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Complete List of Authors:	Vitturi, Bruno; University of Genoa, Health Sciences Rahmani, Alborz; University of Genoa, Health Sciences; IRCCS Ospedale Policlinico San Martino Dini, Guglielmo; University of Genoa, Health Sciences; IRCCS Ospedale Policlinico San Martino Montecucco, Alfredo; University of Genoa, Health Sciences Debarbieri, Nicoletta; IRCCS Ospedale Policlinico San Martino Sbragia, Elvira; IRCCS Ospedale Policlinico San Martino; University of Genoa, DINOGMI Bandiera, Paolo; Italian MS Association Ponzio, Michela; Italian MS Association, Research Area Battaglia, Mario Alberto; Italian Multiple Sclerosis Foundation; University of Siena, Department of Life Science Manacorda, Tommaso; Italian MS Association Persechino, Benedetta; INAIL Buresti, Giuliana; INAIL Inglese, Matilde; IRCCS Ospedale Policlinico San Martino; University of Genoa, DINOGMI Durando, P; University of Genoa; IRCCS Ospedale Policlinico San Martino
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Occupational outcomes of patients with Multiple Sclerosis: a scoping review

Bruno Kusznir Vitturi[1], Alborz Rahmani[1,2], Guglielmo Dini[1,2], Alfredo Montecucco[1,2], Nicoletta Debarbieri[2], Elvira Sbragia[3,4], Paolo Bandiera[5], Michela Ponzio[6], Mario Alberto Battaglia[6,7], Tommaso Manacorda[5], Benedetta Persechino[8], Giuliana Buresti[8], Matilde Inglese[3,4], Paolo Durando[1,2]

1. Department of Health Sciences, University of Genoa, Italy
2. IRCCS Ospedale Policlinico San Martino, Occupational Medicine Unit, Genoa, Italy
3. Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI) and Center of Excellence for Biomedical Research (CEBR), University of Genoa, Genoa, Italy
4. IRCCS Ospedale Policlinico San Martino, Genoa, Italy
5. Italian Multiple Sclerosis Association (AISM)
6. Scientific Research Area, Italian Multiple Sclerosis Foundation (FISM), Italy
7. Department of Life Science, University of Siena, Siena, Italy
8. Italian Workers' Compensation Authority (INAIL)

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Corresponding author

Bruno Kusznir Vitturi, MD

Research Fellow in Occupational Medicine

E-mail: bruno.kusznir.vitturi@edu.unige.it

Department of Health Sciences, University of Genoa, Italy

Building 3, Lgo R. Benzi 10 - 16132 Genoa, Italy

Abstract

Objectives. To update the knowledge on the occupational outcomes associated with MS, systematically examine the extent, scope, and nature of the pre-existent literature, and identify research gaps in the existing literature.

Design. Scoping review.

Data sources. A comprehensive database search of PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science was performed. There were no time limits.

Eligibility criteria. We included any peer-reviewed original article reporting the occupational outcomes of patients with MS between the ages of 18 and 65 years.

Methods. This review was conducted following the JBI recommendations and the PRISMA-ScR flowchart. Screening, reading of full-texts and data extraction was performed in a standardized way by an expert reviewer.

Results. The initial systematic search yielded 104,228 results. After removing duplicates and applying the exclusion criteria, 403 articles were included in the review. In total, the studies evaluated 492,062 subjects with MS. One hundred fifty-four (38.2%) articles were published in the last 5 years and most came from Europe and North America (50.9% and 33.0%, respectively). Three hundred and fourteen (77.9%) studies were cross-sectional, 12 (3.0%) were interventional, and 77 (19.1%) were longitudinal. The assessment of disability and quality of life, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms were the most frequent MS-related variables. Concerning the occupational outcomes, studies mostly addressed unemployment (311, 77.2%), early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%).

Conclusions

This is the first scoping review dedicated to the occupational outcomes of patients with MS. Despite the huge amount of articles already published on the subject, there are still several issues that deserve further in-depth study by the scientific community in order to promote the occupational outcomes of patients with MS.

Keywords

Multiple sclerosis; public health; occupational and industrial medicine; health economics; epidemiology

Article summary

Strengths and limitations of this study

- This is the first scoping review dedicated to the occupational outcomes of PwMS.
- We chose a broad search methodology to be able to sketch an accurate and comprehensive picture of the relationship between the occupational outcomes and MS.
- In line with the scoping review approach, we didn’t formally assess the quality of included studies.
- We could have missed some data for not including results from the grey literature.

1. Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system causing demyelination and neurodegeneration. It mainly affects young people between 20 and 40 years of age and it is the main cause of non-traumatic disability among young adults in the Western world [1]. MS is a global disease, affects 2.5 million people worldwide, the incidence and prevalence are known to be increasing in both developed and developing countries [2]. The symptoms are extremely varied and the clinical course is within a spectrum that extends from relapsing-remitting to progressive [1-3].

Besides the inherent clinical complexity of MS, the age of onset of the disease brings inevitable repercussions to work activity, once it coincides with the moment in which patients find themselves managing the already expected difficulties of the job market and the beginning of the professional career [4]. As long as MS symptoms remain 'invisible', people with MS are reluctant to inform their employer about their disease for fear of losing their job [4].Concerns about disclosure in the workplace stem from a range of issues including heightened perceptions of vulnerability through fear of discrimination and of termination of employment [5].MS imposes essential adjustments in the work environment and in the way of delivering satisfactory work. Often limiting and disabling, symptoms such as fatigue, neuropsychiatric impairment, and motor disturbances constantly threaten the full performance at work and the search for new professional skills, if they are not responsible for unemployment and early retirement. Besides, the consequences of MS to the occupational setting are directly associated with the patient's quality of life (QoL), which makes this issue even less negligible [6].

Indeed, the impact of MS on work activities has already been evaluated in many studies carried out in different parts of the world. Kobelt et al. demonstrated that workforce participation can decline from 82% to 8% and employment rates vary between 31% and 65% [7], being influenced by a myriad of factors such as the degree of disability, the duration of disease, the level of education and the type of work activity. Another study outlined the complexity of the association between employment and MS and revealed that 56.2% of patients with MS (PwMS) were unemployed and had low odds of re-entering the workforce in a second moment [8].

Although the damage caused by MS in professional life is already sufficiently eloquent at the individual level, it is impossible not to recognize the impact of the disease at the community level as well. In Italy, long-term absence, invalidity, and early retirement may generate social costs amounting to 17,945 € per patient in the late stages of MS [9]. Besides, an Australian study demonstrated that loss of productivity at work and change of occupation due to MS account for an annual cost of 2,310 € and US$ 2,560 € for each patient, respectively [10]. In other terms, the impact of MS on occupational outcomes is also responsible for a significant economic burden and represents a matter of public health all around the world.

Despite being relatively easy to find some information about MS and work in the literature, it is still imperative to address this topic since the occupational outcomes of patients with MS are far from being considered acceptable yet. In 2021, being a victim of MS still poses a great risk for unemployment, early retirement, loss of work capacity, reduced monthly income, job dissatisfaction, and impaired QoL. Moreover, the recent advances in the treatment of MS and the emergence of new types and modalities of work oblige scientists to keep studying the delicate association between MS and work. In parallel, it is also true that amidst the diversity of articles on this topic, researchers can easily find themselves in a kind of scientific cacophony that has the potential to inhibit the idealization of new relevant studies in this area and, in contrast, promote redundant and unnecessary research. Based on this scenario, we decided to conduct the first scoping review related to the occupational outcomes of patients with MS, as it has the appealing capacity of producing a broad map of the existing evidence and identifying gaps for potential future studies.

2. Objectives

The objectives of the present scoping review are (1) to update the knowledge on the occupational outcomes associated with MS, (2) to systematically examine the extent, scope, and nature of the pre-existent literature, (3) to summarize and disseminate the research results deriving from the already published articles, (4) to identify research gaps in the existing literature and (5) to provide an accurate rationale to develop further relevant research in the area.

3. Methods

We performed this scoping review following the guidelines outlined by Arksey and O'Malley, the Joanna Briggs Institute recommendations, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for scoping review (PRISMA-ScR) guidelines [11,12]. As this was a literature review, it didn't involve the recruitment of subjects and it analysed data from already published original articles and, therefore, the ethical approval wasn't necessary.

3.1. Study selection/search strategy

From July 14, 2021, to July 31, 2021, we systematically searched on PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science the following keywords (Employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "work resumption" OR workplace* OR "return to work" OR "work force" OR "workforce" OR "labour force" OR "labor force" OR Career* OR Job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("Multiple sclerosis" OR "Disseminated Sclerosis" OR "Demyelinating Autoimmune Diseases" OR "Demyelinating Autoimmune Disorders" OR "Clinically Isolated Syndrome" OR "Demyelinating"). The details of the search strategy used is reported in Table 1. After the preliminary identification, the articles were exported and managed in Mendeley 1.19.8 (Elsevier, New York, USA).

PubMed	(Employ* OR unemploy* OR occupation* OR “work” OR vocation* OR “workplace” OR “workforce” OR “labour force” OR “labor force” OR Career* OR Job* OR retire* OR “disability pension” OR “worker” OR “fitness for work”) AND (“Multiple sclerosis” OR “Demyelinating Autoimmune Diseases” OR “Demyelinating Autoimmune Disorders” OR “Clinically Isolated Syndrome” OR “Demyelinating”)
Scopus	TITLE-ABS KEY [(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR “workplace” OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("Multiple sclerosis" OR "Demyelinating Autoimmune Diseases" OR "Demyelinating Autoimmune Disorders" OR "Clinically Isolated Syndrome" OR "Demyelinating")]
SciVerse Science Direct	("Employ" OR "occupation" OR "work" OR "vocation" OR “labour” OR "Job" OR "retire" OR “disability pension”) AND “Multiple sclerosis”
Web of Science	(Employ* OR unemploy* OR occupation* OR “work” OR vocation* OR “workplace” OR “workforce” OR “labour force” OR “labor force” OR Career* OR Job* OR retire* OR “disability pension” OR “worker” OR “fitness for work”) AND (“Multiple sclerosis” OR “Demyelinating Autoimmune Diseases” OR “Demyelinating Autoimmune Disorders” OR “Clinically Isolated Syndrome” OR “Demyelinating”)

Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

3.2. Inclusion and exclusion criteria

A priori, we chose a broad search methodology to be able to sketch an accurate and comprehensive picture of the relationship between the occupational outcomes and MS. The PCC (Population/Concept/Context) framework was used to define inclusion criteria. We included any peer-reviewed original article reporting the occupational outcomes (concept) of PwMS between the ages of 18 and 65 years (population). MS must have been diagnosed according to accepted international criteria at the time of the study. No time limits were set for the search. The context was broad and we accepted articles whose full text was published in English, Italian, Spanish, French, and Portuguese, as these are the languages spoken in our research group.

After we removed duplicate entries, we performed an initial screen of titles or abstracts to assess potential relevance and remove those off-topic. Screening of titles, abstracts, and full texts for each article was conducted by two experienced and trained investigators, each blinded to the other's ratings. In case of discrepancy, a final decision was made by a consensus. Afterward, we obtained relevant full-text articles, revaluated their eligibility, and determined their final inclusion or exclusion.

Studies written in languages other than the five pre-specified above and studies designed as reviews, letters to the editor, expert opinions, commentaries, case reports, case series, editorials were excluded. In case of lack of essential information or full-text not being available, we tried to contact the corresponding author twice to obtain the information by email. Whenever our contact attempt failed, the study was excluded. We didn't accept studies whose sample deliberately included patients with more than a chronic disease or in which MS was not the primary condition. Figure 1 provides the PRISMA flowchart overview of the search and screening strategy performed.

3.3. Data extraction

Data extraction was performed in a standardized way by an expert reviewer. Among the basic characteristics, we gathered information about the authors' names, the title of the study, the year of publication, the country of origin of the study, the study design, the number of subjects with and without MS, the subtype of the disease, the prevalence of each clinical symptom, the duration of the disease, the distribution by age and sex, the level of education, the marital status, the description of any neuroradiological finding, treatment data, assessment of the QoL and disability, and prevalence of fatigue, psychiatric symptoms, and cognitive symptoms. Regarding the occupational outcomes, data were collected related to the description of the profession, the prevalence of unemployment and early retirement, the influence of the disease on monthly income, the need for disability pension, the indirect cost of MS, the stigma and prejudice faced in the workplace, job characteristics, strategies of vocational rehabilitation and work adaptation, patient opinion on work and working life in general, job limitations, degree of job satisfaction, need for a change of employment due to MS, the prevalence of work handicap and information on the disclosure of the diagnosis in the workplace (outcomes).

3.4. Data synthesis

Following data extraction, due to the range of outcomes assessed and different study designs included in the review, we used a narrative synthesis to report data. One expert reviewer performed a thematic categorization of the findings, which was verified by two other reviewers. Based on the approved categorization, data were summarized and compared between studies.

4. Results

The initial systematic search yielded 104,228 results, of which 7,486 were from PubMed, 8,346 were from Scopus, 63,731 were from SciVerse Science Direct 24,665 were from Web of Science. Removing duplicates and applying the eligibility criteria resulted in a total of 1,136 articles whose full texts were read in the subsequent step. At the end, 403 articles were included in the review, and information about the baseline clinical-epidemiological characteristics and the occupational outcomes was properly extracted (Table S1). Figure 1 describes the entire PRISMA-ScR flowchart.

The amount of studies published on the topic over time has unquestionably increased as 154 (38.2%) of the studies included in the review were published in the last 5 years. Most of the studies come from Europe and North America (50.9% and 33.0%, respectively). Asia and Oceania produced n = 32 (7.9%) and n = 24 (6.0%) of the studies on the subject, respectively. There were no published data on the association between MS and work from the African continent. Italy, with less than 1% of the world population, promoted the publication of n = 29 (7.2%) articles on the subject of our study. Regarding the study design, 314 (77.9%) were cross-sectional, 12 (3.0%) were interventional, and 77 (19.1%) were longitudinal. Only 63 (15.6%) studies included a control group in their analysis. In total, the 403 studies evaluated 492,062 subjects with MS. Among the characteristics of MS explored, the assessment of disability and QoL, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms figure as the most mentioned variables (Table 2). Neuroimaging data and the use of disease-modifying drugs (DMDs) were explored in 10 (2.5%) and 117 (29.0%) studies, respectively.

Clinical and demographic characteristics			**Work/occupational characteristics**		
	n	%		n	%
Age	394	97.8	Job description	55	13.6
Sex	389	96.5	Work performance	57	14.1
Educational level	288	71.5	Unemployment	311	77.2
Civil status	180	44.7	Sick leave	77	19.1
Socioeconomic conditions	47	11.7	Early retirement	120	29.8
EDSS	212	52.6	Disability pension	117	29.3
Disease duration	274	68.0	Impact on monthly income	52	12.9
Type of MS	258	64.0	Indirect cost of MS	74	18.4
Neuroimaging findings	10	2.4	Professional absenteeism	85	21.1
Description of symptoms	59	14.6	Stigma and prejudice	23	5.7
Quality of Life	139	34.4	Work characteristics	57	14.1
Disability assessment	234	58.1	Vocational rehabilitation	19	4.7
Fatigue	169	41.9	Adaptation to work	45	11.2
Psychiatric symptoms	209	51.9	Patients opinion about work	85	21.9
Cognitive symptoms	160	39.7	Workplace limitations	65	16.1
Motor symptoms	84	20.8	Disclose of the diagnosis in the workplace	17	4.2
Treatment (DMDs)	117	29.0	Job satisfaction	19	4.7
			Occupational change	78	19.3
			Work handicap	38	9.4

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Work was considered as a dependent variable in 285 (70.7%) articles. Studies could be classified into 6 types according to their sub-topic: 82 (28.8%) studies dealt with the description of employment outcomes, 85 (29.8%) aimed to assess the economic impact of MS, 14 (4.9%) described any strategy of vocational rehabilitation, 17 (6.0%) evaluated the QoL in MS in general, 81 (28.4%) determined possible risk factors associated with occupational outcomes and 6 (2.1%) aimed to develop a possible assessment scale of occupational outcomes. The prevalence of unemployment was the most explored variable (311, 77.2%). Other addressed issues were early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the influence of MS on monthly income (52, 12.9%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). Workplace limitations were reported in 65 (16.1%) studies and the work adaptation strategies in 45 (11.2%) studies. Perceived stigma in the workplace, job satisfaction, and knowledge of colleagues about MS were less common aspects explored in studies (5.7%, 4.7%, and 4.2%, respectively). Finally, 59 (14.6%) articles examined occupational absenteeism, 85 (21.1%) aimed to understand the patient's opinion on aspects of his professional life, and 19 (4.7%) evaluated strategies of occupational rehabilitation.

The occupational outcomes

MS is a disease that directly influences the patient's professional life. A Norwegian study demonstrated that after 19 years of disease, only 45% of patients are still employed[13]. In a Swedish cohort, only 28% and 23% of PwMS were working full- and part-time after a follow-up of 10 years, respectively [14]. Even for those who remain employed, more than a quarter show some deterioration in employment status and 56% observe a work performance loss in the short term after the diagnosis [15,16]. Unfortunately, once unemployed, it is also difficult for workers with MS to return to the workforce [17]. The literature also highlights the influence of that the occupational setting displays in the QoL. Persons with MS who are employed tend to rate their levels of QoL nearly one third of a standard deviation higher than their unemployed counterparts[18].

The economic impact of MS

MS is a debilitating disease that poses a substantial burden in terms of absenteeism, presenteeism, disability pension, and sick leave costs. Employees with MS are significantly more likely to have disability days than an employee without MS (21.4% vs 5.2%). Overall, MS employees had just over 4 times more workdays lost than their controls (37.7 vs 8.8 days) [19]. In a cohort of 8350 MS patients, two-thirds received some kind of benefit [20]. Increased disability (EDSS) is strongly associated with reduced earnings and increased benefits [20,21] but it is noteworthy that even mild disability can pose a significant economic burden at the expense of premature retirement, premature work disability, and time lost from work [22]. Interestingly, Jennun et al. demonstrated that employment and health costs are affected up to 8 years before the patient receives an MS diagnosis [23]. Neusser et al. reported that adding up all cases of interventions to enable work-life integration results in an estimated total expenditure of 4.3 billion euros annually [24].

Risk factors for occupational outcomes

Multiple studies have addressed the risk factors associated with worse professional outcomes. The progressive phenotype of the disease is certainly a negative predictor of occupational outcomes in PwMS compared to the relapsing-remitting form [13,25]. Older age, longer disease duration, and high EDSS are also associated with a higher risk of unemployment [26,27]. Recently, it was demonstrated that neuroimaging findings are also linked to occupational status. Tauhid et al. showed that the T1 lesion load, the ratio between the T1 and T2 burden, and the overall brain volume are significantly different between employed and non-employed MS patients [28]. In a cohort of 145 patients followed up to 12 years, severe brain atrophy, T1 and T2 injury load were the best predictors of deterioration of the occupational status [29]. Cognitive impairment, neuropsychiatric symptoms, and fatigue are also well-described risk factors for labor force withdrawal and work productivity loss [15,30,31].

Work limitations

Some studies described the main barriers at work for PwMS, which may result from the disease itself or circumstances related to the workplace. Cognitive symptoms, pain, fatigue, psychiatric disorders, disease severity, mobility/gait impairment are illness-related factors considered as major limitations at work [32–35]. In addition, jobs requiring long-distance travel, overly stressful work, limited feedback on performance, hostile supervisors, high-temperature level and inflexible work schedules are some working conditions considered difficult for PwMS [35–37]. Negative work events have been reported as an important barrier as well. Workers with MS may be particularly vulnerable to verbal reprimands, decrease in scheduled work hours, diminution of job responsibilities, and mandatory additional retraining [38]. Kordovski et al. and Frindak et al. both demonstrated that negative work events may act as an indicator of an increased risk of unemployment in the short and middle term [39,40].

Work accommodation and vocational rehabilitation

Work accommodations are associated with greater chances of keeping a job. The studies considered work accommodations as reasonable adjustments in the workplace or strategies related to professional re-training and vocational rehabilitation. In a study with 746 workers with MS, participants with a progressive course of the disease, cognitive impairment, a higher number of MS symptoms, and greater symptom severity were more likely to use work accommodations [41]. More than 60% of PwMS who kept their jobs described any type of accommodation and adopting flexible hours as the most frequently reported accommodation [42]. Other common and useful accommodations are the possibility of working from home and have available some memory aids, additional time to complete tasks, preferential parking, written job instructions, and air conditioning [42,43]. Rumrill Jr. et al. listed the use of equipment/assistive technological resources as being of great importance among the possible accommodations [44].

Dorstyn et al. verified that sending a standardized, mail-delivered, resource-based package to job seekers with MS improved their vocational self-efficacy, optimism, and identity [45]. Chiu et al. examined the effect of rehabilitation technology interventions on job retention and concluded that this kind of technological tool may ensure better occupational outcomes as well [46]. Vocational rehabilitation is a topic that interest PwMS, who already demonstrated to be pretty receptive to this initiative [47]. According to them, a program of vocational rehabilitation must address two main points: managing work performance and expectations [48].

Job satisfaction, stigma, and disclosing the diagnosis in the workplace

Almost one-third of patients who remain employed are dissatisfied at work [32] and 20% to 30% of workers do not feel comfortable disclosing their diagnosis in the work environment [37]. Approximately 40% of the patients did not even communicate the occupational physician about MS [49]. Patients with increased disease severity and who had been at work for a longer time disclosed more often the diagnosis [50]. A quarter of MS patients have robust feelings of stigmatization at work. Stigma is directly associated with poorer QoL, work handicap, and depression [33,51].

Rating clinical scales

The EDSS and the MS functional composite scale have both been associated with employability [52]. Andries et al. designed the Work and Handicap Questionnaire (WHQ) aiming to estimate the degree of work handicap in PwMS, neuromuscular diseases, and asthma based on the association of daily life disabilities and job demands [53]. Although it was not specifically created for PwMS, it showed good reliability. Honan et al. developed a shortened version of the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ) that consists of a 23-item measure of self-reported perceived workplace difficulties in PwMS [54]. Raggi et al. designed and validated the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job), which demonstrated to be an useful tool for measuring the work-related difficulties in PwMS [55]. Both MSWDQ and MSQ-Job proved to be a comprehensive tool for tracking subjective work-related problems but unfortunately, they couldn’t be compared with objective occupational outcomes in a longitudinal perspective and were not validated as a predictive tool of.

5. Discussion

The scientific literature on occupational outcomes and MS is vast. Nevertheless, it is possible to identify some important gaps in this subject. The quality of the scientific evidence in this field is still limited since there is a significant lack of longitudinal and interventional research, and no studies have described the evolution of occupational outcomes of MS patients over time. Over the past 20 years, there have been notable advances in the treatment of MS due to a significant increase in the number and effectiveness of disease-modifying drugs (DMDs) that, in theory, may have influenced various occupational outcomes as well [56]. In this scenario, research assessing the specific role of DMDs on occupational outcomes is highly encouraged. Likewise, there is a lack of studies that compare the variables related to work between countries, considering a global perspective.

