of patient care (Zhai et al., 2023). Moreover, ICs themselves also tend to prioritize their loved ones' well-being over their own (Chan et al., 2022): they may feel guilty about focusing on their own needs, fearing it could lessen the quality of care they provide. Schulz and Sherwood (2008) have discussed the emotional toll of caregiving, including feelings of guilt and inadequacy, and how these emotions are shaped by societal and self-imposed expectations.

4.1. *Target of the interventions and tools*

As regards the IC type (in terms of relationship), most of the ICs included in the reviewed studies are partners or spouses of PwMS, in line with findings from various studies on ICs demographics, where spouses play a predominant role in caregiving because of their close relationship and shared responsibilities (Maguire and Maguire, 2020; Benini et al., 2023). However, it is important to note that the studies did not set specific criteria for including ICs, and therefore none of the interventions appear to be specifically tailored to subgroups of ICs in terms of role with the patients. This raises the issue of underrepresentation of some categories, such as parent caregivers of pediatric PwMS, as highlighted by Ghai et al. (2021).

In terms of patients' clinical characteristics, the majority of PwMS in the analyzed interventions had relapsing-remitting multiple sclerosis (RRMS), likely due to its higher prevalence (Perrone et al., 2022). However, different types of MS may present varying needs for assistance and demands on ICs (McKenzie et al., 2015; Lorefice et al., 2013), even considering the evolving nature of SM. In this regard, only an included study (Strupp et al., 2017) addressed specific needs MS-related, particularly in the context of palliative and hospice care as the intervention targeted patients in advanced stages of illness.

These considerations suggest that certain ICs sub-groups, whether defined by their caregiving role or by the type and stage of MS, may have specific needs that require tailored interventions, highlighting an important area for further exploration and development.

4.2. *Aims, contents and effectiveness of the interventions and tools*

The eight interventions included have been categorized into two broad categories, depending on their specific goals (see Fig. 2): those that focus on promoting skills that help reduce burden, anxiety,

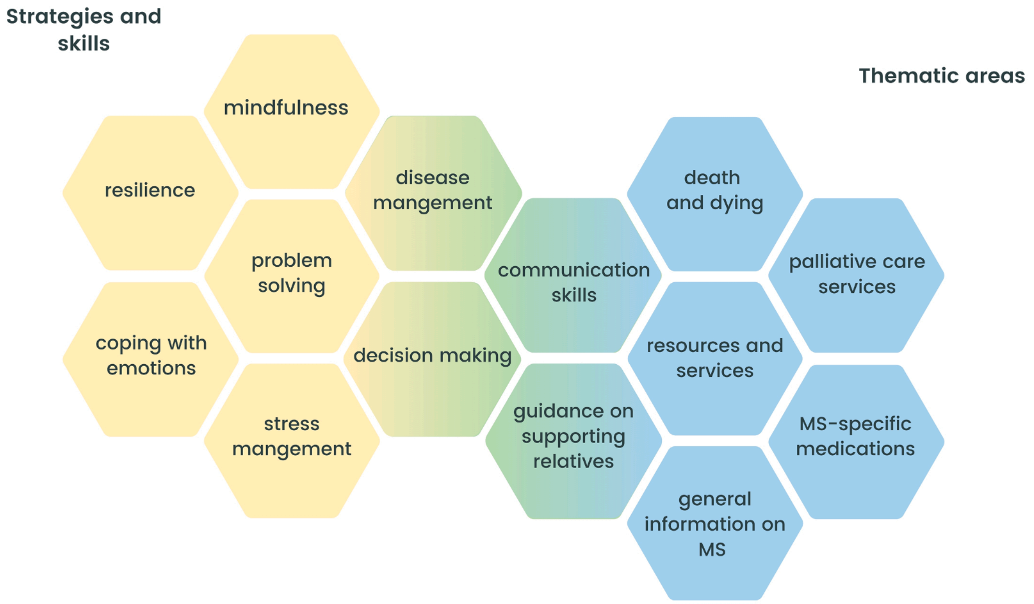

Fig. 2. Main strategies, skills, and thematic areas of included interventions. In this image, the skills related to the first interventions group (i.e., "promoting skills") are repersented in shades of yellow while topics addressed by interventions from the second group (i.e., "informational and support) apperar in blue. The overlapping areas, even visually, illustrate these aspects from a continuum rather than two distinct, separate components.

depression, and improve quality of life (Cavalera et al., 2016; Motaharinezhad et al., 2024; Halstead et al., 2020; Potter et al., 2021; Khazaeili et al., 2019); those that instead have a more broad informational and support function, dealing with providing information on MS diagnosis and progress of the disease and responding to the needs and problems related to the caregiving role (Kalb et al., 2023; Douglas et al., 2023; Strupp et al., 2017). In the figure, we provide a visual representation of the themes addressed, illustrating the two main categories while also highlighting that they lie along a continuum.