The literature is unanimous regarding the MS burden on the economy and public health; indeed, the economic impact of the influence of MS on work has driven several research projects. However, the cost-effectiveness of the new DMDs has not been properly studied yet, considering both the occupational items and the feasible strategies of professional integration concerning their potential benefit in promoting better occupational outcomes with consequent decrease of the economic impact of MS.

Moreover, despite the literature provides a wide description of possible risk factors and work accommodations for PwMS, little evidence exists concerning the possible protective factors associated with occupational outcomes, and most studies are concentrated on the aspects related to the disease, and few are dedicated to the work-related risk factors. Besides, the real role of each type of accommodation in promoting favourable occupational outcomes is still unclear, since a lack of studies providing strong evidence to this issue (longitudinal and interventional studies) still exists.

Furthermore, our scoping review identified gaps between the patient's interest in receiving technical guidance on how to improve the occupational outcomes and the degree of evidence on this topic; in this context, few studies dedicated to identifying strategies capable of promoting job retention, work performance, and even return to work have been published. Moreover, most of the strategies of vocational rehabilitation were studied in small samples of subjects and didn’t consider the particular characteristics of PwMS. Given the still unsatisfactory unemployment rates among MS patients, vocational rehabilitation may be a valuable complementary resource.

There is also extremely limited evidence related to job satisfaction, stigma, and prejudice in the workplace; in this view, it is important to study these outcomes to gauge an individual’s overall level of work adjustment. Furthermore, studying and understanding the reasons for not communicating the diagnosis of MS, including to the occupational physician, should be the first step to promote the worker's full integration.

Surprisingly, we couldn’t find any peer-reviewed publication that had the objective of proposing and validating some standardized and systematized form of evaluation of PwMS considering their risks of deterioration of occupational status in a longitudinal perspective. Few studies tried to develop a scale associated with the occupational outcomes of PwMS. All the proposed scales described the work handicap or job difficulties in restricted samples and a cross-sectional design. Most of them revealed to be excessively extensive and complex, which can represent a limitation for their wide use in clinical practice. The EDSS is the only scale that has already been associated with occupational outcomes as it generally reflects the severity and progression of the disease. However, this evidence comes from secondary analysis of studies and, despite being simple, the EDSS does not include several other factors already proven to specifically influence the professional outcomes, which can raise concerns about its sensitivity as well. The development of a simple and validated scale should be the subject of future studies, as it may represent an easy-to-use tool capable of supporting a more objective and uniform assessment of PwMS by physicians with different professional backgrounds.

Finally, no study addressed how the new ways of working in the 21st century interfered with the occupational outcomes of PwMS. The nature and the pattern of work have undoubtedly changed in the last 20 years [57], and it is reasonable to imagine that PwMS may find more alternatives and resources to ensure a fruitful professional life. Possibly, technological advances in the workplace may even relativize the concept of work disability in specific cases of PwMS.

This is the first scoping review specifically focused on the occupational outcomes of PwMS. A broad and rigorous search strategy was used to properly include all the relevant studies describing the occupational outcomes of MS and to promote reliable and accurate results. We applied a range of outcome possibilities that allowed us to accurately understand the evidence related to the impact of MS in the occupational setting. Moreover, this review identified several opportunities for new research on the topic. Among the limitations of the study, as we respected the scoping review approach, we didn't formally assess the quality of included studies. We could also have missed some data for not including results from the grey literature. Notwithstanding, we intended to disclose the current reality regarding the highest scientific evidence in the field of MS and work and, therefore, the selection of peer-reviewed articles seemed more appropriate.

6. Conclusions

This is the first scoping review dedicated to the occupational outcomes of PwMS. MS is a chronic neurological disorder that is often associated with disabilities and significant impairment of professional life. Many studies have already been published on the subject and several outcomes have been described. Nevertheless, there are still several issues that deserve further in-depth study by the scientific community in order to match the quality of scientific evidence to the undeniable complexity inherent in this topic.

Author contributions: All authors approved the final version. BKV designed the study, performed database search, data extraction, and wrote the manuscript. AR designed, integrated the research group and reviewed the manuscript. GD, AM, ND integrated the research group and reviewed the manuscript. PB, TM, MP, MAB, BP, GB, MI, ES globally supported the research and reviewed the manuscript. PD coordinated, supervised and reviewed the manuscript.

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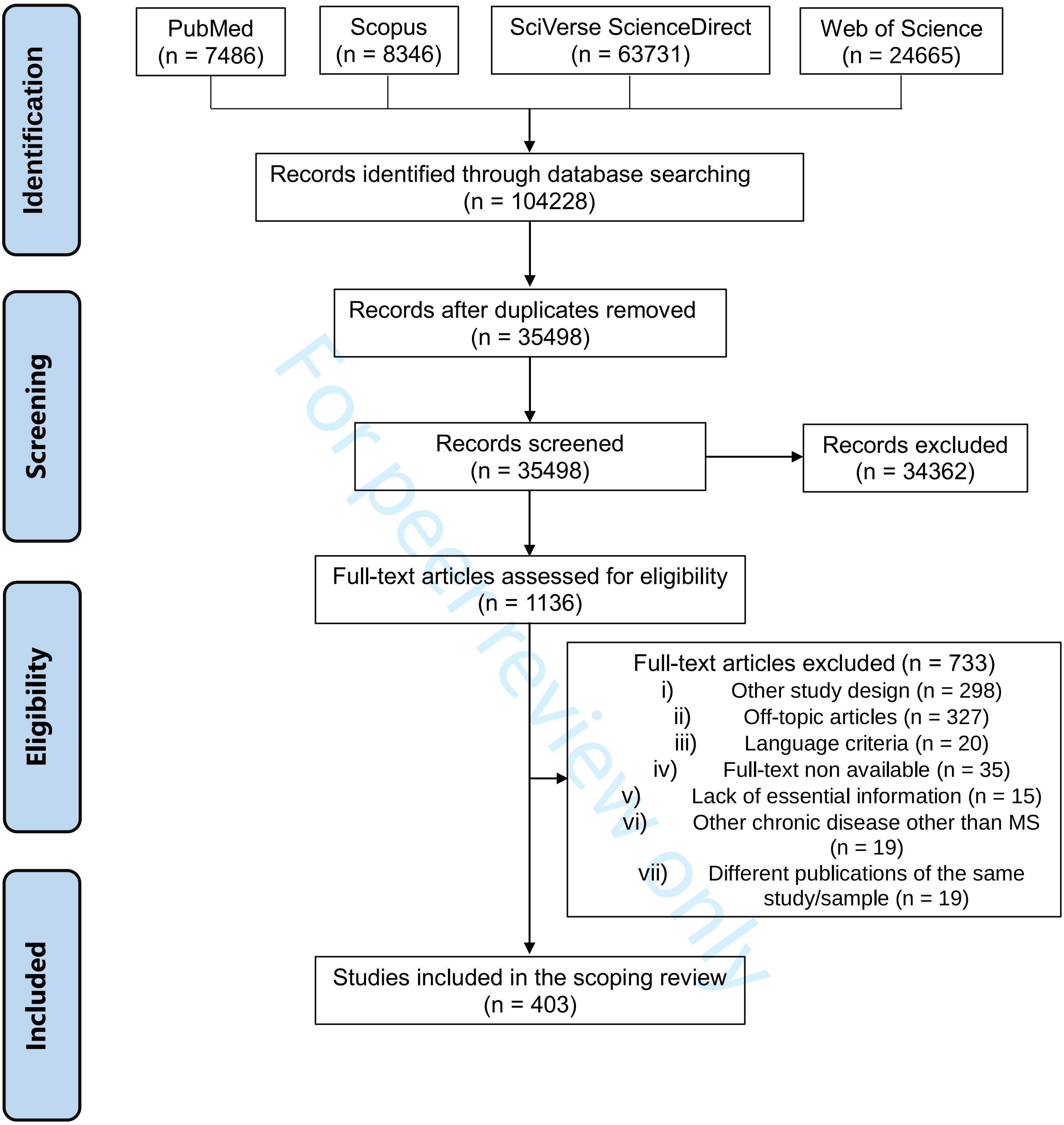
Legends

Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Figure 1. PRISMA flowchart.

Table S1. Complete list of all articles included in the scoping review.


Identification
Screening
Eligibility
Included
PubMed (n = 7486)
Scopus (n = 8346)
SciVerse ScienceDirect (n = 63731)
Web of Science (n = 24665)
Records identified through database searching (n = 104228)
Records after duplicates removed (n = 35498)
Records screened (n = 35498)
Records excluded (n = 34362)
Full-text articles assessed for eligibility (n = 1136)
Full-text articles excluded (n = 733)
i) Other study design (n = 298)
ii) Off-topic articles (n = 327)
iii) Language criteria (n = 20)
iv) Full-text non available (n = 35)
v) Lack of essential information (n = 15)
vi) Other chronic disease other than MS (n = 19)
vii) Different publications of the same study/sample (n = 19)
Studies included in the scoping review (n = 403)

AUTHOR	**TITLE**	**YEAR**	**COUNTRY**
ABBAS et al.	Caractéristiques des personnes atteintes d'une sclérose en plaques selon la situation professionnelle	2008	Francia
Abdullah et al.	MS People's Performance and Satisfaction With Daily Occupations: Implications for Occupational Therapy	2017	Kuwait
Abolhassani et al.	Social aspects of multiple sclerosis for Iranian individuals	2014	Iran
Bass et al.	Effect of Multiple Sclerosis on Daily Activities, Emotional Well-being, and Relationships: The Global vsMS Survey.	2020	Europe
Bayas et al.	Combination treatment of fingolimod with antidepressants in relapsing–remitting multiple sclerosis patients with depression: a multicentre, open-label study – REGAIN	2016	Germany
Beatty et al.	emographic, Clinical, and Cognitive Characteristics of Multiple Sclerosis Patients Who Continue to Work	1995	US
Beatty et al.	Changes in neuropsychological test performance over the workday in multiple sclerosis	2003	US/Italy
Benedict et al.	Negative work events and accommodations in employed multiple sclerosis patients.	2013	US
Benedict et al.	Predicting neuropsychological abnormalities in multiple sclerosis	2006	US
Bøe Lunde et al.	Employment among Patients with Multiple Sclerosis-A Population Study	2014	Norway
Buchanan et al.	A Pilot Study of Latinos With MultipleSclerosis: Demographic, Disease, MentalHealth, and Psychosocial Characteristics	2011	US
Cambier-Langrand	Impact socio professionnel précoce de la sclérose en plaques : une étude prospective d'une série de 24 patients	2016	France
Carnero Contentti	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Carrieri et al.	Determinants of on-the-job-barriers in employed persons with multiple sclerosis: The role of disability severity and cognitive indices	2014	Italy
Castelo-Branco	Clinical course of multiple sclerosis and labour-force absenteeism: a longitudinal population-based study.	2019	Sweden
Cervera-Deval et al.	Social handicaps of multiple sclerosis and their relation to neurological alterations	1994	Spain
Chamot et al.	Item response theory-based measure of global disability in multiple sclerosis derived from the Performance Scales and related items.	2014	USA
Conradsson et al.	Employment status of people with multiple sclerosis in relation to 10-year changes in functioning and perceived impact of the disease.	2020	Sweden
Contentti et al.	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Cores et al.	Work status and cognitive performance in patients with relapsing remitting multiple sclerosis	2019	Argentina
Cowan et al.	Psychosocial aspects of the lived experience of multiple sclerosis: personal perspectives	2018	Australia

Dehghan et al.	Occupational performance of individuals with Multiple Sclerosis based on disability level in Iran.	2019	Iran
Devins et al.	Differences in illness intrusiveness across rheumatoid arthritis, end-stage renal disease, and multiple sclerosis	1993	Canada
D'hooghe et al.	Self-reported levels of education and disability progression in multiple sclerosis.	2016	Belgium/The Netherlands
Estrutti et al.	Employment status of people diagnosed with multiple sclerosis in Brazil.	2019	Brazil
Farnoush et al.	Educational, psycho mental and socio economical needs of an Iranian cohort with multiple sclerosis	2010	Iran
Finlayson et al.	Self-care, productivity and leisure limitations of people with multiple sclerosis in Manitoba	1998	Canada
Flensner et al.	Work capacity and health-related quality of life among individuals with multiple sclerosis reduced by fatigue: A cross-sectional study	2013	Sweden
Fragoso et al.	The effect of multiple sclerosis on the professional life of a group of Brazilian patients.	2010	Brazil
Genevie et al.	Job Retention Among People with Multiple Sclerosis	1987	USA
Gill et al.	Disclosing a Diagnosis in the Workplace: Perspective of People with Multiple Sclerosis	2021	Ireland
Gordon et al.	Employment issues and knowledge regarding ADA of persons with multiple sclerosis	1997	USA
Gregory et al.	Employment and multiple sclerosis in New Zealand.	1993	New Zealand
Gross et al.	Characteristics, burden of illness, and physical functioning of patients with relapsing-remitting and secondary progressive multiple sclerosis: a cross-sectional US survey.	2017	USA
Gulick et al.	Work performance by persons with multiple sclerosis: conditions that impede or enable the performance of work.	1989	USA
Gulick et al.	Health status, work impediments, and coping related to work roles of women with multiple sclerosis.	1996	USA
Hakim et al.	The social impact of multiple sclerosis-a study of 305 patients and their relatives.	2000	UK
Heinonen et al.	The retirement rate due to multiple sclerosis has decreased since 1995- A retrospective study in a Finnish central hospital.	2020	Finland
Heredia-Torres et al.	Occupational performance in multiple sclerosis and its relationship with quality of life and fatigue	2020	Spain
Hersch et al.	The implications of suboptimal year-1 outcomes with disease-modifying therapy in employees with multiple sclerosis.	2021	USA
Incerti et al.	Adverse working events in patients with multiple sclerosis.	2017	Italy
Jaworski et al.	Conscientiousness and deterioration in employment status in multiple sclerosis over 3 years.	2021	USA
Johansson et al.	THE SWEDISH OCCUPATIONAL FATIGUE INVENTORY IN PEOPLE WITH MULTIPLE SCLEROSIS	2008	Sweden

Johnson et al.	Social-services support for multiple sclerosis patients in West of Scotland.	1977	Scotland
Julian et al.	Employment in multiple sclerosis. Exiting and re-entering the work force.	2008	USA
Kornblith et al.	Employment in individuals with multiple sclerosis.	1986	USA
Krause et al.	Employment and Gainful Earnings Among Those With Multiple Sclerosis	2019	USA
Krokavkova et al.	Self-rated health and employment status in patients with multiple sclerosis.	2010	Slovakia/The Netherlands
Kwiatkowski	Social participation in patients with multiple sclerosis: correlations between disability and economic burden.	2014	France
Lehmann et al.	Factors associated with employment and expected work retention among persons with multiple sclerosis: findings of a cross-sectional citizen science study.	2020	Swizerland
Leslie et al.	Patterns in workplace accommodations for people with multiple sclerosis to overcome cognitive and other disease-related limitations.	2015	USA
Li et al.	Employment retention expectations of working adults with multiple sclerosis: A multinomial logistic regression analysis	2018	USA
Lorefice et al.	What do multiple sclerosis patients and their caregivers perceive as unmet needs?	2013	Italy
Lundmark et al.	Relationship between occupation and life satisfaction in people with multiple sclerosis.	1996	Sweden
Maurino et al.	Workplace difficulties, health-related quality of life, and perception of stigma from the perspective of patients with Multiple Sclerosis.	2020	Spain
McCabe et al.	Satisfaction with service needs among people living with multiple sclerosis.	2015	Australia
McDonnell et al.	An assessment of the spectrum of disability and handicap in multiple sclerosis: a population-based study.	2001	UK
Midgard et al.	Impairment, disability and handicap in multiple sclerosis - A cross-sectional study in an incident cohort in More and Romsdal County, Norway	1996	Norway
Mitchell et al.	Multiple Sclerosis and the Prospects for Employment*	1981	UK
Morrow et al.	Predicting loss of employment over three years in multiple sclerosis: clinically meaningful cognitive decline.	2010	USA
Murley et al.	Types of working-life sequences among people recently diagnosed with multiple sclerosis in Sweden: a nationwide register-based cohort study.	2020	Sweden
Neath et al.	Patterns in perceived employment discrimination for adults with multiple sclerosis.	2007	USA
Neuberger et al.	Work Productivity Outcomes Associatedwith Ocrelizumab Compared with Other Disease-Modifying Therapies for Multiple Sclerosis	2021	USA
Ongagna et al.	Difficultés ressenties au travail par les patients atteints de sclérose en plaques	2015	France
Papantoniou et al.	Rotating night shift work and risk of multiple sclerosis in the Nurses' Health Studies.	2019	USA

Patten et al.	Health status, stress and life satisfaction in a community population with MS	2012	Canada
Patti et al.	Symptoms, prevalence and impact of multiple sclerosis in younger patients: a multinational survey.	2014	Italy/Spain/Norway/Germany
Pfleger et al.	Social consequences of multiple sclerosis (1): Early pension and temporary unemployment-a historical prospective cohort study	2010	Denmark
Pina Latorre et al.	Evaluation of handicap and socio-economic status in patients with multiple sclerosis--data from a population-based survey in the sanitary area of Calatayud, northern Spain.	2001	Spain
Ponzio et al.	Workers with disability: the case of multiple sclerosis.	2015	Italy
Rivera-Navarro et al.	Informal caregiving in multiple sclerosis patients: Data from the Madrid demyelinating disease group study	2003	Spain
Rodriguez et al.	Impairment, disability, and handicap in multiple sclerosis: a population-based study in Olmsted County, Minnesota.	1994	USA
Roessler et al.	High-priority employment concerns of Hispanics/Latinos with multiple sclerosis in the United States	2016	USA
Ruet et al.	Cognitive impairment, health-related quality of life and vocational status at early stages of multiple sclerosis: a 7-year longitudinal study.	2013	France
Rumrill et al.	The employment concerns of Americans with multiple sclerosis: Perspectives from a national sample.	2015	USA
Rumrill et al.	Multiple sclerosis and workplace discrimination: The national EEOC ADA research project	2005	USA
Salter et al.	Employment and absenteeism in working-age persons with multiple sclerosis.	2017	USA
Scheinberg et al.	Vocational disability and rehabilitation in multiple sclerosis.	1981	Germany
Ahmad et al.	The increasing economic burden of multiple sclerosis by disability severity in Australia in 2017: Results from updated and detailed data on types of costs	2020	Australia
Battaglia et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Italy	2017	Italy
Berg et al.	Costs and quality of life of multiple sclerosis in Sweden.	2006	Sweden
Birnbaum et al.	Economic impact of multiple sclerosis disease-modifying drugs in an employed population: direct and indirect costs	2008	US
Björkenstam et al.	Heterogeneity of sickness absence and disability pension trajectories among individuals with MS	2015	Sweden
Blinkenberg et al.	Increased socioeconomic burden in patients with primary progressive multiple sclerosis: A Danish nationwide population-based study	2020	Denmark
Bo et al.	Access to social security benefits among multiple sclerosis patients in Italy: A cross-sectional study.	2018	Italy

Bonafede	Productivity Loss and Associated Costs Among Employed Patients Receiving Disease-Modifying Treatment for Multiple Sclerosis	2021	US
Boyko et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Russia	2017	Russia
Brook et al.	Absenteeism and health-benefit costs among employees with MS.	2009	US
Brown et al.	Societal costs of primary progressive multiple sclerosis in Australia and the economic impact of a hypothetical disease-modifying treatment that could delay disease progression.	2021	Australia
Brundin et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Sweden	2017	Sweden
Bruno et al.	Economic burden of multiple sclerosis in France estimated from a regional medical registry and national sick fund claims	2019	France
Butepage et al.	Cost-of-illness trajectories among people with multiple sclerosis by comorbidity: A register-based prospective study in Sweden	2020	Sweden
Calabrese et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Switzerland.	2017	Swizerland
Campbell et al.	Burden of multiple sclerosis on direct, indirect costs and quality of life: National US estimates.	2014	US
Carney et al.	Societal costs of multiple sclerosis in Ireland.	2018	Ireland
Casado et al.	Direct and indirect costs of Multiple Sclerosis in Baix Llobregat (Catalonia, Spain), according to disability	2006	Spain
Catanzaro et al.	Economic status of families living with multiple sclerosis.	1992	USA
Chruzander et al.	Longitudinal changes in sickness absence and disability pension, and associations between disability pension and disease-specific and contextual factors and functioning, in people with multiple sclerosis.	2016	Sweden
da Silva et al.	Cost analysis of multiple sclerosis in Brazil: a cross-sectional multicenter study	2016	Brazil
Dubois et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Belgium.	2017	Belgium
Dusankova et al.	Cost of multiple sclerosis in the Czech Republic: the COMS study.	2012	Czech Republic
Earnshaw et al.	Cost effectiveness of glatiramer acetate and natalizumab in relapsing-remitting multiple sclerosis.	2009	USA
Flachenecker et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Germany.	2017	Germany
Fogarty et al.	Direct and indirect economic consequences of multiple sclerosis in Ireland.	2014	Ireland
Garcia-Dominguez et al.	Economic burden of multiple sclerosis in a population with low physical disability	2019	Spain
Gyllensten et al.	Costs of illness of multiple sclerosis in Sweden: a population-based register study of people of working age.	2018	Sweden
Gyllensten et al.	Comparing costs of illness of multiple sclerosis in three different years: A population-based study.	2018	Sweden

Gyllensten et al.	Costs of illness progression for different multiple sclerosis phenotypes: a population-based study in Sweden	2019	Sweden
Gyllensten et al.	How does work disability of patients with MS develop before and after diagnosis? A nationwide cohort study with a reference group.	2016	Sweden
Heiznlef et al.	Economic Burden of the Out-of-Pocket Expenses for People with Multiple Sclerosis in France	2020	France
Ivanova et al.	The cost of disability and medically related absenteeism among employees with multiple sclerosis in the US.	2009	USA
Jennum et al.	The socioeconomic consequences of multiple sclerosis: A controlled national study	2012	Denmark
Jennum et al.	The socioeconomic consequences of optic neuritis with and without multiple sclerosis: a controlled national study	2012	Denmark
Johnson et al.	Disability in multiple sclerosis and the provision of social and medical services: Findings in Wellington, New Zealand	1984	New Zealand
Johnson et al.	The Cost and Benefits of Employment: A Qualitative Study of Experiences of Persons With Multiple Sclerosis	2004	USA
Kavaliunas et al.	Earnings and Financial Compensation from Social Security Systems Correlate Strongly with Disability for Multiple Sclerosis Patients.	2015	Sweden
Kobelt et al.	Costs and quality of life of multiple sclerosis in Austria.	2006	Austria
Kobelt et al.	Costs and quality of life in multiple sclerosis in The Netherlands.	2006	Belgium
Kobelt et al.	Burden and cost of multiple sclerosis in Brazil.	2019	Brazil
Kobelt et al.	Costs and quality of life of multiple sclerosis in the United Kingdom.	2006	Europe
Kobelt et al.	The burden of multiple sclerosis 2015: Methods of data collection, assessment and analysis of costs, quality of life and symptoms.	2006	Europe
Kobelt et al.	New insights into the burden and costs of multiple sclerosis in Europe.	2017	Europe
Kobelt et al.	Costs and quality of life in multiple sclerosis. An observational study in Germany	2001	Germany
Kobelt et al.	Costs and quality of life in multiple sclerosis in The Netherlands.	2006	Germany
Kobelt et al.	Costs and quality of life of multiple sclerosis in Italy.	2006	Italy
Kobelt et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Poland.	2017	Poland
Kobelt et al.	Costs and quality of life of multiple sclerosis in Spain.	2006	Spain
Kobelt et al.	Costs and quality of life of multiple sclerosis in Switzerland.	2006	Swizerland
Kobelt et al.	Costs and quality of life in multiple sclerosis in The Netherlands.	2006	The Netherlands
Kobelt et al.	Costs and quality of life of multiple sclerosis in the United Kingdom.	2006	UK
Kobelt et al.	Costs and quality of life in multiple sclerosis: a cross-sectional study in the United States.	2006	United States