Specifically, looking at the five studies included in the first group, they place greater emphasis on promoting skills and strategies. This group includes two interventions based on mindfulness training (Cavalera et al., 2016; Khazaeili et al., 2019), an intervention focused on the development of resilience strategies (Halstead et al., 2020), one using occupational therapy (Motaharinezhad et al., 2024), and one based on ACT (Potter et al., 2021). Looking at the main psychological strategies included, those based on mindfulness and acceptance are found in three of them (Cavalera et al., 2016; Khazaeili et al., 2019; Potter et al., 2021). According with the existing literature, mindfulness-based interventions are useful in helping ICs in chronic illness contexts managing stress, improving emotional regulation, and enhancing overall wellbeing (Epstein-Lubow et al., 2011; Whitebird et al. 2013; Brown, 2016; Hearn, 2019). Furthermore, the mindfulness approach can easily be implemented digitally (Tkatch et al., 2017; Kubo et al., 2019).

Two included studies (Motaharinezhad et al., 2024; Halstead et al., 2020) address communication aspects, including the enhancement of skills and techniques for helping ICs in interacting with their cared ones. Communication and health literacy can significantly improve the quality of care provided and reduce caregiver stress (Demiris et al., 2019). Furthermore, this aspect is closely linked to health literacy and to decision-making, areas addressed in the study by Strupp and colleagues, included in the second group of interventions (Strupp et al., 2017). This highlights, as previously introduced, that the categorization does not sharply differentiate interventions; rather, it represents a continuum, in which each intervention predominantly focuses specific domains while still incorporating skills and themes belonging to the other group.

In the second group, we can find three interventions primarily aimed at providing practical support to caregivers: Kalb et al., 2023; Douglas et al., 2023; Strupp et al., 2017. We refer to these as informational and support interventions. Themes such as general information on MS and MS-specific medications, death and dying, and palliative care services, as well as guidance on supporting the care of relatives, are highlighted. Informational and support interventions play a critical role in supporting ICs, facilitating the contact between the PwMS and their ICs with services and offering both practical and emotional guidance.

In support of the conceptual continuum adopted, applied in this review, the aspects promoted in the two interventions' groups are closely interconnected and integrated; indeed, research indicates that when ICs receive both types of support (i.e., practical and emotional), they experience reduced stress and improved overall well-being (Mikkelsen et al., 2021). This dual approach enhances health literacy, enabling ICs to make better-informed decisions about care, which fosters a greater sense of control (Sørensen et al., 2012). However, only one of the studies included attempts to integrate both components (Douglas et al., 2023); this leads us to say that there is a notable lack of studies that integrate both informational and supportive elements along with the promotion of psychological strategies. To contextualize these findings, it is useful to compare them with digital interventions for ICs in other chronic conditions, such as cancer or dementia. Similar to MS, caregivers in these populations face high levels of stress, anxiety, and role burden. Digital interventions for caregivers of patients with cancer or dementia often combine informational support, skills training, and psychosocial strategies (Kaltenbaugh et al., 2015; Boots et al., 2014). For instance, web-based psychoeducational programs for dementia caregivers have been shown to reduce stress and improve coping strategies, while mobile apps for cancer caregivers enhance care coordination and provide timely emotional support. Notably, these interventions frequently integrate both practical and emotional support, paralleling the dual approach highlighted in our review of MS interventions.

At post-intervention and follow-up measures, when evaluated, overall results in terms of effectiveness of the interventions seem to be promising: two works (Douglas et al., 2023; Khazaeili et al., 2019) demonstrated significant reductions in stress and anxiety through targeted interventions. Both Motaharinezhad et al. (2024) and Halstead et al. (2020) highlighted improvements in caregiver performance and satisfaction, though Halstead noted no significant change in overall satisfaction scores.

4.3. Characteristics of the digital format of the intervention and feasibility

All the included interventions adopted a fully remote approach, entirely based on eHealth modalities. The predominant modality utilized was tele-consulting, employed by seven out of eight studies, which facilitated remote interactions between ICS and healthcare professionals. Tele-consulting has proven valuable in various ICs and chronic disease contexts, enhancing care access and support and greater satisfaction and reduced stress (Kruse et al., 2017).

One of the primary advantages of eHealth is the ability to participate in programs from home (Donisi et al., 2022; Ossebaard and Van Gemert-Pijnen, 2016). This convenience is crucial for ICs who often have limited time due to their caregiving responsibilities as also highlighted in some of the included studies, such as that by Douglas et al. (2023) which considered the advantage brought by eHealth solutions for ICs that feel unable to leave the family members they attend to. The severity of MS and other disease-specific factors may influence the type of caregiving tasks, and the time required of caregivers. For example, caregivers supporting individuals with MS and higher levels of disability may benefit from more time-efficient, home-based interventions that enhance their well-being without requiring them to leave the person they are caring for unattended. However, while aspects related to the diagnosis were sometimes considered in relation to the purpose of the intervention (Strupp et al., 2017), no data or comments were provided regarding the feasibility of the interventions according to the disease-specific factors or the caregiving tasks.Theoretically, eHealth platforms allow ICs to connect with a broader network of ICs, facilitating social support, reducing isolation (Sitges-Maciá et al., 2021; Douglas et al., 2023; Motaharinezhad et al., 2024), and potentially decreasing the stigma associated with seeking help (Clement et al., 2015). However, neither of these aspects is addressed in the interventions included and may be points to watch out for in future research.

Among the analyzed studies, none explicitly discuss the influence of cultural factors on the feasibility or acceptability of digital interventions aimed at caregivers of people with MS. However, some works provide insights into demographic aspects: Cavalera et al. (2016) included participants with a mean age of 51 years, while Halstead et al. (2020) reported a mean caregiver age of 57 years, both emphasizing that age was considered in tailoring interventions to the needs of the target population, but no specific reflections were made regarding how age influences the feasibility or acceptability of digital tools. Age can be a significant factor when it comes to digital health literacy. While this topic has been primarily studied concerning patients, it is equally relevant to caregivers, who are often their partners and therefore similar in age. Evidence shows that older adults generally tend to have lower levels of digital literacy compared to younger cohorts, which represents one of the main barriers to adopting digital devices for health-related purposes

(De Lucia et al., 2024). To conclude, none of the studies explicitly examine the feasibility of digital interventions considering these factors, indicating a gap in the literature and the need to further analyze the potential role of the target population's cultural, demographic and clinical elements demographic and clinical elements of the target population in evaluating the practicality of implementing such tools. Many included studies do not report on the time demands of caregiving or caregivers' health conditions, which may affect ability to be employed, availability of financial resources, access to traditional support and preferences for digital interventions. These factors can impact overall well-being and feasibility of interventions, underscoring the need for interventions that are tailored to the practical, contextual and health-related constraints of ICs. Only two of the included studies (Halstead et al., 2020; Potter et al., 2021) did provide feasibility data, both reporting encouraging findings. Participants demonstrated strong engagement and acceptance of the eHealth interventions in those studies, suggesting that such tools are promising in terms of practical implementation. Nonetheless, the limited number of studies assessing these dimensions clearly indicates feasibility remains under-investigated and suggests the need for its systematic assessment in future interventional studies. This issue is particularly crucial when targeting informal caregivers, as their substantial burden may hinder participation in psychosocial interventions. Therefore, it is important to assess feasibility dimensions such as acceptability, barriers, and facilitators to participation (e.g., Hopwood et al., 2018).

4.4. Quality of the studies

The quality of the studies included was overall evaluated as moderate, highlighting the need for further research that can overcome existing methodological limitations. While most studies demonstrated a solid methodological foundation, some did not present all relevant outcomes or failed to provide a complete account of their findings. Another important aspect is that only half of the studies assessed the effects of interventions at follow-up. In particular, the lack of long-term follow-up restricts the ability to evaluate the enduring effects of interventions, a gap that is especially critical given the chronic and progressive nature of MS-related needs and the resulting caregiver tasks. Furthermore, all included studies relied on self-reported questionnaires for outcome assessment, which may introduce potential biases. These considerations naturally lead into the reflection on the strengths and limitations of the present review.