Kotsopoulos et al.	The fiscal consequences of public health investments in disease-modifying therapies for the treatment of multiple sclerosis in Sweden.	2020	Sweden
Landfeldt et al.	Sick leave and disability pension before and after diagnosis of multiple sclerosis.	2016	Sweden
Landfeldt et al.	The long-term impact of early treatment of multiple sclerosis on the risk of disability pension.	2018	Sweden
Landfeldt et al.	Personal Income Before and After Diagnosis of Multiple Sclerosis.	2018	Sweden
Lau et al.	Employment among multiple sclerosis patients in Hong Kong	2016	Hong Kong
Lebrun-Fernay et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for France.	2017	France
McCrone et al.	Multiple sclerosis in the UK: service use, costs, quality of life and disability.	2008	UK
Murley et al.	Disposable income trajectories of working-aged individuals with diagnosed multiple sclerosis.	2018	Sweden
Murley et al.	Diagnosis-specific sickness absence and disability pension before and after multiple sclerosis diagnosis: An 8-year nationwide longitudinal cohort study with matched references.	2020	Sweden
Neusser et al.	Economic burden of multiple sclerosis to the social insurance system in Germany	2018	Germany
Nicholas et al.	Personal and societal costs of multiple sclerosis in the UK: A population-based MS Registry study.	2020	UK
Noyes et al.	Cost-effectiveness of disease-modifying therapy for multiple sclerosis: a population-based study.	2011	USA
Nuijten et al.	Cost-Effectiveness Analysis of Interferon Beta in Multiple Sclerosis: A Markov Process Analysis	2002	Norway
Orlewska et al.	A prospective study of the financial costs of multiple sclerosis at different stages of the disease	2005	Poland
Palmer et al.	The economic impact of multiple sclerosis in Australia in 2010.	2013	Australia
Parise et al.	Direct and indirect cost burden associated with multiple sclerosis relapses: Excess costs of persons with MS and their spouse caregivers	2013	Canada
Péntek et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Hungary.	2017	Hungary
Pike et al.	Social and economic burden of walking andmobility problems in multiple sclerosis	2012	UK
Pope et al.	Prevalence, expenditures, utilization, and payment for persons with MS in insured populations.	2002	Italy
Rajagopalan et al.	Comparing costs and absences for multiplesclerosis among US employees: pre- andpost-treatment initiation	2011	USA
Rasmussen et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Denmark.	2017	Denmark
Rzepinski et al.	New insights into the socio-economic aspects of multiple sclerosis in a cohort of Polish patients	2015	Poland
Sa et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for Portugal	2017	Portugal
Svendsen et al.	The cost of multiple sclerosis in Norway.	2012	Norway
Svendsen et al.	The economic impact of multiple sclerosis to the patients and their families in Norway.	2018	Norway

Chiu et al.	Employment as a health promotion intervention for persons with multiple sclerosis.	2016	USA
Chiu et al.	State vocational rehabilitation services and employment in multiple sclerosis.	2013	USA
Chiu et al.	Effect of Rehabilitation Technology Services on Vocational Rehabilitation Outcomes of Individuals With Multiple Sclerosis	2015	USA
Dorstyn et al.	Online Resource to Promote Vocational Interests Among Job Seekers With Multiple Sclerosis: A Randomized Controlled Trial in Australia.	2018	Australia
Dorstyn et al.	Piloting an email-based resource package for job seekers with multiple sclerosis.	2017	Australia
Fraser et al.	Vocational rehabilitation in multiple sclerosis (MS): a profile of clients seeking services.	2003	USA
LaRocca et al.	A program to facilitate retention of employment among persons with multiple sclerosis.	1996	USA
Rozin et al.	Vocational rehabilitation of multiple sclerosis (MS) patients I. Analysis of clinical and demographic factors first in a series of articles	1982	Israel
Rumrill et al.	Improving career re-entry outcomes for people with multiple sclerosis: A comparison of two approaches	1998	USA
Rumrill et al.	Employment and workplace accommodation outcomes among participants in a vocational consultation service for people with multiple sclerosis	2013	USA
Sundstrom et al.	Sick leave and professional assistance for multiple sclerosis individuals in Vasterbotten County, northern Sweden	2003	Sweden
Sweetland et al.	Vocational rehabilitation services for people with multiple sclerosis: what patients want from clinicians and employers.	2007	UK
Baroin et al.	Validation of a new quality of life scale related to multiple sclerosis and relapses.	2013	France
Benedict et al.	Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder,personality, and behavior change	2005	US
Carnero Contentti	Impact of multiple sclerosis on quality of life: Comparison with systemic lupus erythematosus	2017	Argentina
Forbes et al.	Health problems and health-related quality of life in people with multiple sclerosis.	2006	UK
Ford et al.	Health status and quality of life of people with multiple sclerosis.	2001	UK
Giordano et al.	Low quality of life and psychological wellbeing contrast with moderate perceived burden in carers of people with severe multiple sclerosis.	2016	Italy
Grima et al.	Cost and health related quality of life consequences of multiple sderosis	2000	Canada
Jonsson et al.	Quality of life as a measure of rehabilitation outcome in patients with multiple sclerosis	1996	Denmark
Kikuchi et al.	Impact and characteristics of quality of life in Japanese patients with multiple sclerosis.	2011	Japan
Miller et al.	Health-related quality of life in multiple sclerosis: The impact of disability, gender and employment status.	2006	Israel
Pack et al.	Quality of life and employment in persons with multiple sclerosis.	2014	USA

Petrovic et al.	Quality of life among persons suffering from multiple sclerosis	2019	Croatia
Pluta-Fuerst et al.	Patient-reported quality of life in multiple sclerosis differs between cultures and countries: a cross-sectional Austrian-German-Polish study.	2011	Austria/Germany /Poland
Rashikj-Canevska et al.	Some determinats of quality of life in patients suffering from multiple sclerosis	2015	Macedonia
Rivera-Navarro et al.	[Searching for more specific dimensions for the measurement of quality of life in multiple sclerosis].	2001	Spain
Rumrill et al.	Personal, health and function, and careermaintenance factors as determinants ofquality of life among employed peoplewith multiple sclerosis	2020	USA
SzczygieŁ et al.	Membership in non-governmental organisations and quality of life among people suffering multiple sclerosis	2011	Poland
Alhussain et al.	Multiple Sclerosis Patients in Saudi Arabia: Prevalence of Depression and its Extent of Severity.	2020	Saudi Arabia
Amato et al.	Cognitive impairment in early-onset multiple sclerosis. Pattern, predictors, and impact on everyday life in a 4-year follow-up.	1995	Italy
Amato et al.	Cognitive Dysfunction in Early-OnsetMultiple Sclerosis	2001	Italy
Archibald et al.	Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients	1994	Canada
Baughman et al.	Staying on the job: The relationship between workperformance and cognition in individuals diagnosed withmultiple sclerosis	2015	US
Beier et al.	Relationship of perceived stress and employment status in individuals with multiple sclerosis.	2019	US
Bessing et al.	Changes in multiple sclerosis symptoms are associated with changes in work productivity of people living with multiple sclerosis	2021	Australia
Bishop et al.	The relationship of self-management anddisease modifying therapy use to employmentstatus among adults with multiple sclerosis	2009	US
Bishop et al.	The relationship between housing accessibility variables and employment status among adults with multiple sclerosis	2013	US
Bishop et al.	Employment Among Working-Age Adults With Multiple Sclerosis: A Data-Mining Approach to Identifying Employment Interventions	2015	US
Busche et al.	Short term predictors of unemployment in multiple sclerosis patients.	2003	Canada
Cadden et al.	Factors associated with employment status in individuals with multiple sclerosis: Cognition, fatigue, and motor function	2015	US
Campbell et al.	Cognitive impairment among patients with multiple sclerosis: associations with employment and qualityof life	2016	UK
Chen et al.	Effects of multiple sclerosis disease-modifying therapies on employment measures using patient-reported data.	2018	Australia

Chen et al.	Estimating MS-related work productivity loss and factors associated with work productivity loss in a representative Australian sample of people with multiple sclerosis.	2019	Australia
Chen et al.	Risk factors of leaving employment due to multiple sclerosis and changes in risk over the past decades: survival analysis with competing risks	2019	Australia
Coleman et al.	Impact of mobility impairment on indirect costs and health-related quality of life in multiple sclerosis.	2013	USA
Concetta Incerti	Occupational stress and personality traits in multiple sclerosis: A preliminary study	2015	Italy
D'hooghe et al.	Perceived neuropsychological impairment inversely related to self-reported health and employment in multiple sclerosis	2019	Belgium
Fantoni-Quinton et al.	Impact of multiple sclerosis on employment and use of job-retention strategies: The situation in France in 2015.	2016	France
Forslin et al.	Predictors for Employment Status in People With Multiple Sclerosis: A 10-Year Longitudinal Observational Study	2018	Sweden
Fraser et al.	Predictors of vocational stability in multiple sclerosis	2009	USA
Frndak et al.	Disclosure of disease status among employed multiple sclerosis patients: Association with negative work events and accommodations	2015	USA
Frndak et al.	Negative work events reported online precede job loss in multiple sclerosis	2015	USA
Ghaffar et al.	Occupational attainment as a marker of cognitive reserve in multiple sclerosis.	2012	Canada
Gill et al.	Depressive Symptoms Are Associated With More Negative Functional Outcomes Than Anxiety Symptoms in Persons With Multiple Sclerosis.	2019	Canada
Glanz et al.	Work productivity in relapsing multiple sclerosis: associations with disability, depression, fatigue, anxiety, cognition, and health-related quality of life.	2012	USA
Graham et al.	Barriers and facilitators to employment as reported by people with physical disabilities: An across disability type analysis	2018	USA
Grytten et al.	The influence of coping styles on long-term employment in multiple sclerosis: A prospective study	2017	Norway
Gulick et al.	Model for predicting work performance among persons with multiple sclerosis.	1992	USA
Hategeka et al.	Association of Unemployment and Informal Care with Stigma in Multiple Sclerosis: Evidence from the Survey on Living with Neurological Conditions in Canada.	2019	Canada
Honarmand et al.	Predicting employment status in multiple sclerosis patients: the utility of the MS functional composite	2010	Canada
Incerti et al.	Can personality traits influence occupational stress in multiple sclerosis patients? A one-year longitudinal study.	2020	Italy

Iwanaga et al.	Person-environment contextual factors as mediators for the relationship between symptom cluster and employment outcome in multiple sclerosis	2018	USA
Jacobsen et al.	Brain atrophy and employment in multiple sclerosis patients: a 10-year follow-up study	2020	Norway
Jiméenez-Lopez et al.	Qualitative impact of cognitive impairment on daily life activities of patients with recently diagnosed multiple sclerosis	2012	Mexico
Johnson et al.	Disease and demographic characteristics associated with unemployment among working-age adults with multiple sclerosis	2013	USA
Jones et al.	Quantifying the relationship between increased disability and health care resource utilization, quality of life, work productivity, health care costs in patients with multiple sclerosis in the US	2016	USA
Jongen et al.	Relationship between working hours and power of attention, memory, fatigue, depression and self-efficacy one year after diagnosis of clinically isolated syndrome and relapsing remitting multiple sclerosis.	2014	The Netherlands
Kadrnozkova et al.	Combining clinical and magnetic resonance imaging markers enhances prediction of 12-year employment status in multiple sclerosis patients.	2018	Czech Republic
Kallmann et al.	Real-life outcomes of teriflunomide treatment in patients with relapsing multiple sclerosis: TAURUS-MS observational study.	2019	Germany
Kavaliunas et al.	Cognitive function is a major determinant of income among multiple sclerosis patients in Sweden acting independently from physical disability.	2019	Sweden
Kirk-Brown et al.	Disclosure of diagnosis of multiple sclerosis in the workplace positively affects employment status and job tenure	2014	Australia
Kordovski et al.	Identifying employed multiple sclerosis patients at-risk for job loss: When do negative work events pose a threat?	2015	USA
Krause et al.	Barriers and Facilitators to Employment: A Comparison of Participants With Multiple Sclerosis and Spinal Cord Injury.	2021	USA
Krause et al.	Employment status in multiple sclerosis: impact of disease-specific and non-disease-specific factors.	2013	Germany
LaRocca et al.	Factors associated with unemployment of patients with multiple sclerosis.	1985	USA
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Li et al.	Factors affecting the job satisfaction of employed adults with multiple sclerosis	2004	USA
Li et al.	Factors Influencing Job Satisfaction for Employed Adults With Multiple Sclerosis	2017	USA
Li et al.	Disease-related and functional predictors of employment status among adults with multiple sclerosis.	2015	USA

Lorefice et al.	The impact of visible and invisible symptoms on employment status, work and social functioning in Multiple Sclerosis	2018	Italy
Marck et al.	Predictors of Change in Employment Status and Associations with Quality of Life: A Prospective International Study of People with Multiple Sclerosis	2019	Australia
McCabe et al.	Role of health, relationships, work and coping on adjustment among people with multiple sclerosis: A longitudinal investigation	2004	Australia
Morrow et al.	Predictors of vocational status among persons with multiple sclerosis	2018	Canada
O'Conner et al.	Factors influencing work retention for people with multiple sclerosis: cross-sectional studies using qualitative and quantitative methods.	2005	UK
Pack et al.	Predicting readiness to return to work in a population with multiple sclerosis	2009	USA
Patten et al.	Depression as a predictor of occupational transition in a multiple sclerosis cohort	2013	Canada
Pérez-Miralles et al.	Short-term data on disease activity, cognition, mood, stigma and employment outcomes in a cohort of patients with primary progressive multiple sclerosis (UPPMS study)	2021	Spain
Pfleger et al.	Social consequences of multiple sclerosis: clinical and demographic predictors - a historical prospective cohort study.	2010	Denmark
Phillips et al.	Predicting continued employment in persons with multiple sclerosis	2006	USA
Povolo et al.	Predictors of vocational status among persons with multiple sclerosis.	2019	Canada
Renner et al.	Working ability in individuals with different disease courses of multiple sclerosis: Factors beyond physical impairment.	2020	Germany
Roessler et al.	Determinants of employment status among people with multiple sclerosis	2001	USA
Roessler et al.	Predictors of Employment Status for People with Multiple Sclerosis	2004	USA
Roessler et al.	Severity, employment, and gender: Factors influencing independence for adults with multiple sclerosis	2013	USA
Salter et al.	Impact of loss of mobility on instrumental activities of daily living and socioeconomic status in patients with MS.	2010	USA
Smith et al.	Factors related to employment status changes in individuals with multiple sclerosis.	2005	USA
Strober et al.	Unemployment in multiple sclerosis: the contribution of personality and disease.	2012	USA
Strober et al.	Unemployment in multiple sclerosis (MS): utility of the MS Functional Composite and cognitive testing.	2014	USA
Strober et al.	Unemployment among women with multiple sclerosis: the role of coping and perceived stress and support in the workplace.	2016	USA
Strober et al.	Unemployment in multiple sclerosis across the ages: How factors of unemployment differ among the decades of life.	2016	USA

Strober et al.	Determinants of unemployment in multiple sclerosis (MS): The role of disease, person-specific factors, and engagement in positive health-related behaviors.	2020	USA
Andries et al.	Working with a chronic disorder--the development of the Work and Handicap Questionnaire.	2004	The Netherlands
Gulick et al.	Reliability and validity of the work assessment scale for persons with multiple sclerosis.	1991	USA
Honan et al.	The Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ):development of a shortened scale	2014	Australia
Kahraman et al.	The multiple sclerosis work difficulties questionnaire: translation and cross-cultural adaptation to Turkish and assessment of validity and reliability.	2019	Turkey
McFadden et al.	Screening for the risk of job loss in multiple sclerosis (MS): development of an MS-specific Work Instability Scale (MS-WIS).	2012	UK
Schiavolin et al	Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job): definition of the cut-off score.	2016	Italy
Abbasi et al.	Risk factors of Multiple sclerosis and their Relation with Disease Severity: A Cross-sectional Study from Iran	2016	Iran
Abdulla et al.	Factors that influence quality of life in patients with multiple sclerosis in Saudi Arabia	2021	Saudi Arabia
Ahmadi et al.	Relationship Between Anxiety and Depression with Disability Over Multiple Sclerosis Patients in Rafsanjan, Iran	2018	Iran
Akbar 2021 et al.	A mixed-methods study of cognitive performance in persons with multiple sclerosis: Association between neuropsychological test performance and interviews about daily cognitive functioning	2021	Canada
Al-Asmi	Magnitude and concurrence of anxiety and depression among attendees with multiple sclerosis at a tertiary care Hospital in Oman	2015	Oman
Alosaimi et al.	Psychosocial predictors of patient adherence to disease-modifying therapies for multiple sclerosis	2017	Saudi Arabia
Alsharie et al.	Stressful life events and the risk of primary progressive multiple sclerosis: A population-based case-control study	2021	Iran
Alshubaili et al.	Relationship of depression, disability, and family caregiver attitudes to the quality of life of Kuwaiti persons with multiple sclerosis: a controlled study	2007	Kuwait
AlZahrani	Association of acute stress with multiple sclerosis onset and relapse in Saudi Arabia	2019	Saudi Arabia
Amaducci et al.	Multiple sclerosis among shoe and leather workers: an epidemiological survey in Florence.	1982	Italy
Aronson et al.	Quality of life among persons with multiple sclerosis and their caregivers	1997	Canada
Arroyo et al.	Correlation between spasticity and quality of life in patients with multiple sclerosis: the CANDLE study	2013	Spain
Artemiadis et al.	Structural MRI correlates of cognitive function in multiple sclerosis	2018	Greece

Babamohamadi et al.	Dimensions of Adaptation, General Health, and life Satisfaction in Multiple Sclerosis	2016	Iran
Bamer et al.	Validation study of prevalence and correlates of depressive symptomatology in multiple sclerosis.	2008	United States
Barin et al.	Patterns of care for Multiple Sclerosis in a setting of universal care access: A cross-sectional study	2019	Swizerland
Barzegar et al.	Comparative study of quality of life, anxiety, depression, and fatigue among patients with neuromyelitis optica spectrum disorder and multiple sclerosis: The first report from Iran	2018	Iran
Baumstarck et al.	Is the Concept of Quality of Life Relevant for Multiple Sclerosis Patients with Cognitive Impairment? Preliminary Results of a Cross-Sectional Study	2012	France
Baumstarck et al.	Health-related quality of life as an independent predictor of long-term disability for patients with relapsing–remitting multiplesclerosis-remittingmultiplesclerosis:A2-yearlongitudinalstudy	2013	France
Becker et al.	Patient satisfaction and healthcare services in specialized multiple sclerosis centres in Germany	2018	Germany
Bishop et al.	Sources of information about multiple sclerosis: Information seeking and personal, demographic, and MS variables	2009	US
Bishop et al.	Quality of life among people with multiple sclerosis: Replication of a three-factor prediction model	2015	US
Bishop et al.	Life domains that are important to quality of life for people with multiple sclerosis: A population-based qualitative analysis	2019	US
Björkenstam et al.	Is disability pension a risk indicator for future need of psychiatric healthcare or suicidal behavior among MS patients- a nationwide register study in Sweden?	2015	Sweden
Broersma et al.	The impact of self-perceived limitations, stigma and sense of coherence on quality of life in multiple sclerosis patients: results of a cross-sectional study.	2018	The Netherlands
Brown et al.	Longitudinal assessment of anxiety, depression, and fatigue in people with multiple sclerosis	2009	Australia
Buchanan et al.	Informal care giving to more disabled people with multiple sclerosis	2008	US
Bueno et al.	Health-related quality of life in patients with longstanding ‘benign multiple sclerosis’	2015	Canada
Buhse et al.	.Factors Associated with Health-Related Quality of Life Among Older People with Multiple Sclerosis	2014	US
Buzgova et al.	Factors Influencing Health-Related Quality of Life of Patients with Multiple Sclerosis and Their Caregivers	2020	Czech Republic
Buzgova et al.	Satisfaction of Patients With Severe Multiple Sclerosis and Their Family Members With Palliative Care: Interventional Study	2020	Czech Republic

Calandri et al.	Young adults' adjustment to a recent diagnosis of multiple sclerosis: The role of identity satisfaction and self-efficacy	2019	Italy
Calandri et al.	Improving the quality of life and psychological well-being of recently diagnosed multiple sclerosis patients: preliminary evaluation of a group-based cognitive behavioral intervention	2017	Italy
Casado et al.	Direct costs of relapses in patients with relapsing-remitting multiple sclerosis	2006	Spain
Cattaneo et al.	Participation Restriction in People With Multiple Sclerosis: Prevalence and Correlations With Cognitive, Walking, Balance, and Upper Limb Impairments	2017	Italy/Belgium
Chen et al.	Impact of depression, fatigue and disability on quality of life in Chinese patients with multiple sclerosis.	2013	China
Chiu et al.	Motivational and Volitional Variables Associated With Stages of Change for Exercise in Multiple Sclerosis: A Multiple Discriminant Analysis	2012	USA
Chiu et al.	Descriptive analysis of free-text comments on healthcare priorities and experiences in a national sample of people with multiple sclerosis.	2019	USA
Chruzander et al.	A 10-year follow-up of a population-based study of people with multiple sclerosis in Stockholm, Sweden: Changes in disability and the value of different factors in predicting disability and mortality	2013	Sweden
Chwastiak et al.	Fatigue and psychiatric illness in a large community sample of persons with multiple sclerosis.	2005	USA
Cioncoloni et al.	Individual factors enhance poor health-related quality of life outcome in multiple sclerosis patients. Significance of predictive determinants.	2014	Italy
Clingerman et al.	The Influence of Resources on Perceived Functional Limitations Among Women with Multiple Sclerosis	2004	USA
Cofield et al.	Shared Decision Making and Autonomy Among US Participants with Multiple Sclerosis in the NARCOMS Registry.	2017	USA
Conradsson et al.	Changes in disability in people with multiple sclerosis: a 10-year prospective study.	2018	Sweden
Conradsson et al.	Activity limitations and participation restrictions in people with multiple sclerosis: a detailed 10-year perspective.	2021	Sweden
Costa et al.	Social support network and quality of life in multiple sclerosis patients.	2017	Portugal
Dayapoglu et al.	Quality of life in relapsing-remitting multiple sclerosis	2011	Pakistan
Esposito et al.	Lifestyle and Mediterranean diet adherence in a cohort of Southern Italian patients with Multiple Sclerosis	2021	Italy
Farran et al.	Quality of life and coping strategies in Lebanese Multiple Sclerosis patients: A pilot study	2016	Lebanon
Fernandez et al.	Patient characteristics and determinants of quality of life in an international population with multiple sclerosis: Assessment using the MusiQoL and SF-36 questionnaires	2011	Europe

Fernandez-Jimenez et al.	Quality of Life and Depressive Symptomatology in Multiple Sclerosis: A Cross-Sectional Study Between the USA and Spain	2021	USA/Spain
Fidao et al.	Depression mediates the relationship between fatigue and mental health-related quality of life in multiple sclerosis	2021	Australia
Freedman et al.	Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: a case-control study based on death certificates.	2000	USA
Fuchs et al.	Response heterogeneity to home-based restorative cognitive rehabilitation in multiple sclerosis: An exploratory study.	2019	USA
Gil-Gonzàlez et al.	Predicting improvement of quality of life and mental health over 18-months in multiple sclerosis patients	2021	Spain
Giovanetti et al.	Individualized quality of life of severely affected multiple sclerosis patients: practicability and value in comparison with standard inventories	2016	Italy
Giovanetti et al.	Cognitive function alone is a poor predictor of health-related quality of life in employed patients with MS: results from a cross-sectional study	2016	Italy
Giovanetti et al.	Conversion to secondary progressive multiple sclerosis: Multi stakeholder experiences and needs in Italy	2020	Italy
Göksel Karatepe et al.	Quality of life in patients with multiple sclerosis: the impact of depression, fatigue, and disability	2011	Spain
Gottberg et al.	Health-related quality of life in a population-based sample of people with multiple sclerosis in Stockholm County.	2006	Sweden
Goverover et al.	The relationship among performance of instrumental activities of daily living, self-report of quality of life, and self-awareness of functional status in individuals with multiple sclerosis.	2009	USA
Gracia et al.	Costs of multiple sclerosis in Panama from societal, patient perspectives and health-related quality of life	2018	USA
Gustavsen et al.	Shift work at young age is associated with increased risk of multiple sclerosis in a Danish population.	2016	Denmark
Hadjigeorgiou	Observational study assessing demographic, economic and clinical factors associated with access and utilization of health care services of patients with multiple sclerosis under treatment with interferon beta-1b (EXTAVIA).	2014	Greece
Hamed et al.	Environmental factors affecting the daily functioning of Jordanian individuals with multiple sclerosis.	2012	Jordan
Henriksson et al.	Costs, quality of life and disease severity in multiple sclerosis: a cross-sectional study in Sweden.	2001	Sweden
Horwitz et al.	Effect of occupation on risk of developing MS: an insurance cohort study.	2013	Denmark

Hyarat et al.	Health Related Quality of Life Among Patients With Multiple Sclerosis: The Role of Psychosocial Adjustment to Illness	2019	Saudi Arabia/Jordan
Iezzoni et al.	Health, disability, and life insurance experiences of working-age persons with multiple sclerosis.	2007	USA
Iezzoni et al.	Experiences acquiring and using mobility aids among working-age persons with multiple sclerosis living in communities in the United States.	2010	USA
Imani et al.	Economic costs incurred by the patients with multiple sclerosis at different levels of the disease: a cross-sectional study in Northwest Iran.	2020	Iran
Jaracz et al.	Quality of life and social support in patients with multiple sclerosis	2020	Poland
Jiang et al.	Stressful life events are associated with the risk of multiple sclerosis.	2020	Sweden
Johansson et al.	Associations between fatigue impact and lifestyle factors in people with multiple sclerosis - The Danish MS hospitals rehabilitation study.	2021	Denmark
Johansson et al.	Use of health services in people with multiple sclerosis with and without fatigue.	2009	Sweden
Johansson et al.	Participation in social/lifestyle activities in people with multiple sclerosis: Changes across 10 years and predictors of sustained participation.	2020	Sweden
Jongen et al.	Improved health-related quality of life, participation, and autonomy in patients with treatment-resistant chronic pain after an intensive social cognitive intervention with the participation of support partners.	2017	The Netherlands
Kahraman et al.	Determinants of physical activity in minimally impaired people with multiple sclerosis.	2015	Turkey
Kahraman et al.	Feasibility of a 6-Month Yoga Program to Improve the Physical and Psychosocial Status of Persons with Multiple Sclerosis and their Family Members	2018	Turkey
Kalantari et al.	Perceived Social Stigma in Patients with Multiple Sclerosis: A Study from Iran.	2018	Iran
Khader et al.	Estimating the prevalence of cognition and mental health among multiple sclerosis patients: A population-based cross-sectional study	2019	Kuwait
Khan et al.	Multiple sclerosis: disability profile and quality of life in an Australian community cohort.	2006	Australia
Khan et al.	Use of International Classification of Functioning, Disability and Health (ICF) to describe patient-reported disability in multiple sclerosis and identification of relevant environmental factors.	2007	Australia
Kleiter et al.	Adherence, satisfaction and functional health status among patients with multiple sclerosis using the BETACONNECT® autoinjector: a prospective observational cohort study.	2017	Germany
Koch et al.	Illness and demographic correlates of quality of life among people with multiple sclerosis	2001	USA
Kohn et al.	Mobility, walking and physical activity in persons with multiple sclerosis	2014	USA
Koltunuik et al.	The Role of Stress Perception and Coping with Stress and the Quality of Life Among Multiple Sclerosis Patients	2021	Poland

Kos et al.	Assessing life balance of European people with multiple sclerosis: A multicenter clinimetric study within the RIMS network	2020	Belgium
Krokavkova et al.	Mastery, functional disability and perceived health status in patients with multiple sclerosis	2008	Slovakia/The Netherlands
Labiano-Fontcuberta et al.	Cognitive impairment in patients with multiple sclerosis predicts worse caregiver's health-related quality of life	2014	Spain
Labiano-Fontcuberta et al.	Impact of anger on the health-related quality of life of multiple sclerosis patients	2015	Spain
Lewis et al.	Disability, depression and suicide ideation in people with multiple sclerosis	2017	UK
Lexell et al.	Self-perceived performance and satisfaction with performance of daily activities in persons with multiple sclerosis following interdisciplinary rehabilitation.	2014	Sweden
Li et al.	Regional, socioeconomic and occupational groups and risk of hospital admission for multiple sclerosis: a cohort study in Sweden.	2008	Sweden
Magyari et al.	Physical and social environment and the risk of multiple sclerosis.	2014	Denmark
Marck et al.	Health outcomes and adherence to a healthy lifestyle after a multimodal intervention in people with multiple sclerosis: Three year follow-up	2018	Australia
Motl et al.	Fatigue, depression, and physical activity in relapsing-remitting multiple sclerosis: Results from a prospective, 18-month study	2012	USA
Nery-Hurwit et al.	Examining the roles of self-compassion and resilience on health-related quality of life for individuals with Multiple Sclerosis	2018	USA
Nickel et al.	Self-assessments and determinants of HRQoL in a German MS population.	2018	Germany
O'Brian et al.	Multiple sclerosis: the relationship among self-esteem, social support, and coping behavior.	1993	USA
Ow et al.	Functioning Profiles of Young People with MS in Inpatient Rehabilitation: Data from the National Rehabilitation Reporting System in Canada.	2020	Canada
Pakenham et al.	The nature of sense making in caregiving for persons with multiple sclerosis.	2008	Australia
Patti et al.	Effects of education level and employment status on HRQoL in early relapsing-remitting multiple sclerosis.	2007	Italy
Patti et al.	Predictors of quality of life among patients with multiple sclerosis: An Italian cross-sectional study	2007	Italy
Ponzio et al.	Disparity between perceived needs and service provision: a cross-sectional study of Italians with multiple sclerosis.	2019	Italy
Ponzio et al.	Unmet needs influence health-related quality of life in people with multiple sclerosis	2020	Italy
Ratajska et al.	Social support in multiple sclerosis: Associations with quality of life, depression, and anxiety	2020	USA
Riazi et al.	Socio-demographic variables are limited predictors of health status in multiple sclerosis.	2003	UK

Šabanagić-Hajrić et al.	Impacts of education level and employment status on health-related quality of life in multiple sclerosis patients	2014	Bosnia and Herzegovina
Salehi et al.	ASSOCIATION BETWEEN DISABILITY AND QUALITY OF LIFE IN MULTIPLE SCLEROSIS PATIENTS IN AHVAZ, IRAN.	2016	Iran
Schmidt et al.	Depression, fatigue and disability are independently associated with quality of life in patients with multiple Sclerosis: Results of a cross-sectional study.	2019	Germany
Shawaryn et al.	Assessing Functional Status: Exploring the Relationship Between the Multiple Sclerosis Functional Composite and Driving	2002	USA
Somerset et al.	Factors that contribute to quality of life outcomes prioritised by people with multiple sclerosis.	2003	UK
Stuifbergen et al.	Predictors and moderators of the disablement process in persons with multiple sclerosis	2009	USA
Stuifbergen et al.	Selected health behaviors moderate the progression of functional limitations in persons with multiple sclerosis: Eleven years of annual follow-up	2016	USA
Tansey et al.	Differential Vocational Rehabilitation Service Patterns Related to the Job Retention and Job-Seeking Needs of Individuals With Multiple Sclerosis	2015	USA
Taylor et al.	Lifestyle factors, demographics and medications associated with depression risk in an international sample of people with multiple sclerosis	2014	Australia
Tepavcevic et al.	Change in quality of life and predictors of change among patients with multiple sclerosis: a prospective cohort study	2013	Serbia
Tinghog et al.	High prevalence of sickness absence and disability pension among multiple sclerosis patients: a nationwide population-based study	2013	Sweden
Unger et al.	A comparative analysis of employment discrimination complaints filed by people with multiple sclerosis and individuals with other disabilities	2004	USA
Valadkeviciene et al.	Working capacity level of patients with multiple sclerosis in Lithuania: Its dynamics and relationship with the employment and lethal outcomes.	2021	Lithuania
van der Hiele et al.	Work Participation and Executive Abilities in Patients with Relapsing-Remitting Multiple Sclerosis	2015	The Netherlands
van der Hiele et al.	Coping strategies in relation to negative work events and accommodations in employed multiple sclerosis patients.	2016	The Netherlands
van der Hiele et al.	A pilot study on factors involved with work participation in the early stages of multiple sclerosis.	2014	The Netherlands
van der Hiele et al.	Self-reported occupational functioning in persons with relapsing-remitting multiple sclerosis: Does personality matter?	2021	The Netherlands
Thompson et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for the United Kingdom.	2017	UK

Uitdehaag et al.	New insights into the burden and costs of multiple sclerosis in Europe: Results for the Netherlands.	2017	The Netherlands
van Egmond et al.	A Dutch validation study of the Multiple Sclerosis Work Difficulties Questionnaire in relapsing remitting multiple sclerosis.	2021	The Netherlands
van Gorp et al.	Cognitive functioning as a predictor of employment status in relapsing-remitting multiple sclerosis: a 2-year longitudinal study.	2019	The Netherlands
van Gorp et al.	The capability set for work - correlates of sustainable employability in workers with multiple sclerosis.	2018	The Netherlands
van Mastrigt et al.	An economic evaluation attached to a single-centre, parallel group, unmasked, randomized controlled trial of a 3-day intensive social cognitive treatment (can do treatment) in patients with relapsing remitting multiple sclerosis and low disability.	2019	The Netherlands
Verdier-Taillefer et al.	Occupational environment as risk factor for unemployment in multiple sclerosis	1995	France
Whetten-Goldstein et al.	A comprehensive assessment of the cost of multiple sclerosis in the United States	1998	USA
Wiberg et al.	Sources and level of income among individuals with multiple sclerosis compared to the general population: A nationwide population-based study.	2015	Sweden
Wiberg et al.	Earnings among people with multiple sclerosis compared to references, in total and by educational level and type of occupation: a population-based cohort study at different points in time.	2019	Sweden
Wickström et al.	Improved ability to work after one year of natalizumab treatment in multiple sclerosis. Analysis of disease-specific and work-related factors that influence the effect of treatment	2013	Sweden
Wickström et al.	Improved working ability in a contemporary MS population compared with a historic non-treated MS population in the same geographic area of Sweden.	2015	Sweden
Wickström et al.	The impact of adjusted work conditions and disease-modifying drugs on work ability in multiple sclerosis	2017	Sweden
Yamabe et al.	Health-related outcomes, health care resource utilization, and costs of multiple sclerosis in Japan compared with US and five EU countries.	2019	Japan

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3, 4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	5
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5, 6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5, 6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Click here to enter text.

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7, 8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	7, 8
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Click here to enter text.
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	8-12
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	8-12
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	12-15
Limitations	20	Discuss the limitations of the scoping review process.	15
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	1

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

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Occupational outcomes of people with Multiple Sclerosis: a scoping review

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Occupational outcomes of people with Multiple Sclerosis: a scoping review

Bruno Kusznir Vitturi[1], Alborz Rahmani[1,2], Guglielmo Dini[1,2], Alfredo Montecucco[1,2], Nicoletta Debarbieri[2], Elvira Sbragia[3,4], Paolo Bandiera[5], Michela Ponzio[6], Mario Alberto Battaglia[6,7], Tommaso Manacorda[5], Benedetta Persechino[8], Giuliana Buresti[8], Matilde Inglese[3,4], Paolo Durando[1,2]

1. Department of Health Sciences, University of Genoa, Italy
2. IRCCS Ospedale Policlinico San Martino, Occupational Medicine Unit, Genoa, Italy
3. Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI) and Center of Excellence for Biomedical Research (CEBR), University of Genoa, Genoa, Italy
4. IRCCS Ospedale Policlinico San Martino, Genoa, Italy
5. Italian Multiple Sclerosis Association (AISM)
6. Scientific Research Area, Italian Multiple Sclerosis Foundation (FISM), Italy
7. Department of Life Science, University of Siena, Siena, Italy
8. Italian Workers' Compensation Authority (INAIL)

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Corresponding author

Bruno Kusznir Vitturi, MD

Department of Health Sciences, University of Genoa, Italy

Building 3, L.go R. Benzi 10 - 16132 Genoa, Italy

E-mail: bruno.kusznir.vitturi@edu.unige.it

Abstract

Objectives. To update the knowledge on the occupational outcomes associated with Multiple Sclerosis (MS), systematically examine the extent, scope, and nature of the pre-existing literature, and identify research gaps in the existing literature.

Design. Scoping review.

Data sources. A comprehensive database search of PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science was performed. There were no time limits.

Eligibility criteria. We included any peer-reviewed original article reporting the occupational outcomes of people with MS between the ages of 18 and 65 years. We excluded those off-topic and with insufficient information.

Methods. This review was conducted following the JBI recommendations and the PRISMA-ScR flowchart. Screening, reading of full-texts and data extraction was performed in a standardized way by expert reviewers from July 14, 2021, to October 31, 2021. We provided a narrative synthesis and an overview of findings.

Results. The initial systematic search yielded 104,228 results. After removing duplicates and applying the exclusion criteria, 403 articles were included in the review. In total, the studies evaluated 492,062 subjects with MS. One hundred fifty-four (38.2%) articles were published in the last 5 years, mostly from Europe and North America (50.9% and 33.0%, respectively). The assessment of disability and quality of life, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms were the most frequent MS-related variables. Concerning the occupational outcomes, studies mostly addressed unemployment (311, 77.2%), early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%).

Conclusions

This is the first scoping review dedicated to the occupational outcomes of patients with MS. Despite a significant number of articles have already been published on the subject, there are several issues that deserve further in-depth study by the scientific community in order to promote the occupational outcomes of people with MS.

Keywords

Multiple sclerosis; occupational & industrial medicine; public health; health economics; epidemiology; neurology

Strengths and limitations of this study

- We chose a broad search methodology to form an accurate and comprehensive picture of the relationship between the occupational outcomes and MS.
- As we respected the scoping review approach, we did not formally assess the quality of included studies.
- We could have missed some data for not including results from the grey literature.

1. Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disease that causes demyelination and neurodegeneration in the central nervous system. It mainly affects young people between 20 and 40 years of age and it is the main cause of non-traumatic disability among young adults in the Western world [1]. MS is a global disease, affects 2.5 million people worldwide, the incidence and prevalence are known to be increasing in both developed and developing countries [2]. The symptoms are extremely varied and the clinical course is within a spectrum that extends from relapsing-remitting to progressive [1-3].

In addition to the inherent clinical complexity of MS, the age of onset of the disease brings inevitable repercussions to work activity, as it often coincides with the moment in which patients find themselves managing the already expected difficulties of the job market and the beginning of the professional career [4]. As long as MS symptoms remain 'invisible', people with MS (PwMS) are reluctant to inform their employer about their disease out of fear of losing their job [4]. Concerns about disclosing the diagnosis in the workplace stem from a range of issues involving the fear of appearing vulnerable, suffering discrimination and losing their jobs. [5]. MS imposes essential accommodations in the work environment and in the way of delivering satisfactory work. Often limiting and disabling, symptoms such as fatigue, neuropsychiatric impairment, and motor disturbances constantly threaten the full performance at work and the search for new professional skills. PwMS are more vulnerable to unemployment and early retirement and the influence of MS on professional life is known to be directly associated with quality of life (QoL) [6].

The impact of MS on work activities has already been evaluated in many studies carried out in different parts of the world [7–10]. Calabrese et al. demonstrated that workforce participation can decline from 82% to 8% and employment rates vary between 31% and 65% [7], being influenced by

factors such as the degree of disability, the duration of disease, the level of education and the type of work activity. Another study outlined the complexity of the association between employment and MS and revealed that 56.2% of PwMS are unemployed and have low odds of re-entering the workforce in a second moment [8].

Besides the potential consequences of MS for people's working life, it is also important to recognize the impact of the disease at the community level. Long-term absence, invalidity, and early retirement may demand an annual expense of 17,945€ per patient in the late stages of MS [11]. Loss of productivity at work and occupation change due to MS account for an annual cost of $2,691 and $2,982 for each patient, respectively [12]. Indeed, the impact of MS on occupational outcomes is responsible for a significant economic burden and represents a matter of public health all around the world.

There is an eminent need for further scientific research on the occupational outcomes of PwMS. Although it is relatively easy to find information on MS and work in the literature, being diagnosed with MS still increases the risk of unemployment, early retirement, loss of working capacity, reduced monthly income, job dissatisfaction and impaired QoL. Recent advances in the treatment of MS and the emergence of new types and modalities of work also call for new studies investigating the role of MS on work. Moreover, previous reviews were focused on specific occupational outcomes that do not reflect the totality of possible outcomes, contributing only partially to the holistic understanding of the relationship between MS and work [13–17]. Due to the large number and heterogeneity of articles already published, there is a significant difficulty in detecting gaps in the pre-existing literature and consolidating evidence on the subject. This scenario favours unnecessary investments in redundant studies that could be reallocated to research with potential to truly influence patients' lives. In this context, we decided to conduct the first scoping review related to the occupational outcomes of PwMS, as it can provide a broad map of the existing evidence and identify gaps for potential future studies.

2. Objectives

The objectives of the present scoping review are related to occupational outcomes associated with MS: the primary objective is to update the knowledge on the occupational outcomes of PwMS compared with people without MS, and among PwMS by clinical characteristics. Our secondary objectives were to systematically examine the extent, scope, and nature of the pre-existent literature, to summarize and disseminate the research results deriving from the already published articles, to identify research gaps in the existing literature and to provide an accurate rationale to develop further relevant research in the area.

3. Methods

We performed this scoping review following the guidelines outlined by Arksey and O'Malley, the Joanna Briggs Institute recommendations, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for scoping review (PRISMA-ScR) guidelines [18,19]. As this was a literature review, it did not involve the recruitment of subjects and it analysed data from already published original articles and, therefore, the ethical approval was not necessary.

3.1. Study selection/search strategy

From July 14, 2021, to July 31, 2021, we systematically searched on PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science the following keywords (employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "work resumption" OR workplace* OR "return to work" OR "work force" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention” OR retire* OR “disability pension” OR “worker” OR “fitness for work”) AND (“multiple sclerosis” OR “disseminated sclerosis” OR “demyelinating autoimmune diseases” OR “demyelinating autoimmune disorders” OR “clinically isolated syndrome” OR “demyelinating”). The details of the search strategy used are reported in Table 1. After the preliminary identification, the articles were exported and managed in Mendeley 1.19.8 (Elsevier, New York, USA).

PubMed	(employ* OR unemploy* OR occupation* OR “work” OR vocation* OR “workplace” OR “workforce” OR “labour force” OR “labor force” OR career* OR job* OR retire* OR “disability pension” OR “worker” OR “fitness for work”) AND (“multiple sclerosis” OR “demyelinating autoimmune diseases” OR “demyelinating autoimmune disorders” OR “clinically isolated syndrome” OR “demyelinating”)
Scopus	TITLE-ABS KEY [(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR “workplace” OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune Diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")]
SciVerse Science Direct	("employ" OR "occupation" OR "work" OR "vocation" OR “labour” OR "Job" OR "retire" OR “disability pension”) AND “multiple sclerosis”
Web of Science	(employ* OR unemploy* OR occupation* OR “work” OR vocation* OR “workplace” OR “workforce” OR “labour force” OR “labor force” OR career* OR job* OR retire* OR “disability pension” OR “worker” OR “fitness for work”) AND (“multiple sclerosis” OR “demyelinating autoimmune diseases” OR “demyelinating autoimmune disorders” OR “clinically isolated syndrome” OR “demyelinating”)

Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

3.2. Inclusion and exclusion criteria

A priori, we chose a broad search methodology to be able to form an accurate and comprehensive picture of the relationship between the occupational outcomes and MS. The PCC (Population/Concept/Context) framework was used to define inclusion criteria. We included any peer-reviewed original article reporting the occupational outcomes of PwMS between the ages of 18 and 65 years (population). MS must have been diagnosed according to accepted international criteria at the time of the study. No time limits were set for the search. The context was broad and we accepted articles published in English, Italian, Spanish, French, and Portuguese, as these are the languages spoken in our research group (context). The term “occupational outcomes” was defined as direct and indirect work-related characteristics/consequences potentially associated with MS (concept).

After removing duplicate entries, we performed an initial screening of titles and abstracts to assess potential relevance and excluded those not directly or indirectly focused on the topic of interest. Screening of titles, abstracts, and full texts for each article was conducted by two experienced and trained investigators (BKV and AR), each blinded to the other’s ratings. In case of discrepancy, a final decision was made by a consensus after a debate with a senior researcher (GD). Afterward, we obtained relevant full-text articles, evaluated their eligibility, and determined their final inclusion or exclusion.