5. Limitations

Several limitations of this review should be acknowledged. The review encompasses only eight studies, which limits the generalizability of the findings. The included studies vary in terms of eHealth interventions, ranging from tele-consulting to online support groups, and target different psychosocial primary and secondary outcomes, precluding a meta-analytic synthesis and making it difficult to draw definitive conclusions about the effectiveness and feasibility of specific modalities. Another significant limitation is the variability in the quality and methodologies of the studies, which affects the comparability of the findings.

However, this systematic review also presents several strengths. It addresses a critical gap in the literature, and the use of broad inclusion criteria allowed us to describe all the existing digital-delivery psychosocial interventions, providing valuable insights in the under-explored area of eHealth interventions for ICs. Moreover, the review follows PRISMA guidelines, and the quality of included studies was thoroughly assessed using the MMAT, suitable for multidisciplinary research.

6. Conclusion

Despite the growing acknowledgment of the importance of supporting caregivers of PwMS and the increasing interest for e-health solutions, the body of literature specifically addressing digital psychosocial interventions and tools designed for ICs in the MS field remains notably limited and only a restricted and recent number of studies have investigated digital tools specifically designed for this group. Overall, these digital interventions showed signal of effectiveness in alleviating stress and anxiety and answering the multifaceted needs of ICs, while also highlighting the critical role of accessible, practical support resources. Only few interventions have addressed key aspects such as communication or decision-making, and only one intervention has attempted to integrate skill-building and tools with informational and support resources for ICs, highlighting the need for further studies that develop and evaluate interventions incorporating both dimensions. Indeed, it is important that caregivers are recognized as integral members of the healthcare team, as they play a crucial role in the care process, but to collaborate effectively and on an equal footing with other team members, caregivers must be provided with the necessary tools and resources. Additionally, the interventions appear to target ICs in a general manner without considering the ICs distinct challenges and diverse needs, depending on factors such as their relationship to the patient, the stage of the disease and caregiving responsibilities, and/or their personal circumstances. Customizing interventions to suit these varying needs would enhance the relevance and effectiveness of support strategies, ensuring that each ICs receives the most appropriate psychosocial resources. Future research should continue to explore tailored interventions that address both the emotional and practical needs of caregivers, foster their competences in caregiving ensuring comprehensive support for this vital group. Indeed, empowering caregivers, can enhance the quality of care and better address the complex needs of individuals with chronic conditions such as MS.

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CRediT authorship contribution statement

Giorgia Giusto: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Data curation, Conceptualization. **Silvia Poli:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Angelica Filosa:** Writing – review & editing, Software, Data curation. **Michela Rimondini:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Valeria Donisi:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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None.

Appendix A. Search strategy

Database	Search Terms	Filters	Results
PubMed	Advanced query ((((((caregiver*[Title/Abstract]) OR (carer*[Title/Abstract])) OR (spous*[Title/Abstract])) OR (partner*[Title/Abstract])) OR (family[Title/Abstract])) OR (families[Title/Abstract])) AND (("multiple sclerosis"[Title/Abstract]) OR (MS[Title/Abstract])) AND (((((((((((((((tele-medicine[Title/Abstract]) OR (telemedicine[Title/Abstract])) OR (tele-health[Title/Abstract])) OR (telehealth[Title/Abstract])) OR (m-health[Title/Abstract])) OR (mhealth[Title/Abstract])) OR (e-health[Title/Abstract])) OR (ehealth[Title/Abstract])) OR (internet[Title/Abstract])) OR (web[Title/Abstract])) OR (online[Title/Abstract])) OR (mobile [Title/Abstract])) OR (app[Title/Abstract])) OR (computer[Title/Abstract])) OR (digital[Title/Abstract]) OR (telephone[Title/Abstract]) OR (video[Title/Abstract]))	Years from 2000 to 2024	658
Web of Science	TS = ((caregiver* OR carer* OR spous* OR partner* OR family OR families) AND ("multiple sclerosis" OR MS) AND (tele-medicine OR telemedicine OR tele-health OR telehealth OR m-health OR mhealth OR e-health OR ehealth OR internet OR web OR online OR mobile OR app OR computer OR digital OR telephone OR video))	years from 2000 to 2024	959
Scopus	TITLE-ABS-KEY ((caregiver* OR carer* OR spous* OR partner* OR family OR families) AND ("multiple sclerosis" OR ms) AND (tele-medicine OR telemedicine OR tele-health OR telehealth OR m-health OR mhealth OR e-health OR ehealth OR internet OR web OR online OR mobile OR app OR computer OR digital OR telephone OR video)) AND PUBYEAR > 1999 AND PUBYEAR < 2025 AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (SUBJAREA, "PSYC") OR LIMIT-TO (SUBJAREA, "COMP") OR LIMIT-TO (SUBJAREA, "HEAL") OR LIMIT-TO (SUBJAREA, "SOCI"))	Years from 2000 to 2024	973
PsycInfo	((caregiver* or carer* or spous* or partner* or family or families) and ("multiple sclerosis" or MS) and (tele-medicine or telemedicine or tele-health or telehealth or m-health or mhealth or e-health or ehealth or internet or web or online or mobile or app or computer or digital or telephone or video)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh word]	Limit to yr="2000-Current"	159