Studies written in languages other than the five pre-specified above and studies designed as reviews, letters to the editor, expert opinions, commentaries, case reports, case series, editorials were excluded. Studies that did not address any aspect of an occupational outcome or that eventually only mentioned it as part of the arguments presented in the introduction or discussion (off-topic articles) were excluded. In case of lack of essential information or full-text not being available, we tried to contact the corresponding author twice to obtain the information by email. Whenever our contact attempt failed, the study was excluded. We did not accept studies where MS was not the primary condition or the subjects had other chronic diseases that could potentially influence the occupational outcomes (e.g. a study that included patients with MS and migraine). Some authors published more than one article with the same study population and reporting the same occupational outcomes. In these cases, we included the most recent one and excluded the others. Figure 1 provides the PRISMA flowchart overview of the search and screening strategy performed.

3.3. Data extraction

Data were extracted in a standardized way by an expert reviewer (BKV) and they were double-checked after two months in order to minimise the intrapersonal variability. We determined the information to extract *a priori*. Among the basic characteristics, we gathered information about the authors' names, the title of the study, the year of publication, the country of origin of the study, the study design, the number of subjects with and without MS, the subtype of the disease, the prevalence of each clinical symptom, the duration of the disease, the distribution by age and sex, the level of education, the marital status, the description of any neuroradiological finding, treatment data, assessment of the QoL and disability, prevalence of fatigue, psychiatric symptoms, and cognitive symptoms. Regarding the occupational outcomes, the following data were collected: the description of the profession, the prevalence of unemployment and early retirement, the influence of the disease on monthly income, the need for disability pension, the indirect cost of MS, the stigma and prejudice faced in the workplace, job characteristics, strategies of vocational rehabilitation and job accommodations, patient opinion on work and working life in general, barriers to employment, degree of job satisfaction, need for a change of employment due to MS, the prevalence of work handicap and information on the disclosure of the diagnosis in the workplace. Job accommodations were defined as any reasonable adjustment to a job or work environment that enables PwMS to perform their job duties. Barriers to employment were defined as any challenge or difficulty that may prevent PwMS from getting or keeping a job, or advancing in their career.

3.4. Data synthesis

Following data extraction, due to the range of outcomes assessed and different study designs included in the review, we used a narrative synthesis to report data. This process was carried out after reading the full-text of all the articles included in the review in order to summarize the results as clearly and accurately as possible and cover all the outcomes found. One expert reviewer (BKV) performed a thematic categorization of the findings, which was verified by two other reviewers (AR and AM). The results were categorised into 7 subtopics: “Changes in work and occupational status due to MS”, “work-related socio-economic consequences of MS”, “risk factors for unfavourable occupational outcomes”, “reported barriers to employment”, “reported job accommodations and vocational rehabilitation strategies”, “job satisfaction, stigma, and disclosing the diagnosis in the workplace” and “rating clinical scales”. These subgroups were created to guide the synthesis of the main results reported in the pre-existing literature. We generated a set of statements to adequately represent each subtopic, based on their relevance and degree of evidence.

3.5. Patient and public involvement

No patients or public were involved in the study.

4. Results

Overview of the literature search

The initial systematic search yielded 104,228 results, of which 7,486 were from PubMed, 8,346 were from Scopus, 63,731 were from SciVerse Science Direct 24,665 were from Web of Science. Removing duplicates and applying the eligibility criteria resulted in a total of 1,136 articles. At the end of the study selection, 403 articles were included in the review, and information about the baseline clinical-epidemiological characteristics and the occupational outcomes was properly extracted (Table S1). Figure 1 describes the entire PRISMA-ScR flowchart.

Characteristics of the included literature

The number of studies published on the topic has increased over time, as 154 (38.2%) of the included studies were published in the last 5 years. Most of the studies were conducted in Europe and North America (50.9% and 33.0%, respectively). Asia and Oceania produced 32 (7.9%) and 24 (6.0%) of the studies on the subject, respectively. There were no published data on the association between MS and work from the African continent. Italy, with less than 1% of the world population, promoted the publication of 29 (7.2%) articles on the subject of our study. Regarding the study design, 314 (77.9%) were cross-sectional, 12 (3.0%) were interventional, and 77 (19.1%) were longitudinal. Only 63 (15.6%) studies included a control group in their analysis. In total, the 403 studies evaluated 492,062 subjects with MS. Among the explored characteristics of MS, the assessment of disability and QoL, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms were the most mentioned variables (Table 2). Neuroimaging data and the use of disease-modifying drugs (DMDs) were explored in 10 (2.5%) and 117 (29.0%) studies, respectively.

Clinical and demographic characteristics			**Occupational outcomes**		
	n	%		n	%
Age	394	97.8	Job description	55	13.6
Sex	389	96.5	Work performance	57	14.1
Educational level	288	71.5	Unemployment	311	77.2
Civil status	180	44.7	Sick leave	77	19.1
Socioeconomic conditions	47	11.7	Early retirement	120	29.8
EDSS	212	52.6	Disability pension	117	29.3
Disease duration	274	68.0	Impact on monthly income	52	12.9
Type of MS	258	64.0	Indirect cost of MS	74	18.4
Neuroimaging findings	10	2.4	Professional absenteeism	85	21.1
Description of symptoms	59	14.6	Stigma and prejudice	23	5.7
Quality of Life	139	34.4	Work characteristics	57	14.1
Disability assessment	234	58.1	Vocational rehabilitation	19	4.7
Fatigue	169	41.9	Job accommodations	45	11.2
Psychiatric symptoms	209	51.9	Patients’ opinion about work	85	21.9
Cognitive symptoms	160	39.7	Barriers to employment	65	16.1

Motor symptoms	84	20.8	Disclose of the diagnosis in the workplace	17	4.2
Treatment (DMDs)	117	29.0	Job satisfaction	19	4.7
			Occupational change	78	19.3
			Work handicap	38	9.4

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Work was considered as a dependent variable in 285 (70.7%) articles. Eighty-two (28.8%) studies dealt with the description of employment outcomes, 85 (29.8%) aimed to assess the economic impact of MS, 14 (4.9%) described any strategy of vocational rehabilitation, 17 (6.0%) evaluated the QoL in MS in general, 81 (28.4%) determined possible risk factors associated with occupational outcomes and 6 (2.1%) aimed to develop a possible assessment scale of occupational outcomes. The prevalence of unemployment was the most explored variable (311, 77.2%). Other addressed issues were early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the influence of MS on monthly income (52, 12.9%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). Barriers to employment were reported in 65 (16.1%) studies and job accommodations in 45 (11.2%) studies. Perceived stigma in the workplace, job satisfaction, and knowledge of colleagues about MS were less commonly explored aspects in the studies (5.7%, 4.7%, and 4.2%, respectively). Finally, 59 (14.6%) articles examined occupational absenteeism, 85 (21.1%) aimed to understand the patient's opinion on aspects of his professional life, and 19 (4.7%) evaluated strategies of occupational rehabilitation. The definition of each outcome is extremely diverse across studies in order to suit the particularities of the study design and the research context.

Changes in work and occupational status due to MS

MS is a disease that directly influences the patient's professional life [20–23]. PwMS are vulnerable to a spectrum of several negative consequences at work, ranging from reduction of working hours to unemployment. In a Swedish cohort, only 28% and 23% of PwMS were working full- and part-time after a follow-up of 10 years, respectively [24]. A Norwegian study demonstrated that after 19 years of disease, only 45% of patients were still employed [10]. Even for those who remain employed, more than a quarter show some deterioration in employment status and 56% observe a work performance loss in the short term after the diagnosis [25,26]. Moreover, once unemployed, it is difficult for workers with MS to return to the workforce [8]. Pfleger et al. found that the probability of remaining without early pension at 20 years was 22% for patients and 86% for controls [27].

Work-related socio-economic consequences of MS

MS is a debilitating disease that poses a substantial burden in terms of absenteeism, presenteeism, disability pension, and sick leave costs [28–31]. Employees with MS are significantly more likely to have disability days compared to employees without MS (21.4% vs 5.2%). Overall, employees with MS had lost over 4 times more workdays compared to their controls (37.7 vs 8.8 days) [32]. In a cohort of 8350 PwMS, two-thirds received a form of benefit [33]. Increased disability as measured on the Expanded Disability Status Scale (EDSS) is strongly associated with reduced earnings and increased benefits [20,33,34] but it is noteworthy that even mild disability can pose a significant economic burden at the expense of premature retirement, premature work disability, and time lost from work [20,28,34,35]. Interestingly, Jennun et al. demonstrated that negative effects on employment and health costs have been shown up to 8 years prior to MS diagnosis [36]. Neusser et al. reported an estimated total expenditure of 4.3 billion euros annually when considering all interventions enabling work-life integration [37]. Studies on the economic impact of MS come from different countries and continents [7,9,38–40], so the interpretation of their findings must necessarily take into account the specific social security systems of different countries.

Risk factors for unfavourable occupational outcomes

Multiple studies have addressed the risk factors associated with worse professional outcomes. The progressive phenotype of the disease is certainly a negative predictor of occupational outcomes in PwMS compared to the relapsing-remitting form [10,35,41]. Older age, longer disease duration, and high EDSS are also associated with a higher risk of unemployment [42–45]. Recently, the link between neuroimaging findings and occupational status has been demonstrated. Tauhid et al. showed that the T1 lesion load, the ratio between the T1 and T2 burden, and the overall brain volume are significantly different between employed and non-employed PwMS [46]. In a cohort of 145 patients followed up to 12 years, severe brain atrophy, T1 and T2 injury load were the best predictors of deterioration of the occupational status [47]. Cognitive impairment, neuropsychiatric symptoms, and fatigue are also well-described risk factors for labor force withdrawal and work productivity loss [25,48,49]. The main reasons reported by people with MS for their loss of employment involved the ineffective management of symptoms of MS in the workplace, rather than workplace-related factors including insufficient flexibility of employment conditions or being layed off.

Reported barriers to employment

Some studies described the main barriers to employment for PwMS, which may result from the disease itself or circumstances related to the workplace. Cognitive symptoms, pain, fatigue, psychiatric disorders, disease severity, mobility/gait impairment are illness-related factors considered as major barriers to employment [50–53]. In addition, jobs requiring long-distance travel, overly stressful work, limited feedback on performance, hostile supervisors, high-temperature level and inflexible work schedules are some working conditions considered difficult for PwMS [53–55]. Moreover, negative work events have been reported as an important barrier. Workers with MS may be particularly vulnerable to verbal reprimands, decrease in scheduled work hours, reduction of job responsibilities, and mandatory additional retraining [26,56–58]. Kordovski et al. and Frindak et al both demonstrated that negative work events may act as an indicator of an increased risk of unemployment in the short and medium term [57,59].

Reported job accommodations and vocational rehabilitation strategies

Job accommodations are associated with greater chances of retaining occupation. The studies considered work accommodations as reasonable adjustments in the workplace or strategies related to professional re-training and vocational rehabilitation. In a study with 746 workers with MS, participants with a progressive course of the disease, cognitive impairment, a higher number of MS symptoms, and greater symptom severity were more likely to use job accommodations [60]. More than 60% of PwMS who kept their jobs described any type of accommodation and adopting flexible hours as the most frequently reported accommodation [26,61,62]. Other common accommodations are the possibility of working from home and availability of memory aids, additional time to complete tasks, preferential parking, written job instructions, and air conditioning [26,56]. Rumrill Jr. et al. listed the use of equipment/assistive technological resources as being of great importance [62].

Dorstyn et al. verified that sending a standardized, mail-delivered, resource-based package to job seekers with MS improved their vocational self-efficacy, optimism, and identity [63]. Chiu et al. examined the effect of rehabilitation technology interventions on job retention and concluded that this kind of technological tool may ensure better occupational outcomes [64]. Vocational rehabilitation is a topic that interests PwMS, a group of people receptive to this type of initiative [65]. According to these subjects, a program of vocational rehabilitation must address two main points: managing work performance and expectations [66].

Job satisfaction, stigma, and disclosing the diagnosis in the workplace

Almost one-third of patients who remain employed are dissatisfied at work [50] and 20% to 30% of workers do not feel comfortable disclosing their diagnosis in the work environment [26,55,59,67]. Approximately 40% of these patients did not inform the occupational physician about their diagnosis [68]. More often, patients with increased disease severity and longer work experience disclosed their diagnosis [59]. A quarter of PwMS report feelings of stigmatization at work. Stigma is directly associated with poorer QoL, work handicap, and depression [41,51,69].

Rating clinical scales

The EDSS and the Multiple Sclerosis Functional Composite (MSFC) scale have both been associated with employability [70]. Andries et al. designed the Work and Handicap Questionnaire (WHQ) aiming to estimate the degree of work handicap in PwMS, neuromuscular diseases, and asthma based on the association of daily life disabilities and job demands [71]. Although it was not specifically created for PwMS, it showed good reliability. Honan et al. developed a shortened version of the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ) that consists of a 23-item measure of self-reported perceived workplace difficulties in PwMS [72]. Schiavolin et al. designed and validated the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job), which demonstrated to be a useful tool for measuring the work-related difficulties in PwMS [73]. Both MSWDQ and MSQ-Job proved to be comprehensive tools for tracking subjective work-related problems, but they could not be compared with objective occupational outcomes$ in a longitudinal perspective and were not validated as a predictive tool of unemployment. McFadden et al. created a 22-item, self-administered scale that indicates if PwMS are at low, medium or high risk of work instability [74]. It was further used in a 3-year longitudinal study aimed at assessing the psychological determinants of job retention [75]. Table 3 summarizes all scales associated with occupational outcomes.

Study	Name	Specific for MS	Specific for work	Longitudinally validated	Usefulness
Andries et al. [71]	Work and Handicap Questionnaire (WHQ)	No	Yes	No	The WHQ makes an inventory of possibly harmful working conditions and of possible strategies to counter health-related work problems by means of the work adjustments.
Gulick et al.[76]	Work Assessment Scale (WAS)	No	Yes	Yes	The WAS evaluates work-impeding and work-enhancing situations and conditions.
Honan et al.[72]	The Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ)	Yes	Yes	No	The MSWDQ measures the workplace difficulties that can predict the necessity of reducing working hours, work withdrawal and expectations in PwMS.
McFadden et al.[74]	MS-specific Work Instability Scale (MS-WIS)	Yes	Yes	No	The MS-WIS indicates low, medium, and high risk of work instability (job retention).
Raggi et al.[73]	Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job)	Yes	Yes	No	The MSQ-Job measures difficulties in work-related tasks.
Honarmand et al.[70]	Multiple Sclerosis Functional Composite (MSFC)	Yes	No	No	The MSFC predicts unemployment.
Busche et al.[44]	EDSS	Yes	No	Yes	The EDSS predicts unemployment.

Table 3. Scales described in the literature associated with occupational outcomes.

5. Discussion

The scientific literature on occupational outcomes and MS is vast. Nevertheless, it is possible to identify some important gaps on this subject. The quality of the scientific evidence in this field is still limited due to a significant lack of longitudinal and interventional studies. No studies have analyzed the evolution of occupational outcomes of PwMS over time, much less the factors that led to an eventual change: there is no scientific evidence that any improvement has occurred in the prevalence of unfavourable occupational outcomes. Indeed, there is no study supporting the hypothesis that a worker with MS in 2022 is not susceptible to the same occupational consequences caused by the disease as 40 years ago. In contrast, over the past 20 years, there have been notable advances in the treatment of MS due to a significant increase in the availability and effectiveness of disease-modifying drugs (DMDs) that, in theory, may have influenced various occupational outcomes [77]. In this scenario, a study that assesses the specific role of DMDs on occupational outcomes is highly encouraged. Likewise, there is a lack of studies that compare the variables related to work based on a geographical perspective (e.g. countries, continents).

Data about occupational outcomes come from different contexts and study designs. In most cases, occupational outcomes are part of the primary objectives of the studies. The geographical distribution of the origin of the studies is uneven and creates a bias in the interpretation of the results. No article defined the term “occupational outcomes” and the definitions of each variable differed substantially. Our scoping review brings the first evidence about the several possibilities of occupational outcomes and shows that it comprises of several possible variables, most of them easily evaluated objectively - such as unemployment or salary reduction. Moreover, the variables described in the literature can be understood as part of a spectrum that comprises potentially reversible outcomes present at the beginning of the illness and outcomes that are generally irreversible and correspond to the end of the occupational career.

The literature is unanimous regarding the MS burden on the economy and public health; indeed, the economic impact of the influence of MS on work has driven several research projects. However, the cost-effectiveness of the new DMDs has not been thoroughly studied, considering both the occupational items and the feasible strategies of professional integration concerning their potential benefit in promoting better occupational outcomes with consequent decrease of the economic impact of MS.

Moreover, despite the literature provides a wide description of possible risk factors and work accommodations for PwMS, little evidence exists concerning the possible protective factors associated with occupational outcomes. Most studies are focused on the aspects related to the disease, and few are dedicated to work-related risk factors. Furthermore, the real role of each type of accommodation in promoting favourable occupational outcomes is still unclear due to a lack of studies providing strong evidence (longitudinal and interventional studies).

Our scoping review identified gaps between the patient's interest in receiving technical guidance on how to improve the occupational outcomes and the degree of evidence on this topic. Few studies were dedicated to identifying strategies capable of promoting job retention, work performance, and even return to work. Moreover, most of the strategies of vocational rehabilitation were studied in small samples of subjects and did not consider the particular characteristics of PwMS. Given the still unsatisfactory unemployment rates among PwMS, vocational rehabilitation may be a valuable complementary resource that deserves further research.

There is also extremely limited evidence related to job satisfaction, stigma, and prejudice in the workplace; in this view, it is important to study these outcomes to gauge an individual's overall level of work adjustment. Furthermore, studying and understanding the reasons for not communicating the diagnosis of MS, including to the occupational physician, should be the first step to promote the worker's full integration.

Only few studies tried to develop a scale associated with the occupational outcomes of PwMS. All the proposed scales described the work handicap or job difficulties in restricted samples and mostly in a cross-sectional design. Most of them revealed to be excessively extensive and complex, which represents a limitation for their wide use in clinical practice. The EDSS is the only scale that has already been associated with occupational outcomes as it generally reflects the severity and progression of the disease. However, this evidence comes from secondary analysis of studies and, despite being simple, the EDSS does not include several other factors already proven to specifically influence the professional outcomes, which can also raise concerns about its sensitivity. The development of a simple and validated scale should be the subject of future studies, as it may represent an easy-to-use tool capable of supporting a more objective and uniform assessment of PwMS by physicians with different backgrounds.

Finally, no study addressed how the new ways of working in the 21st century interfered with the occupational outcomes of PwMS. The nature and the pattern of work have undoubtedly changed in the last 20 years [78] and it is reasonable to imagine that PwMS may find more alternatives and resources to ensure a fruitful professional life. Possibly, technological advances in the workplace may even relativize the concept of work disability. PwMS with the same clinical characteristics can be classified with different degrees of work disability depending on the technological adjustments that help them perform their work. It is reasonable to imagine that a few decades ago, a worker with MS could easily be considered unfit for work, while today's modernisation of types of work and the provision of various technological resources may contribute to delay the definitive endpoint of inability to work.

This is the first scoping review dedicated to the occupational outcomes of PwMS. We highlight that a broad and rigorous search strategy was used to properly include all relevant studies describing the occupational outcomes of MS and promote reliable and accurate results. We applied a range of outcome possibilities that allowed us to accurately understand the evidence related to the impact of MS in the occupational setting. The wide variability of aspects, outcomes, and measures identified motivated the breadth of our methods. This review highlighted several opportunities for new research on the topic. Among the limitations of the study, we did not formally assess the quality of included studies, as we respected the scoping review approach. We could also have missed some data for not including results from the grey literature. Notwithstanding, we intended to disclose the current reality regarding the highest scientific evidence in the field of MS and work and, therefore, the selection of peer-reviewed articles seemed more appropriate. We decided not to use specific terms in our search strategy which may have excluded some articles from our review. Nevertheless, there is an infinite number of possible specific words and synonyms that could be characterised as occupational outcomes so that it would be impossible to cover all the possibilities. Finally, the definitions of each variable changed significantly according to the study, so that, as usually happens with systematic reviews, it was not possible to standardise a definition for each one of them.

6. Conclusions

This is the first scoping review dedicated to the occupational outcomes of PwMS. MS is a chronic neurological disorder that is often associated with disabilities and significant impairment of professional life. Many studies have already been published on the subject and several outcomes have been described. Nevertheless, there are still several issues that deserve further in-depth study by the scientific community in order to match the quality of scientific evidence to the undeniable complexity inherent in this topic.

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Legends

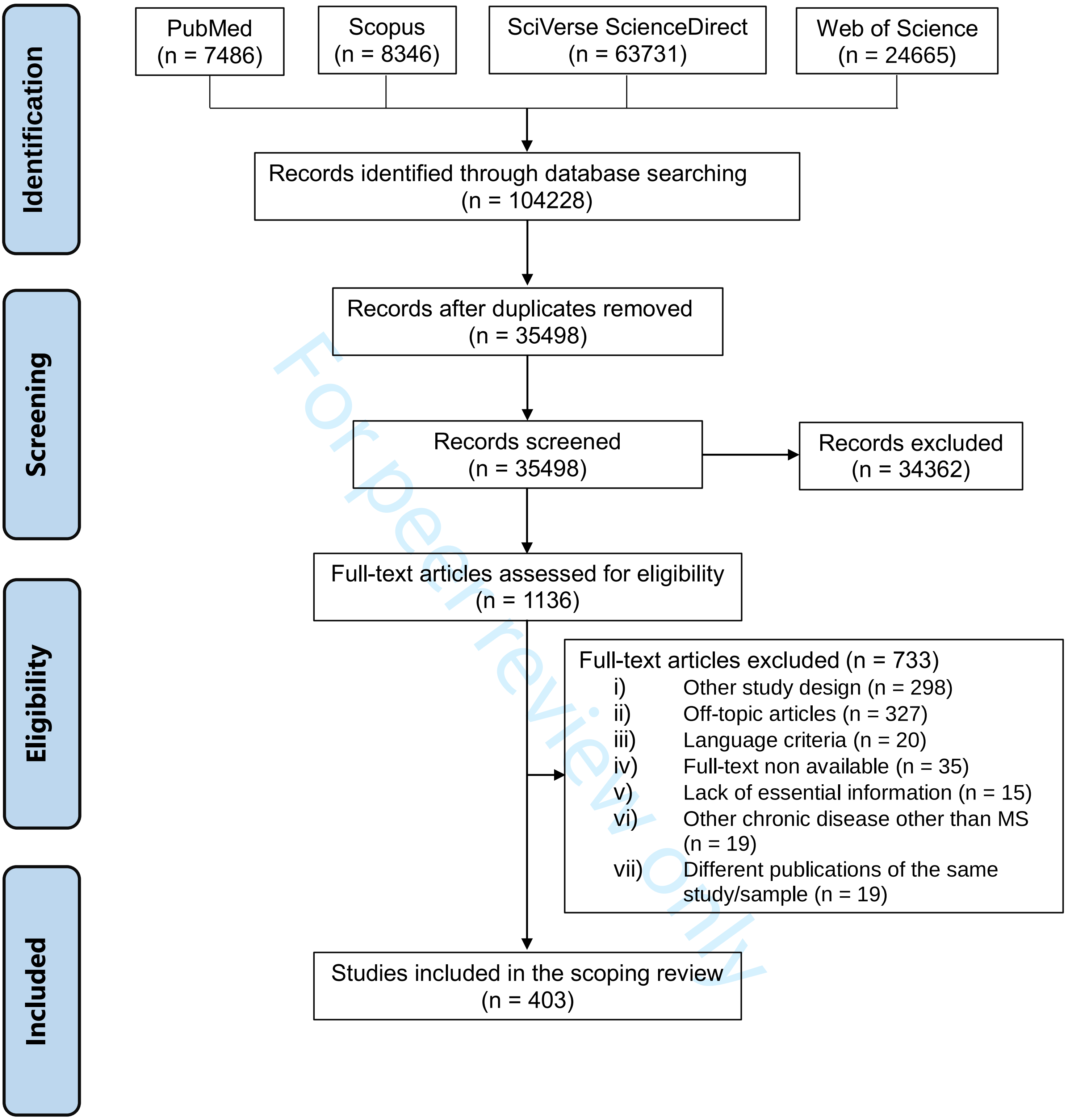
Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Table 3. Scales described in the literature associated with occupational outcomes.

Figure 1. PRISMA flowchart.

Table S1. Complete list of all articles included in the scoping review.


Identification
Screening
Eligibility
Included
PubMed (n = 7486)
Scopus (n = 8346)
SciVerse ScienceDirect (n = 63731)
Web of Science (n = 24665)
Records identified through database searching (n = 104228)
Records after duplicates removed (n = 35498)
Records screened (n = 35498)
Records excluded (n = 34362)
Full-text articles assessed for eligibility (n = 1136)
Full-text articles excluded (n = 733)
i) Other study design (n = 298)
ii) Off-topic articles (n = 327)
iii) Language criteria (n = 20)
iv) Full-text non available (n = 35)
v) Lack of essential information (n = 15)
vi) Other chronic disease other than MS (n = 19)
vii) Different publications of the same study/sample (n = 19)
Studies included in the scoping review (n = 403)

AUTHOR	TITLE	YEAR	COUNTRY
Abbas et al. [1]	Caractéristiques des personnes atteintes d'une sclérose en plaques selon la situation professionnelle	2008	France
Abbasi et al.[2]	Risk factors of Multiple sclerosis and their Relation with Disease Severity: A Cross-sectional Study from Iran	2016	Iran
Abdulla et al.[3]	Factors that influence quality of life in patients with multiple sclerosis in Saudi Arabia	2021	Saudi Arabia
Abdullah et al.[4]	MS People's Performance and Satisfaction With Daily Occupations: Implications for Occupational Therapy	2017	Kuwait
Abolhassani et al. [5]	Social aspects of multiple sclerosis for Iranian individuals	2014	Iran
Ahmad et al.[6]	The increasing economic burden of multiple sclerosis by disability severity in Australia in 2017: Results from updated and detailed data on types of costs	2020	Australia
Ahmadi et al.[7]	Relationship Between Anxiety and Depression with Disability Over Multiple Sclerosis Patients in Rafsanjan, Iran	2018	Iran
Akbar et al.[8]	A mixed-methods study of cognitive performance in persons with multiple sclerosis: Association between neuropsychological test performance and interviews about daily cognitive functioning	2021	Canada
Al-Asmi et al. [9]	Magnitude and concurrence of anxiety and depression among attendees with multiple sclerosis at a tertiary care Hospital in Oman	2015	Oman
Alhussain et al. [10]	Multiple Sclerosis Patients in Saudi Arabia: Prevalence of Depression and its Extent of Severity.	2020	Saudi Arabia
Alosaimi et al. [11]	Psychosocial predictors of patient adherence to disease-modifying therapies for multiple sclerosis	2017	Saudi Arabia
Alsharie et al. [12]	Stressful life events and the risk of primary progressive multiple sclerosis: A population-based case-control study	2021	Iran
Alshubaili et al. [13]	Relationship of depression, disability, and family caregiver attitudes to the quality of life of Kuwaiti persons with multiple sclerosis: a controlled study	2007	Kuwait
AlZahrani et al. [14]	Association of acute stress with multiple sclerosis onset and relapse in Saudi Arabia	2019	Saudi Arabia
Amaducci et al.[15]	Multiple sclerosis among shoe and leather workers: an epidemiological survey in Florence.	1982	Italy
Amato et al.[16]	Cognitive impairment in early-onset multiple sclerosis. Pattern, predictors, and impact on everyday life in a 4-year follow-up.	1995	Italy
Amato et al.[17]	Cognitive Dysfunction in Early-Onset Multiple Sclerosis	2001	Italy

Andries et al.[18]	Working with a chronic disorder--the development of the Work and Handicap Questionnaire.	2004	The Netherlands
Archibald et al. [19]	Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients	1994	Canada
Aronson et al.[20]	Quality of life among persons with multiple sclerosis and their caregivers	1997	Canada
Arroyo et al.[21]	Correlation between spasticity and quality of life in patients with multiple sclerosis: the CANDLE study	2013	Spain
Artemiadis et al.[22]	Structural MRI correlates of cognitive function in multiple sclerosis	2018	Greece
Babamohamadi et al. [23]	Dimensions of Adaptation, General Health, and life Satisfaction in Multiple Sclerosis	2016	Iran
Bamer et al.[24]	Validation study of prevalence and correlates of depressive symptomatology in multiple sclerosis.	2008	United States
Barin et al.[25]	Patterns of care for Multiple Sclerosis in a setting of universal care access: A cross-sectional study	2019	Switzerland
Baroin et al.[26]	Validation of a new quality of life scale related to multiple sclerosis and relapses.	2013	France
Barzegar et al.[27]	Comparative study of quality of life, anxiety, depression, and fatigue among patients with neuromyelitis optica spectrum disorder and multiple sclerosis: The first report from Iran	2018	Iran
Bass et al.[28]	Effect of Multiple Sclerosis on Daily Activities, Emotional Well-being, and Relationships: The Global vsMS Survey.	2020	Europe
Battaglia et al. [29]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Italy	2017	Italy
Baughman et al. [30]	Staying on the job: The relationship between work performance and cognition in individuals diagnosed with multiple sclerosis	2015	US
Baumstarck et al. [31]	Health-related quality of life as an independent predictor of long-term disability for patients with relapsing–remitting multiplesclerosis-remittingmultiplesclerosis:A2-yearlongitudinalstudy	2013	France
Baumstarck et al. [32]	Is the Concept of Quality of Life Relevant for Multiple Sclerosis Patients with Cognitive Impairment? Preliminary Results of a Cross-Sectional Study	2012	France
Bayas et al.[33]	Combination treatment of fingolimod with antidepressants in relapsing–remitting multiple sclerosis patients with depression: a multicentre, open-label study – REGAIN	2016	Germany
Beatty et al.[34]	Demographic, Clinical, and Cognitive Characteristics of Multiple Sclerosis Patients Who Continue to Work	1995	US
Beatty et al.[35]	Changes in neuropsychological test performance over the workday in multiple sclerosis	2003	US/Italy

Becker et al.[36]	Patient satisfaction and healthcare services in specialized multiple sclerosis centres in Germany	2018	Germany
Beier et al.[37]	Relationship of perceived stress and employment status in individuals with multiple sclerosis.	2019	US
Benedict et al.[38]	Predicting neuropsychological abnormalities in multiple sclerosis	2006	US
Benedict et al.[39]	Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change	2005	US
Benedict et al.[40]	Negative work events and accommodations in employed multiple sclerosis patients.	2013	US
Berg et al.[41]	Costs and quality of life of multiple sclerosis in Sweden.	2006	Sweden
Bessing et al.[42]	Changes in multiple sclerosis symptoms are associated with changes in work productivity of people living with multiple sclerosis	2021	Australia
Birnbaum et al.[43]	Economic impact of multiple sclerosis disease-modifying drugs in an employed population: direct and indirect costs	2008	US
Bishop et al. [44]	The relationship between housing accessibility variables and employment status among adults with multiple sclerosis	2013	US
Bishop et al. [45]	Employment Among Working-Age Adults With Multiple Sclerosis: A Data-Mining Approach to Identifying Employment Interventions	2015	US
Bishop et al. [46]	Life domains that are important to quality of life for people with multiple sclerosis: A population-based qualitative analysis	2019	US
Bishop et al. [47]	Sources of information about multiple sclerosis: Information seeking and personal, demographic, and MS variables	2009	US
Bishop et al. [48]	The relationship of self-management and disease modifying therapy use to employment status among adults with multiple sclerosis	2009	US
Bishop et al. [49]	Quality of life among people with multiple sclerosis: Replication of a three-factor prediction model	2015	US
Björkenstam et al.[50]	Heterogeneity of sickness absence and disability pension trajectories among individuals with MS	2015	Sweden
Björkenstam et al.[51]	Is disability pension a risk indicator for future need of psychiatric healthcare or suicidal behavior among MS patients- a nationwide register study in Sweden?	2015	Sweden
Blinkenberg et al.[52]	Increased socioeconomic burden in patients with primary progressive multiple sclerosis: A Danish nationwide population-based study	2020	Denmark

Bo et al.[53]	Access to social security benefits among multiple sclerosis patients in Italy: A cross-sectional study.	2018	Italy
Bøe Lunde et al.[54]	Employment among Patients with Multiple Sclerosis-A Population Study	2014	Norway
Bonafede et al. [55]	Productivity Loss and Associated Costs Among Employed Patients Receiving Disease-Modifying Treatment for Multiple Sclerosis	2021	US
Boyko et al.[56]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Russia	2017	Russia
Broersma et al.[57]	The impact of self-perceived limitations, stigma and sense of coherence on quality of life in multiple sclerosis patients: results of a cross-sectional study.	2018	The Netherlands
Brook et al.[58]	Absenteeism and health-benefit costs among employees with MS.	2009	US
Brown et al.[59]	Societal costs of primary progressive multiple sclerosis in Australia and the economic impact of a hypothetical disease-modifying treatment that could delay disease progression.	2021	Australia
Brown et al.[60]	Longitudinal assessment of anxiety, depression, and fatigue in people with multiple sclerosis	2009	Australia
Brundin et al.[61]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Sweden	2017	Sweden
Bruno et al.[62]	Economic burden of multiple sclerosis in France estimated from a regional medical registry and national sick fund claims	2019	France
Buchanan et al. [63]	Informal care giving to more disabled people with multiple sclerosis	2008	US
Buchanan et al. [64]	A Pilot Study of Latinos With Multiple Sclerosis: Demographic, Disease, Mental Health, and Psychosocial Characteristics	2011	US
Bueno et al.[65]	Health-related quality of life in patients with longstanding 'benign multiple sclerosis'	2015	Canada
Buhse et al.[66]	Factors Associated with Health-Related Quality of Life Among Older People with Multiple Sclerosis	2014	US
Busche et al.[67]	Short term predictors of unemployment in multiple sclerosis patients.	2003	Canada
Butepage et al.[68]	Cost-of-illness trajectories among people with multiple sclerosis by comorbidity: A register-based prospective study in Sweden	2020	Sweden
Buzgova et al.[69]	Factors Influencing Health-Related Quality of Life of Patients with Multiple Sclerosis and Their Caregivers	2020	Czech Republic
Buzgova et al.[70]	Satisfaction of Patients With Severe Multiple Sclerosis and Their Family Members With Palliative Care: Interventional Study	2020	Czech Republic

Cadden et al.[71]	Factors associated with employment status in individuals with multiple sclerosis: Cognition, fatigue, and motor function	2015	US
Calabrese et al. [72]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Switzerland.	2017	Swizerland
Calandri et al.[73]	Improving the quality of life and psychological well-being of recently diagnosed multiple sclerosis patients: preliminary evaluation of a group-based cognitive behavioral intervention	2017	Italy
Calandri et al.[74]	Young adults' adjustment to a recent diagnosis of multiple sclerosis: The role of identity satisfaction and self-efficacy	2019	Italy
Cambier-Langrand et al. [75]	Impact socio professionnel précoce de la sclérose en plaques : une étude prospective d'une série de 24 patients	2016	France
Campbell et al.[76]	Cognitive impairment among patients with multiple sclerosis: associations with employment and quality of life	2016	UK
Campbell et al.[77]	Burden of multiple sclerosis on direct, indirect costs and quality of life: National US estimates.	2014	US
Carnero Contentti et al. [78]	Impact of multiple sclerosis on quality of life: Comparison with systemic lupus erythematosus	2017	Argentina
Carnero Contentti et al. [79]	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Carney et al.[80]	Societal costs of multiple sclerosis in Ireland.	2018	Ireland
Carrieri et al.[81]	Determinants of on-the-job-barriers in employed persons with multiple sclerosis: The role of disability severity and cognitive indices	2014	Italy
Casado et al. [82]	Direct costs of relapses in patients with relapsing-remitting multiple sclerosis	2021	Spain
Casado et al. [83]	Direct and indirect costs of Multiple Sclerosis in Baix Llobregat (Catalonia, Spain), according to disability	2006	Spain
Castelo-Branco et al. [84]	Clinical course of multiple sclerosis and labour-force absenteeism: a longitudinal population-based study.	2019	Sweden
Catanzaro et al.[85]	Economic status of families living with multiple sclerosis.	1992	USA
Cattaneo et al.[86]	Participation Restriction in People With Multiple Sclerosis: Prevalence and Correlations With Cognitive, Walking, Balance, and Upper Limb Impairments	2017	Italy/Belgium
Cervera-Deval et al.[87]	Social handicaps of multiple sclerosis and their relation to neurological alterations	1994	Spain

Chamot et al.[88]	Item response theory-based measure of global disability in multiple sclerosis derived from the Performance Scales and related items.	2014	USA
Chen et al. [89]	Risk factors of leaving employment due to multiple sclerosis and changes in risk over the past decades: survival analysis with competing risks	2019	Australia
Chen et al. [90]	Effects of multiple sclerosis disease-modifying therapies on employment measures using patient-reported data.	2018	Australia
Chen et al. [91]	Estimating MS-related work productivity loss and factors associated with work productivity loss in a representative Australian sample of people with multiple sclerosis.	2019	Australia
Chen et al.[92]	Impact of depression, fatigue and disability on quality of life in Chinese patients with multiple sclerosis.	2013	China
Chiu et al.[93]	Descriptive analysis of free-text comments on healthcare priorities and experiences in a national sample of people with multiple sclerosis.	2019	USA
Chiu et al.[94]	Effect of Rehabilitation Technology Services on Vocational Rehabilitation Outcomes of Individuals With Multiple Sclerosis	2015	USA
Chiu et al.[95]	Motivational and Volitional Variables Associated With Stages of Change for Exercise in Multiple Sclerosis: A Multiple Discriminant Analysis	2012	USA
Chiu et al.[96]	State vocational rehabilitation services and employment in multiple sclerosis.	2013	USA
Chiu et al.[97]	Employment as a health promotion intervention for persons with multiple sclerosis.	2016	USA
Chruzander et al.[98]	A 10-year follow-up of a population-based study of people with multiple sclerosis in Stockholm, Sweden: Changes in disability and the value of different factors in predicting disability and mortality	2013	Sweden
Chruzander et al.[99]	Longitudinal changes in sickness absence and disability pension, and associations between disability pension and disease-specific and contextual factors and functioning, in people with multiple sclerosis.	2016	Sweden
Chwastiak et al.[100]	Fatigue and psychiatric illness in a large community sample of persons with multiple sclerosis.	2005	USA
Cioncoloni et al.[101]	Individual factors enhance poor health-related quality of life outcome in multiple sclerosis patients. Significance of predictive determinants.	2014	Italy
Clingerman et al.[102]	The Influence of Resources on Perceived Functional Limitations Among Women with Multiple Sclerosis	2004	USA
Cofield et al.[103]	Shared Decision Making and Autonomy Among US Participants with Multiple Sclerosis in the NARCOMS Registry.	2017	USA

Coleman et al.[104]	Impact of mobility impairment on indirect costs and health-related quality of life in multiple sclerosis.	2013	USA
Concetta Incerti et al. [105]	Occupational stress and personality traits in multiple sclerosis: A preliminary study	2015	Italy
Conradsson et al.[106]	Changes in disability in people with multiple sclerosis: a 10-year prospective study.	2018	Sweden
Conradsson et al.[107]	Activity limitations and participation restrictions in people with multiple sclerosis: a detailed 10-year perspective.	2021	Sweden
Conradsson et al.[108]	Employment status of people with multiple sclerosis in relation to 10-year changes in functioning and perceived impact of the disease.	2020	Sweden
Contentti et al.[109]	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Cores et al.[110]	Work status and cognitive performance in patients with relapsing remitting multiple sclerosis	2019	Argentina
Costa et al.[111]	Social support network and quality of life in multiple sclerosis patients.	2017	Portugal
Cowan et al.[112]	Psychosocial aspects of the lived experience of multiple sclerosis: personal perspectives	2018	Australia
da Silva et al.[113]	Cost analysis of multiple sclerosis in Brazil: a cross-sectional multicenter study	2016	Brazil
Dayapoglu et al.[114]	Quality of life in relapsing-remitting multiple sclerosis	2011	Pakistan
Dehghan et al.[115]	Occupational performance of individuals with Multiple Sclerosis based on disability level in Iran.	2019	Iran
Devins et al.[116]	Differences in illness intrusiveness across rheumatoid arthritis, end-stage renal disease, and multiple sclerosis	1993	Canada
D'hooghe et al.[117]	Self-reported levels of education and disability progression in multiple sclerosis.	2016	Belgium/The Netherlands
D'hooghe et al.[118]	Perceived neuropsychological impairment inversely related to self-reported health and employment in multiple sclerosis	2019	Belgium
Dorstyn et al.[119]	Piloting an email-based resource package for job seekers with multiple sclerosis.	2017	Australia
Dorstyn et al.[120]	Online Resource to Promote Vocational Interests Among Job Seekers With Multiple Sclerosis: A Randomized Controlled Trial in Australia.	2018	Australia
Dubois et al.[121]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Belgium.	2017	Belgium
Dusankova et al.[122]	Cost of multiple sclerosis in the Czech Republic: the COMS study.	2012	Czech Republic

Earnshaw et al.[123]	Cost effectiveness of glatiramer acetate and natalizumab in relapsing-remitting multiple sclerosis.	2009	USA
Esposito et al.[124]	Lifestyle and Mediterranean diet adherence in a cohort of Southern Italian patients with Multiple Sclerosis	2021	Italy
Estrutti et al.[125]	Employment status of people diagnosed with multiple sclerosis in Brazil.	2019	Brazil
Fantoni-Quinton et al.[126]	Impact of multiple sclerosis on employment and use of job-retention strategies: The situation in France in 2015.	2016	France
Farnoush et al.[127]	Educational, psycho mental and socio economical needs of an Iranian cohort with multiple sclerosis	2010	Iran
Farran et al.[128]	Quality of life and coping strategies in Lebanese Multiple Sclerosis patients: A pilot study	2016	Lebanon
Fernandez et al.[129]	Patient characteristics and determinants of quality of life in an international population with multiple sclerosis: Assessment using the MusiQoL and SF-36 questionnaires	2011	Europe
Fernandez-Jimenez et al.[130]	Quality of Life and Depressive Symptomatology in Multiple Sclerosis: A Cross-Sectional Study Between the USA and Spain	2021	USA/Spain
Fidao et al.[131]	Depression mediates the relationship between fatigue and mental health-related quality of life in multiple sclerosis	2021	Australia
Finlayson et al.[132]	Self-care, productivity and leisure limitations of people with multiple sclerosis in Manitoba	1998	Canada
Flachenecker et al.[133]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Germany.	2017	Germany
Flensner et al.[134]	Work capacity and health-related quality of life among individuals with multiple sclerosis reduced by fatigue: A cross-sectional study	2013	Sweden
Fogarty et al.[135]	Direct and indirect economic consequences of multiple sclerosis in Ireland.	2014	Ireland
Forbes et al.[136]	Health problems and health-related quality of life in people with multiple sclerosis.	2006	UK
Ford et al. [137]	Health status and quality of life of people with multiple sclerosis.	2001	UK
Forslin et al.[138]	Predictors for Employment Status in People With Multiple Sclerosis: A 10-Year Longitudinal Observational Study	2018	Sweden
Fragoso et al.[139]	The effect of multiple sclerosis on the professional life of a group of Brazilian patients.	2010	Brazil
Fraser et al.[140]	Vocational rehabilitation in multiple sclerosis (MS): a profile of clients seeking services.	2003	USA
Fraser et al.[141]	Predictors of vocational stability in multiple sclerosis	2009	USA

Freedman et al.[142]	Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: a case-control study based on death certificates.	2000	USA
Frndak et al.[143]	Negative work events reported online precede job loss in multiple sclerosis	2015	USA
Frndak et al.[144]	Disclosure of disease status among employed multiple sclerosis patients: association with negative work events and accommodations	2015	USA
Fuchs et al.[145]	Response heterogeneity to home-based restorative cognitive rehabilitation in multiple sclerosis: An exploratory study.	2019	USA
Garcia-Dominguez et al.[146]	Economic burden of multiple sclerosis in a population with low physical disability	2019	Spain
Genevie et al.[147]	Job Retention Among People with Multiple Sclerosis	1987	USA
Ghaffar et al.[148]	Occupational attainment as a marker of cognitive reserve in multiple sclerosis.	2012	Canada
Gil-Gonzàlez et al.[149]	Predicting improvement of quality of life and mental health over 18-months in multiple sclerosis patients	2021	Spain
Gill et al.[150]	Disclosing a Diagnosis in the Workplace: Perspective of People with Multiple Sclerosis	2021	Ireland
Gill et al.[151]	Depressive Symptoms Are Associated With More Negative Functional Outcomes Than Anxiety Symptoms in Persons With Multiple Sclerosis.	2019	Canada
Giordano et al.[152]	Low quality of life and psychological wellbeing contrast with moderate perceived burden in carers of people with severe multiple sclerosis.	2016	Italy
Giovannetti et al.[153]	Individualized quality of life of severely affected multiple sclerosis patients: practicability and value in comparison with standard inventories	2016	Italy
Giovannetti et al.[154]	Conversion to secondary progressive multiple sclerosis: Multi stakeholder experiences and needs in Italy	2020	Italy
Giovannetti et al.[155]	Cognitive function alone is a poor predictor of health-related quality of life in employed patients with MS: results from a cross-sectional study	2016	Italy
Glanz et al.[156]	Work productivity in relapsing multiple sclerosis: associations with disability, depression, fatigue, anxiety, cognition, and health-related quality of life.	2012	USA
Göksel Karatepe et al.[157]	Quality of life in patients with multiple sclerosis: the impact of depression, fatigue, and disability	2011	Spain
Gordon et al.[158]	Employment issues and knowledge regarding ADA of persons with multiple sclerosis	1997	USA
Gottberg et al.[159]	Health-related quality of life in a population-based sample of people with multiple sclerosis in Stockholm County.	2006	Sweden