*Topic-based filters were applied on Scopus to enhance relevance and manage the high volume of indexed records.

Appendix B. MMAT (Mixed Method Appraisal Tool)

METHODOLOGICAL QUALITY CRITERIA	INCLUDED STUDIES					
	Douglas et al., 2023	Motaharinezhad et al., 2024	Halstead et al., 2020	Potter et al., 2021	Khazaeili et al., 2019	Strupp et al., 2017
S1. Are there clear research questions?	YES	YES	YES	YES	YES	YES
S2. Do the collected data allow to address the research questions?	YES	YES	YES	YES	YES	YES
1. Qualitative						
1.1. Is the qualitative approach appropriate to answer the research question?				YES		YES
1.2. Are the qualitative data collection methods adequate to address the research question?				YES		YES
1.3. Are the findings adequately derived from the data?				YES		YES
1.4. Is the interpretation of results sufficiently substantiated by data?				YES		YES
1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				YES		YES
2. Quantitative randomized controlled trials						
2.1 Is randomization appropriately performed?	YES	YES		YES	CAN'T TELL	
2.2 Are the groups comparable at baseline?	YES	CAN'T TELL		YES	CAN'T TELL	
2.3 Are there complete outcome data?	NO No baseline and follow up results clearly presented in a table for the two subgroups in the two time points	YES		YES	YES	
2.4 Are outcome assessors blinded to the intervention provided?	CAN'T TELL Patient reported outcome.	YES		CAN'T TELL Patient reported outcome.	CAN'T TELL	
2.5 Did the participants adhere to the assigned intervention?	CAN'T TELL Dropout rates are low but no data on compliance to the intervention's sessions is reported.	CAN'T TELL		YES Attrition is low. Some problems with adherence are reported but thoroughly discussed.	CAN'T TELL No dropout rates or attrition rates are reported.	
3. Quantitative non-randomized						

(*continued on next page*)

(*continued*)

METHODOLOGICAL QUALITY CRITERIA	INCLUDED STUDIES					
	Douglas et al., 2023	Motaharinezhad et al., 2024	Halstead et al., 2020	Potter et al., 2021	Khazaeili et al., 2019	Strupp et al., 2017
3.1. Are the participants representative of the target population?			CAN'T TELL			
3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?			YES			
3.3. Are there complete outcome data?			NO Data for all variables are only reported in the text for a small number of variables.			
3.4. Are the confounders accounted for in the design and analysis?			NO			
3.5. During the study period, is the intervention administered (or exposure occurred) as intended?			CAN'T TELL			
5. Mixed methods						
5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				YES		
5.2. Are the different components of the study effectively integrated to answer the research question?				YES		
5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				YES		
5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				YES		
5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				YES		

Legend: Cells marked as "Yes" indicate that the study meets the specific criterion, "No" indicates that the criterion was not met, and "Can't Tell" reflects insufficient information to assess the criterion. Blank cells denote criteria that were not applicable to the study's design or methodology. Additionally, only the sections related to the specific design adopted by each study were evaluated and filled out (e.g., qualitative, quantitative randomized controlled trials, etc.).

*The evaluation was systematically conducted using the tool's criteria, which focus on the following five key domains:

1. Appropriateness of the research questions and objectives.
2. Relevance and rigor of the data collection methods.
3. Adequacy of the analytical approach (statistical or qualitative).
4. Minimization of bias and confounding factors.
5. Clarity and validity of the study's conclusions.

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