Goverover et al.[160]	The relationship among performance of instrumental activities of daily living, self-report of quality of life, and self-awareness of functional status in individuals with multiple sclerosis.	2009	USA
Gracia et al.[161]	Costs of multiple sclerosis in Panama from societal, patient perspectives and health-related quality of life	2018	USA
Graham et al.[162]	Barriers and facilitators to employment as reported by people with physical disabilities: An across disability type analysis	2018	USA
Gregory et al.[163]	Employment and multiple sclerosis in New Zealand.	1993	New Zealand
Grima et al.[164]	Cost and health related quality of life consequences of multiple sderosis	2000	Canada
Gross et al.[165]	Characteristics, burden of illness, and physical functioning of patients with relapsing-remitting and secondary progressive multiple sclerosis: a cross-sectional US survey.	2017	USA
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Heredia-Torres et al.[183]	Occupational performance in multiple sclerosis and its relationship with quality of life and fatigue	2020	Spain
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Horwitz et al.[187]	Effect of occupation on risk of developing MS: an insurance cohort study.	2013	Denmark
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Kobelt et al.[238]	Costs and quality of life of multiple sclerosis in Switzerland.	2006	Switzerland
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Kobelt et al.[240]	Costs and quality of life of multiple sclerosis in the United Kingdom.	2006	UK
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Koch et al.[245]	Illness and demographic correlates of quality of life among people with multiple sclerosis	2001	USA
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Pfleger et al.[325]	Social consequences of multiple sclerosis: clinical and demographic predictors - a historical prospective cohort study.	2010	Denmark
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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3, 4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	5
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5, 6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5, 6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7, 8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	7, 8
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	8-12
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	8-12
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	12-15
Limitations	20	Discuss the limitations of the scoping review process.	15
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	1

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

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Occupational outcomes of people with Multiple Sclerosis: a scoping review

Bruno Kusznir Vitturi[1], Alborz Rahmani[1,2], Guglielmo Dini[1,2], Alfredo Montecucco[1,2], Nicoletta Debarbieri[2], Elvira Sbragia[3,4], Paolo Bandiera[5], Michela Ponzio[6], Mario Alberto Battaglia[6,7], Tommaso Manacorda[5], Benedetta Persechino[8], Giuliana Buresti[8], Matilde Inglese[3,4], Paolo Durando[1,2]

1. Department of Health Sciences, University of Genoa, Italy
2. IRCCS Ospedale Policlinico San Martino, Occupational Medicine Unit, Genoa, Italy
3. Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI) and Center of Excellence for Biomedical Research (CEBR), University of Genoa, Genoa, Italy
4. IRCCS Ospedale Policlinico San Martino, Genoa, Italy
5. Italian Multiple Sclerosis Association (AISM)
6. Scientific Research Area, Italian Multiple Sclerosis Foundation (FISM), Italy
7. Department of Life Science, University of Siena, Siena, Italy
8. Italian Workers' Compensation Authority (INAIL)

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Corresponding author

Bruno Kusznir Vitturi, MD

Department of Health Sciences, University of Genoa, Italy

Building 3, L.go R. Benzi 10 - 16132 Genoa, Italy

E-mail: z_azul@hotmail.com

Abstract

Objectives. To update the knowledge on the occupational outcomes associated with Multiple Sclerosis (MS), systematically examine the extent, scope, and nature of the pre-existing literature, and identify research gaps in the existing literature.

Design. Scoping review.

Data sources. A comprehensive database search of PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science was performed. There were no time limits.

Eligibility criteria. We included any peer-reviewed original article reporting the occupational outcomes of people with MS between the ages of 18 and 65 years. We excluded those off-topic and with insufficient information.

Methods. This review was conducted following the JBI recommendations and the PRISMA-ScR flowchart. Screening, reading of full-texts and data extraction was performed in a standardized way by expert reviewers from July 14, 2021, to October 31, 2021. We provided a narrative synthesis and an overview of findings.

Results. The initial systematic search yielded 104,228 results. After removing duplicates and applying the exclusion criteria, 403 articles were included in the review. In total, the studies evaluated 492,062 subjects with MS. One hundred fifty-four (38.2%) articles were published in the last 5 years, mostly from Europe and North America (50.9% and 33.0%, respectively). Concerning the occupational outcomes, studies mostly addressed unemployment (311, 77.2%), early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). The results were categorised into 7 subtopics: “Changes in work and occupational status due to MS”, “work-related socio-economic consequences of MS”, “risk factors for unfavourable occupational outcomes”, “reported barriers to employment”, “reported job accommodations and vocational rehabilitation strategies", "job satisfaction, stigma, and disclosing the diagnosis in the workplace" and "rating clinical scales".

Conclusions. There are several issues that deserve further in-depth study by the scientific community in order to improve the occupational outcomes of people with MS.

Keywords

Multiple sclerosis; occupational & industrial medicine; public health; health economics; epidemiology; neurology

Strengths and limitations of this study

- The scoping design allowed a summary of the diverse/heterogeneous range of terms and conceptualisations or even the multidimensional relationship of work and MS.
- All original peer-reviewed articles included were reviewed by our research group.
- As we respected the scoping review approach, we did not formally assess the quality of included studies.
- We could have missed some data for not including results from the grey literature.

1. Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disease that causes demyelination and neurodegeneration in the central nervous system. It mainly affects young people between 20 and 40 years of age and it is the main cause of non-traumatic disability among young adults in the Western world [1]. MS is a global disease, affects 2.5 million people worldwide, the incidence and prevalence are known to be increasing in both developed and developing countries [2]. The symptoms are extremely varied and the clinical course is within a spectrum that extends from relapsing-remitting to progressive [1-3].

In addition to the inherent clinical complexity of MS, the age of onset of the disease brings inevitable repercussions to work activity, as it often coincides with the moment in which patients find themselves managing the already expected difficulties of the job market and the beginning of the professional career [4]. As long as MS symptoms remain 'invisible', people with MS (PwMS) are reluctant to inform their employer about their disease out of fear of losing their job [4]. Concerns about disclosing the diagnosis in the workplace stem from a range of issues involving the fear of appearing vulnerable, suffering discrimination and losing their jobs. [5]. PwMS often require essential accommodations in the work environment to continue providing satisfactory work. Often limiting and disabling, symptoms such as fatigue, neuropsychiatric impairment, and motor disturbances constantly threaten the full performance at work and the search for new professional skills. PwMS are more vulnerable to unemployment and early retirement and the influence of MS on professional life is known to be directly associated with quality of life (QoL) [6].

The impact of MS on work activities has already been evaluated in many studies carried out in different parts of the world [7–10]. Calabrese et al. demonstrated that workforce participation can decline from 82% to 8% and employment rates vary between 31% and 65% [7], being influenced by

factors such as the degree of disability, the duration of disease, the level of education and the type of work activity. Another study outlined the complexity of the association between employment and MS and revealed that 56.2% of PwMS are unemployed and face great difficulty in returning to the workforce [8].

Besides the potential consequences of MS for people's working life, it is also important to recognize the impact of the disease at the community level. Long-term absence, invalidity, and early retirement may demand an annual expense of 17,945€ per patient in the late stages of MS [11]. Loss of productivity at work and occupation change due to MS account for an annual cost of $2,691 and $2,982 for each patient, respectively [12]. Indeed, the impact of MS on occupational outcomes is responsible for a significant economic burden and represents a matter of public health all around the world.

There is an eminent need for further scientific research on the occupational outcomes of PwMS. Furthermore, research in this area is highly encouraged as it contributes to address the eighth Sustainable Development Goal set up by the United Nations. Although it is relatively easy to find information on MS and work in the literature, being diagnosed with MS still increases the risk of unemployment, early retirement, loss of working capacity, reduced monthly income, job dissatisfaction and impaired QoL. Recent advances in the treatment of MS and the emergence of new types and modalities of work also call for new studies investigating the role of MS on work. Moreover, previous reviews were focused on specific occupational outcomes that do not reflect the totality of possible outcomes, contributing only partially to the holistic understanding of the relationship between MS and work [13–17]. Due to the large number and heterogeneity of articles already published, there is a significant difficulty in detecting gaps in the pre-existing literature and consolidating evidence on the subject. This scenario favours unnecessary investments in redundant studies that could be reallocated to research with potential to truly influence patients' lives. In this context, we decided to conduct the first scoping review related to the occupational outcomes of PwMS, as it can provide a broad map of the existing evidence and identify gaps for potential future studies.

2. Objectives

The objectives of the present scoping review are related to occupational outcomes associated with MS: the primary objective is to update the knowledge on the occupational outcomes of PwMS compared with people without MS, and among PwMS by clinical characteristics. Our secondary objectives were to systematically examine the extent, scope, and nature of the pre-existent literature, to summarize and disseminate the research results deriving from the already published articles, to identify research gaps in the existing literature and to provide an accurate rationale to develop further relevant research in the area.

3. Methods

We performed this scoping review following the guidelines outlined by Arksey and O'Malley, the Joanna Briggs Institute recommendations, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for scoping review (PRISMA-ScR) guidelines [18–20]. As this was a literature review, it did not involve the recruitment of subjects and it analysed data from already published original articles and, therefore, the ethical approval was not necessary.

3.1. Study selection/search strategy

From July 14, 2021, to July 31, 2021, we systematically searched on PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science the following keywords (employ* OR unemploy* OR occupation* OR “work” OR vocation* OR “work resumption” OR workplace* OR “return to work” OR “work force” OR “workforce” OR “labour force” OR “labor force” OR career* OR job* OR “job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "disseminated sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating"). The details of the search strategy used are reported in Table 1. We decided not to include specific terms due to the expected diversity in concepts and terms related to the central argument of the study. Furthermore, this choice is supported by the traditional scoping review methodology. After the preliminary identification, the articles were exported and managed in Mendeley 1.19.8 (Elsevier, New York, USA).

PubMed	(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")
Scopus	TITLE-ABS KEY [(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune Diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")]
SciVerse Science Direct	("employ" OR "occupation" OR "work" OR "vocation" OR "labour" OR "Job" OR "retire" OR "disability pension") AND "multiple sclerosis"
Web of Science	(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")

Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

3.2. Inclusion and exclusion criteria

A priori, we chose a broad search methodology to be able to form an accurate and comprehensive picture of the relationship between the occupational outcomes and MS. The PCC (Population/Concept/Context) framework was used to define inclusion criteria. We included any peer-reviewed original article reporting the occupational outcomes of PwMS between the ages of 18 and 65 years (population). MS must have been diagnosed according to accepted international criteria at the time of the study. No time limits were set for the search. The context was broad and we accepted articles published in English, Italian, Spanish, French, and Portuguese, as these are the languages spoken in our research group (context). The term “occupational outcomes” was defined as direct and indirect work-related characteristics/consequences potentially associated with MS (concept).

After removing duplicate entries, we performed an initial screening of titles and abstracts to assess potential relevance and excluded those not directly or indirectly focused on the topic of interest. Screening of titles, abstracts, and full texts for each article was conducted by two experienced and trained investigators (BKV and AR), each blinded to the other’s ratings. In case of discrepancy, a final decision was made by a consensus after a debate with a senior researcher (GD). Afterward, we obtained relevant full-text articles, read all of them, evaluated their eligibility, and determined their final inclusion or exclusion.

Studies written in languages other than the five pre-specified above and studies designed as reviews, letters to the editor, expert opinions, commentaries, case reports, case series, editorials were excluded. Studies that did not address any aspect of an occupational outcome or that eventually only mentioned it as part of the arguments presented in the introduction or discussion (off-topic articles) were excluded. In case of lack of essential information or full-text not being available, we tried to contact the corresponding author twice to obtain the information by email. Whenever our contact attempt failed, the study was excluded. We did not accept studies where MS was not the primary condition or the subjects had other chronic diseases that could potentially influence the occupational outcomes (e.g. a study that included patients with MS and migraine). Some authors published more than one article with the same study population and reporting the same occupational outcomes. In these cases, we included the most recent one and excluded the others. Figure 1 provides the PRISMA flowchart overview of the search and screening strategy performed.

3.3. Data extraction

Data were extracted in a standardized way by an expert reviewer (BKV) and they were double-checked after two months in order to minimise the intrapersonal variability. We determined the information to extract *a priori*. Among the basic characteristics, we gathered information about the authors' names, the title of the study, the year of publication, the country of origin of the study, the study design, the number of subjects with and without MS, the subtype of the disease, the prevalence of each clinical symptom, the duration of the disease, the distribution by age and sex, the level of education, the marital status, the description of any neuroradiological finding, treatment data, assessment of the QoL and disability, prevalence of fatigue, psychiatric symptoms, and cognitive symptoms. Regarding the occupational outcomes, the following data were collected: the description of the profession, the prevalence of unemployment and early retirement, the influence of the disease on monthly income, the need for disability pension, the indirect cost of MS, the stigma and prejudice faced in the workplace, job characteristics, strategies of vocational rehabilitation and job accommodations, patient opinion on work and working life in general, barriers to employment, degree of job satisfaction, need for a change of employment due to MS, the prevalence of work handicap and information on the disclosure of the diagnosis in the workplace. Job accommodations were defined as any reasonable adjustment to a job or work environment that enables PwMS to perform their job duties. Barriers to employment were defined as any challenge or difficulty that may prevent PwMS from getting or keeping a job, or advancing in their career. Sick leave is characterized as when the absence is granted because of illness. Usually it takes many days and are due to a specific necessity provoked by the illness. Absenteeism refers to the habitual non-presence of an employee at their job that is not formally justified to the employer or linked to the illness. Usually it takes just a couple of days but may be more frequent.

3.4. Data synthesis

Following data extraction, due to the range of outcomes assessed and different study designs included in the review, we used a narrative synthesis to report data. This process was carried out after reading the full-text of all the articles included in the review in order to summarize the results as clearly and accurately as possible and cover all the outcomes found. One expert reviewer (BKV) performed a thematic categorization of the findings, which was verified by two other reviewers (AR and AM). The results were categorised into 7 subtopics: “Changes in work and occupational status due to MS”, “work-related socio-economic consequences of MS”, “risk factors for unfavourable occupational outcomes”, “reported barriers to employment”, “reported job accommodations and vocational rehabilitation strategies”, “job satisfaction, stigma, and disclosing the diagnosis in the workplace” and “rating clinical scales”. These subgroups were created to guide the synthesis of the main results reported in the pre-existing literature. We generated a set of statements to adequately represent each subtopic, based on their relevance and degree of evidence.

3.5. Patient and public involvement

No patients or public were involved in the study.

4. Results

Overview of the literature search

The initial systematic search yielded 104,228 results, of which 7,486 were from PubMed, 8,346 were from Scopus, 63,731 were from SciVerse Science Direct 24,665 were from Web of Science. Removing duplicates and applying the eligibility criteria resulted in a total of 1,136 articles. At the end of the study selection, 403 articles were included in the review, and information about the baseline clinical-epidemiological characteristics and the occupational outcomes was properly extracted (Table S1). Figure 1 describes the entire PRISMA-ScR flowchart.

Characteristics of the included literature

The number of studies published on the topic has increased over time, as 154 (38.2%) of the included studies were published in the last 5 years. Most of the studies were conducted in Europe and North America (50.9% and 33.0%, respectively). Asia and Oceania produced 32 (7.9%) and 24 (6.0%) of the studies on the subject, respectively. There were no published data on the association between MS and work from the African continent. Italy, with less than 1% of the world population, promoted the publication of 29 (7.2%) articles on the subject of our study. Regarding the study design, 314 (77.9%) were cross-sectional, 12 (3.0%) were interventional, and 77 (19.1%) were longitudinal. Only 63 (15.6%) studies included a control group in their analysis. In total, the 403 studies evaluated 492,062 subjects with MS. Among the explored characteristics of MS, the assessment of disability and QoL, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms were the most mentioned variables (Table 2). Neuroimaging data and the use of disease-modifying drugs (DMDs) were explored in 10 (2.5%) and 117 (29.0%) studies, respectively.

Clinical and demographic characteristics			**Occupational outcomes**		
	n	%		n	%
Age	394	97.8	Job description	55	13.6
Sex	389	96.5	Work performance	57	14.1
Educational level	288	71.5	Vocational rehabilitation	19	4.7
Civil status	180	44.7	Unemployment	311	77.2
Socioeconomic conditions	47	11.7	Early retirement	120	29.8
EDSS	212	52.6	Disability pension	117	29.3
Disease duration	274	68.0	Sick leave	77	19.1
Type of MS	258	64.0	Impact on monthly income	52	12.9

Neuroimaging findings	10	2.4	Indirect cost of MS	85	21.1
Description of symptoms	59	14.6	Work characteristics	57	14.1
Quality of Life	139	34.4	Barriers to employment	65	16.1
Disability assessment	234	58.1	Job accommodations	45	11.2
Fatigue	169	41.9	Stigma and prejudice	23	5.7
Psychiatric symptoms	209	51.9	Job satisfaction	19	4.7
Cognitive symptoms	160	39.7	**Disclosure** of the diagnosis in the workplace	17	4.2
Motor symptoms	84	20.8	Professional absenteeism	74	18.4
Treatment (DMDs)	117	29.0	Patients' opinion about work	85	21.9
			Occupational change	78	19.3
			Work **disability**	38	9.4

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Work was considered as a dependent variable in 285 (70.7%) articles. Eighty-two (28.8%) studies dealt with the description of employment outcomes, 85 (29.8%) aimed to assess the economic impact of MS, 14 (4.9%) described any strategy of vocational rehabilitation, 17 (6.0%) evaluated the QoL in MS in general, 81 (28.4%) determined possible risk factors associated with occupational outcomes and 6 (2.1%) aimed to develop a possible assessment scale of occupational outcomes. The prevalence of unemployment was the most explored variable (311, 77.2%). Other addressed issues were early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the influence of MS on monthly income (52, 12.9%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). Barriers to employment were reported in 65 (16.1%) studies and job accommodations in 45 (11.2%) studies. Perceived stigma in the workplace, job satisfaction, and knowledge of colleagues about MS were less commonly explored aspects in the studies (5.7%, 4.7%, and 4.2%, respectively). Finally, 59 (14.6%) articles examined occupational absenteeism, 85 (21.1%) aimed to understand the patient's opinion on aspects of his professional life, and 19 (4.7%) evaluated strategies of occupational rehabilitation. The definition of each outcome is extremely diverse across studies in order to suit the particularities of the study design and the research context.

Changes in work and occupational status due to MS

MS is a disease that directly influences the patient's professional life [21–24]. PwMS are vulnerable to a spectrum of several negative consequences at work, ranging from reduction of working hours to unemployment. In a Swedish cohort, only 28% and 23% of PwMS were working full- and part-time after a follow-up of 10 years, respectively [25]. A Norwegian study demonstrated that after 19 years of disease, only 45% of patients were still employed [10]. Even for those who remain employed, more than a quarter show some deterioration in employment status and 56% observe a work performance loss in the short term after the diagnosis [26,27]. Moreover, once unemployed, it is difficult for workers with MS to return to the workforce [8]. Pfleger et al. found that the probability of remaining without early pension at 20 years was 22% for patients and 86% for controls [28].

Work-related socio-economic consequences of MS

MS is a debilitating disease that poses a substantial burden in terms of absenteeism, presenteeism, disability pension, and sick leave costs [29–32]. Both employees and employers bear the socio-economic consequences of MS. Employees with MS are significantly more likely to have disability days compared to employees without MS (21.4% vs 5.2%) [33]. Overall, employees with MS had lost over 4 times more workdays compared to their controls (37.7 vs 8.8 days) [34]. In a cohort of 8350 PwMS, two-thirds received a form of benefit [35]. Increased disability as measured on the Expanded Disability Status Scale (EDSS) is strongly associated with reduced earnings and increased benefits [21,35,36] but it is noteworthy that even mild disability can pose a significant economic burden at the expense of premature retirement, premature work disability, and time lost from work [21,29,36,37]. Interestingly, Jennun et al. demonstrated that negative effects on employment and health costs have been shown up to 8 years prior to MS diagnosis [38]. Neusser et al. reported an estimated total expenditure of 4.3 billion euros annually when considering all interventions enabling work-life integration [39]. Studies on the economic impact of MS come from different countries and continents [7,9,40–42], so the interpretation of their findings must necessarily take into account the specific social security systems of different countries.

Risk factors for unfavourable occupational outcomes

Multiple studies have addressed the risk factors associated with worse professional outcomes. The progressive phenotype of the disease is certainly a negative predictor of occupational outcomes in PwMS compared to the relapsing-remitting form [10,37,43]. Older age, longer disease duration, and high EDSS are also associated with a higher risk of unemployment [44–47]. Recently, the link between neuroimaging findings and occupational status has been demonstrated. Tauhid et al. showed that the T1 lesion load, the ratio between the T1 and T2 burden, and the overall brain volume are significantly different between employed and non-employed PwMS [48]. In a cohort of 145 patients followed up to 12 years, severe brain atrophy, T1 and T2 injury load were the best predictors of deterioration of the occupational status [49]. Cognitive impairment, neuropsychiatric symptoms, and fatigue are also well-described risk factors for labor force withdrawal and work productivity loss [26,50,51]. The main reasons reported by people with MS for their loss of employment involved the ineffective management of symptoms of MS in the workplace, rather than workplace-related factors including insufficient flexibility of employment conditions or being dismissed.

Reported barriers to employment

Some studies described the main barriers to employment for PwMS, which may result from the disease itself or circumstances related to the workplace. Cognitive symptoms, pain, fatigue, psychiatric disorders, disease severity, mobility/gait impairment are illness-related factors considered as major barriers to employment [52–55]. In addition, jobs requiring long-distance travel, overly stressful work, limited feedback on performance, hostile supervisors, high-temperature level and inflexible work schedules are some working conditions considered difficult for PwMS [55–57]. Moreover, negative work events have been reported as an important barrier. Workers with MS may be particularly vulnerable to verbal reprimands, decrease in scheduled work hours, reduction of job responsibilities, and mandatory additional retraining [27,58–60]. Kordovski et al. and Frindak et al both demonstrated that negative work events may act as an indicator of an increased risk of unemployment in the short and medium term [59,61].

Reported job accommodations and vocational rehabilitation strategies

Job accommodations are associated with greater chances of retaining occupation. The studies considered work accommodations as reasonable adjustments in the workplace or strategies related to professional re-training and vocational rehabilitation. In a study with 746 workers with MS, participants with a progressive course of the disease, cognitive impairment, a higher number of MS symptoms, and greater symptom severity were more likely to use job accommodations [62]. More than 60% of PwMS who kept their jobs described any type of accommodation and adopting flexible hours as the most frequently reported accommodation [27,63,64]. Other common accommodations are the possibility of working from home and availability of memory aids, additional time to complete tasks, preferential parking, written job instructions, and air conditioning [27,58]. Rumrill Jr. et al. listed the use of equipment/assistive technological resources as being of great importance [64].

Dorstyn et al. verified that sending a standardized, mail-delivered, resource-based package to job seekers with MS improved their vocational self-efficacy, optimism, and identity [65]. Chiu et al. examined the effect of rehabilitation technology interventions on job retention and concluded that this kind of technological tool may ensure better occupational outcomes [66]. Vocational rehabilitation is a topic that interests PwMS, a group of people receptive to this type of initiative [67]. According to these subjects, a program of vocational rehabilitation must address two main points: managing work performance and expectations [68].

Job satisfaction, stigma, and disclosing the diagnosis in the workplace

Almost one-third of patients who remain employed are dissatisfied at work [52] and 20% to 30% of workers do not feel comfortable disclosing their diagnosis in the work environment [27,57,61,69]. Approximately 40% of these patients did not inform the occupational physician about their diagnosis [70]. More often, patients with increased disease severity and longer work experience disclosed their diagnosis [61]. In parallel, PwMS with "invisible" symptoms tend not to disclose. A quarter of PwMS report feelings of stigmatization at work. Stigma is directly associated with poorer QoL, work handicap, and depression [43,53,71].

Rating clinical scales

The EDSS and the Multiple Sclerosis Functional Composite (MSFC) scale have both been associated with employability [72]. Andries et al. designed the Work and Handicap Questionnaire (WHQ) aiming to estimate the degree of work handicap in PwMS, neuromuscular diseases, and asthma based on the association of daily life disabilities and job demands [73]. Although it was not specifically created for PwMS, it showed good reliability. Honan et al. developed a shortened version of the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ) that consists of a 23-item measure of self-reported perceived workplace difficulties in PwMS [74]. Schiavolin et al. designed and validated the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job), which demonstrated to be a useful tool for measuring the work-related difficulties in PwMS [75]. Both MSWDQ and MSQ-Job proved to be comprehensive tools for tracking subjective work-related problems, but they could not be compared with objective occupational outcomes in a longitudinal perspective and were not validated as a predictive tool of unemployment. McFadden et al. created a 22-item, self-administered scale that indicates if PwMS are at low, medium or high risk of work instability [76]. It was further used in a 3-year longitudinal study aimed at assessing the psychological determinants of job retention [77].

Table 3 summarizes all scales associated with occupational outcomes.

Study	**Name**	**Specific for MS**	**Specific for work**	**Longitudinally validated**	**Usefulness**
Andries et al. [73]	Work and Handicap Questionnaire (WHQ)	No	Yes	No	The WHQ makes an inventory of possibly harmful working conditions and of possible strategies to counter health-related work problems by means of the work adjustments.
Gulick et al.[78]	Work Assessment Scale (WAS)	No	Yes	Yes	The WAS evaluates work-impeding and work-enhancing situations and conditions.
Honan et al.[74]	The Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ)	Yes	Yes	No	The MSWDQ measures the workplace difficulties that can predict the necessity of reducing working hours, work withdrawal and expectations in PwMS.
McFadden et al.[76]	MS-specific Work Instability Scale (MS-WIS)	Yes	Yes	No	The MS-WIS indicates low, medium, and high risk of work instability (job retention).
Raggi et al.[75]	Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job)	Yes	Yes	No	The MSQ-Job measures difficulties in work-related tasks.
Honarmand et al.[72]	Multiple Sclerosis Functional Composite (MSFC)	Yes	No	No	The MSFC predicts unemployment.
Busche et al.[46]	EDSS	Yes	No	Yes	The EDSS predicts unemployment.

Table 3. Identified scales described in the literature associated with occupational outcomes.

5. Discussion

The scientific literature on occupational outcomes and MS is vast. Nevertheless, it is possible to identify some important gaps on this subject. The quality of the scientific evidence in this field is still limited due to a significant lack of longitudinal and interventional studies. Few studies have analyzed the evolution of occupational outcomes of PwMS over time, much less the factors that led to an eventual change: there is no scientific evidence that any improvement has occurred in the prevalence of unfavourable occupational outcomes. Indeed, there is no study supporting the hypothesis that a worker with MS in 2022 is not susceptible to the same occupational consequences caused by the disease as 40 years ago. In contrast, over the past 20 years, there have been notable advances in the treatment of MS due to a significant increase in the availability and effectiveness of disease-modifying drugs (DMDs) that, in theory, may have influenced various occupational outcomes [79]. In this scenario, a study that assesses the specific role of DMDs on occupational outcomes is highly encouraged. Likewise, there is a lack of studies that compare the variables related to work based on a geographical perspective (e.g. countries, continents). Furthermore, there is little evidence on the biopsychosocial context related to work disability, as most articles focus only on the relationship between work trajectories and morbidity.

Data about occupational outcomes come from different contexts and study designs. In most cases, occupational outcomes are part of the primary objectives of the studies. The geographical distribution of the origin of the studies is uneven and creates a bias in the interpretation of the results. No article defined the term “occupational outcomes” and the definitions of each variable differed substantially. Our scoping review brings an evidence-based description about the several possibilities of occupational outcomes and shows that it comprises of several possible variables, most of them easily evaluated objectively - such as unemployment or salary reduction. The variables described in the literature comprise potentially reversible outcomes present at the beginning of the illness and outcomes that are generally irreversible and are associated with the end of the professional career.

The literature is unanimous regarding the MS burden on the economy and public health; indeed, the economic impact of the influence of MS on work has driven several research projects. However, the cost-effectiveness of the new DMDs has not been thoroughly studied, considering both the occupational items and the feasible strategies of professional integration concerning their potential benefit in promoting better occupational outcomes with consequent decrease of the economic impact of MS.

Moreover, despite the literature provides a wide description of possible risk factors and work accommodations for PwMS, little evidence exists concerning the possible protective factors associated with occupational outcomes. Most studies are focused on the aspects related to the disease, and few are dedicated to work-related risk factors. Furthermore, the real role of each type of accommodation in promoting favourable occupational outcomes is still unclear due to a lack of studies providing strong evidence (longitudinal and interventional studies).

Our scoping review identified gaps between the patient's interest in receiving technical guidance on how to improve the occupational outcomes and the degree of evidence on this topic. Few studies were dedicated to identifying strategies capable of promoting job retention, work performance, and even return to work. Moreover, most of the strategies of vocational rehabilitation were studied in small samples of subjects and did not consider the particular characteristics of PwMS. Given the still unsatisfactory unemployment rates among PwMS, vocational rehabilitation may be a valuable complementary resource that deserves further research.

There is also extremely limited evidence related to job satisfaction, stigma, and prejudice in the workplace; in this view, it is important to study these outcomes to gauge an individual's overall level of work adjustment. More studies are needed to understand the reasons for not communicating the diagnosis of MS, including to the occupational physician, since the disclosure may be the first step to promote the worker's full integration.

Only few studies tried to develop a scale associated with the occupational outcomes of PwMS. All the proposed scales described the work handicap or job difficulties in restricted samples and mostly in a cross-sectional design. Most of them revealed to be excessively extensive and complex, which represents a limitation for their wide use in clinical practice. The EDSS is the only scale that has already been associated with occupational outcomes as it generally reflects the severity and progression of the disease. However, this evidence comes from secondary analysis of studies and, despite being simple, the EDSS does not include several other factors already proven to specifically influence the professional outcomes, which can also raise concerns about its sensitivity. The development of a simple and validated scale should be the subject of future studies, as it may represent an easy-to-use tool capable of supporting a more objective and uniform assessment of PwMS by physicians with different backgrounds.

Finally, no study addressed how the new ways of working in the 21st century interfered with the occupational outcomes of PwMS. The nature and the pattern of work have undoubtedly changed in the last 20 years [80] and it is reasonable to imagine that PwMS may find more alternatives and resources to ensure a fruitful professional life. Possibly, technological advances in the workplace may even relativize the concept of work disability. PwMS with the same clinical characteristics can be classified with different degrees of work disability depending on the technological adjustments that help them perform their work. It is reasonable to imagine that a few decades ago, a worker with MS could easily be considered unfit for work, while today's modernisation of types of work and the provision of various technological resources may contribute to delay the definitive endpoint of inability to work.

This is the first scoping review dedicated to the occupational outcomes of PwMS. We highlight that a broad and rigorous search strategy was used to properly include all relevant studies describing the occupational outcomes of MS and promote reliable and accurate results. We applied a range of outcome possibilities that allowed us to accurately understand the evidence related to the impact of MS in the occupational setting. The wide variability of aspects, outcomes, and measures identified motivated the breadth of our methods. This review highlighted several opportunities for new research on the topic. Among the limitations of the study, we did not formally assess the quality of included studies, as we respected the scoping review approach. We could also have missed some data for not including results from the grey literature. Notwithstanding, we intended to disclose the current reality regarding the highest scientific evidence in the field of MS and work and, therefore, the selection of peer-reviewed articles seemed more appropriate. We decided not to use specific terms in our search strategy which may have excluded some articles from our review. Nevertheless, there is an infinite number of possible specific words and synonyms that could be characterised as occupational outcomes so that it would be impossible to cover all the possibilities. Finally, the definitions of each variable changed significantly according to the study, so that, as usually happens with systematic reviews, it was not possible to standardise a definition for each one of them.

6. Conclusions

This is the first scoping review dedicated to the occupational outcomes of PwMS. MS is a chronic neurological disorder that is often associated with disabilities and significant impairment of professional life. Many studies have already been published on the subject and several outcomes have been described. Nevertheless, there are still several issues that deserve further in-depth study by the scientific community in order to match the quality of scientific evidence to the undeniable complexity inherent in this topic.

Author contributions: All authors approved the final version. BKV designed the study, performed database search, data extraction, and wrote the manuscript. AR designed, integrated the research group and reviewed the manuscript. GD, AM, ND integrated the research group and reviewed the manuscript. PB, TM, MP, MAB, BP, GB, MI, ES globally supported the research and reviewed the manuscript. PD coordinated, supervised and reviewed the manuscript.

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Legends

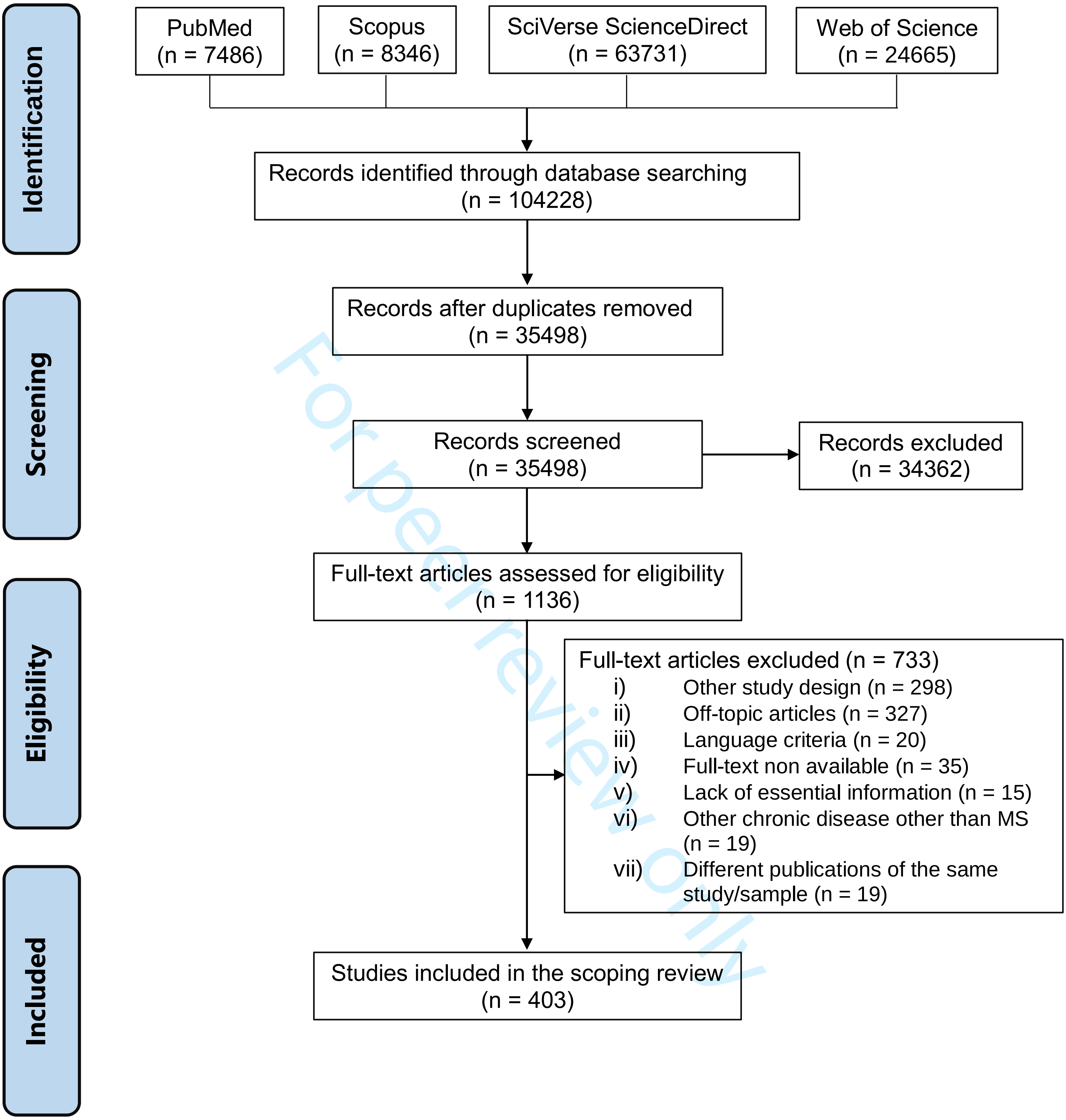
Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Table 3. Identified scales described in the literature associated with occupational outcomes.

Figure 1. PRISMA flowchart.

Table S1. Complete list of all articles included in the scoping review.


Identification
Screening
Eligibility
Included
PubMed (n = 7486)
Scopus (n = 8346)
SciVerse ScienceDirect (n = 63731)
Web of Science (n = 24665)
Records identified through database searching (n = 104228)
Records after duplicates removed (n = 35498)
Records screened (n = 35498)
Records excluded (n = 34362)
Full-text articles assessed for eligibility (n = 1136)
Full-text articles excluded (n = 733)
i) Other study design (n = 298)
ii) Off-topic articles (n = 327)
iii) Language criteria (n = 20)
iv) Full-text non available (n = 35)
v) Lack of essential information (n = 15)
vi) Other chronic disease other than MS (n = 19)
vii) Different publications of the same study/sample (n = 19)
Studies included in the scoping review (n = 403)

AUTHOR	TITLE	YEAR	COUNTRY
Abbas et al. [1]	Caractéristiques des personnes atteintes d'une sclérose en plaques selon la situation professionnelle	2008	France
Abbasi et al.[2]	Risk factors of Multiple sclerosis and their Relation with Disease Severity: A Cross-sectional Study from Iran	2016	Iran
Abdulla et al.[3]	Factors that influence quality of life in patients with multiple sclerosis in Saudi Arabia	2021	Saudi Arabia
Abdullah et al.[4]	MS People's Performance and Satisfaction With Daily Occupations: Implications for Occupational Therapy	2017	Kuwait
Abolhassani et al. [5]	Social aspects of multiple sclerosis for Iranian individuals	2014	Iran
Ahmad et al.[6]	The increasing economic burden of multiple sclerosis by disability severity in Australia in 2017: Results from updated and detailed data on types of costs	2020	Australia
Ahmadi et al.[7]	Relationship Between Anxiety and Depression with Disability Over Multiple Sclerosis Patients in Rafsanjan, Iran	2018	Iran
Akbar et al.[8]	A mixed-methods study of cognitive performance in persons with multiple sclerosis: Association between neuropsychological test performance and interviews about daily cognitive functioning	2021	Canada
Al-Asmi et al. [9]	Magnitude and concurrence of anxiety and depression among attendees with multiple sclerosis at a tertiary care Hospital in Oman	2015	Oman
Alhussain et al. [10]	Multiple Sclerosis Patients in Saudi Arabia: Prevalence of Depression and its Extent of Severity.	2020	Saudi Arabia
Alosaimi et al. [11]	Psychosocial predictors of patient adherence to disease-modifying therapies for multiple sclerosis	2017	Saudi Arabia
Alsharie et al. [12]	Stressful life events and the risk of primary progressive multiple sclerosis: A population-based case-control study	2021	Iran
Alshubaili et al. [13]	Relationship of depression, disability, and family caregiver attitudes to the quality of life of Kuwaiti persons with multiple sclerosis: a controlled study	2007	Kuwait
AlZahrani et al. [14]	Association of acute stress with multiple sclerosis onset and relapse in Saudi Arabia	2019	Saudi Arabia
Amaducci et al.[15]	Multiple sclerosis among shoe and leather workers: an epidemiological survey in Florence.	1982	Italy
Amato et al.[16]	Cognitive impairment in early-onset multiple sclerosis. Pattern, predictors, and impact on everyday life in a 4-year follow-up.	1995	Italy
Amato et al.[17]	Cognitive Dysfunction in Early-Onset Multiple Sclerosis	2001	Italy

Andries et al.[18]	Working with a chronic disorder--the development of the Work and Handicap Questionnaire.	2004	The Netherlands
Archibald et al. [19]	Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients	1994	Canada
Aronson et al.[20]	Quality of life among persons with multiple sclerosis and their caregivers	1997	Canada
Arroyo et al.[21]	Correlation between spasticity and quality of life in patients with multiple sclerosis: the CANDLE study	2013	Spain
Artemiadis et al.[22]	Structural MRI correlates of cognitive function in multiple sclerosis	2018	Greece
Babamohamadi et al. [23]	Dimensions of Adaptation, General Health, and life Satisfaction in Multiple Sclerosis	2016	Iran
Bamer et al.[24]	Validation study of prevalence and correlates of depressive symptomatology in multiple sclerosis.	2008	United States
Barin et al.[25]	Patterns of care for Multiple Sclerosis in a setting of universal care access: A cross-sectional study	2019	Switzerland
Baroin et al.[26]	Validation of a new quality of life scale related to multiple sclerosis and relapses.	2013	France
Barzegar et al.[27]	Comparative study of quality of life, anxiety, depression, and fatigue among patients with neuromyelitis optica spectrum disorder and multiple sclerosis: The first report from Iran	2018	Iran
Bass et al.[28]	Effect of Multiple Sclerosis on Daily Activities, Emotional Well-being, and Relationships: The Global vsMS Survey.	2020	Europe
Battaglia et al. [29]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Italy	2017	Italy
Baughman et al. [30]	Staying on the job: The relationship between work performance and cognition in individuals diagnosed with multiple sclerosis	2015	US
Baumstarck et al. [31]	Health-related quality of life as an independent predictor of long-term disability for patients with relapsing–remitting multiplesclerosis-remittingmultiplesclerosis:A2-yearlongitudinalstudy	2013	France
Baumstarck et al. [32]	Is the Concept of Quality of Life Relevant for Multiple Sclerosis Patients with Cognitive Impairment? Preliminary Results of a Cross-Sectional Study	2012	France
Bayas et al.[33]	Combination treatment of fingolimod with antidepressants in relapsing–remitting multiple sclerosis patients with depression: a multicentre, open-label study – REGAIN	2016	Germany
Beatty et al.[34]	Demographic, Clinical, and Cognitive Characteristics of Multiple Sclerosis Patients Who Continue to Work	1995	US
Beatty et al.[35]	Changes in neuropsychological test performance over the workday in multiple sclerosis	2003	US/Italy

Becker et al.[36]	Patient satisfaction and healthcare services in specialized multiple sclerosis centres in Germany	2018	Germany
Beier et al.[37]	Relationship of perceived stress and employment status in individuals with multiple sclerosis.	2019	US
Benedict et al.[38]	Predicting neuropsychological abnormalities in multiple sclerosis	2006	US
Benedict et al.[39]	Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change	2005	US
Benedict et al.[40]	Negative work events and accommodations in employed multiple sclerosis patients.	2013	US
Berg et al.[41]	Costs and quality of life of multiple sclerosis in Sweden.	2006	Sweden
Bessing et al.[42]	Changes in multiple sclerosis symptoms are associated with changes in work productivity of people living with multiple sclerosis	2021	Australia
Birnbaum et al.[43]	Economic impact of multiple sclerosis disease-modifying drugs in an employed population: direct and indirect costs	2008	US
Bishop et al. [44]	The relationship between housing accessibility variables and employment status among adults with multiple sclerosis	2013	US
Bishop et al. [45]	Employment Among Working-Age Adults With Multiple Sclerosis: A Data-Mining Approach to Identifying Employment Interventions	2015	US
Bishop et al. [46]	Life domains that are important to quality of life for people with multiple sclerosis: A population-based qualitative analysis	2019	US
Bishop et al. [47]	Sources of information about multiple sclerosis: Information seeking and personal, demographic, and MS variables	2009	US
Bishop et al. [48]	The relationship of self-management and disease modifying therapy use to employment status among adults with multiple sclerosis	2009	US
Bishop et al. [49]	Quality of life among people with multiple sclerosis: Replication of a three-factor prediction model	2015	US
Björkenstam et al.[50]	Heterogeneity of sickness absence and disability pension trajectories among individuals with MS	2015	Sweden
Björkenstam et al.[51]	Is disability pension a risk indicator for future need of psychiatric healthcare or suicidal behavior among MS patients- a nationwide register study in Sweden?	2015	Sweden
Blinkenberg et al.[52]	Increased socioeconomic burden in patients with primary progressive multiple sclerosis: A Danish nationwide population-based study	2020	Denmark

Bo et al.[53]	Access to social security benefits among multiple sclerosis patients in Italy: A cross-sectional study.	2018	Italy
Bøe Lunde et al.[54]	Employment among Patients with Multiple Sclerosis-A Population Study	2014	Norway
Bonafede et al. [55]	Productivity Loss and Associated Costs Among Employed Patients Receiving Disease-Modifying Treatment for Multiple Sclerosis	2021	US
Boyko et al.[56]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Russia	2017	Russia
Broersma et al.[57]	The impact of self-perceived limitations, stigma and sense of coherence on quality of life in multiple sclerosis patients: results of a cross-sectional study.	2018	The Netherlands
Brook et al.[58]	Absenteeism and health-benefit costs among employees with MS.	2009	US
Brown et al.[59]	Societal costs of primary progressive multiple sclerosis in Australia and the economic impact of a hypothetical disease-modifying treatment that could delay disease progression.	2021	Australia
Brown et al.[60]	Longitudinal assessment of anxiety, depression, and fatigue in people with multiple sclerosis	2009	Australia
Brundin et al.[61]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Sweden	2017	Sweden
Bruno et al.[62]	Economic burden of multiple sclerosis in France estimated from a regional medical registry and national sick fund claims	2019	France
Buchanan et al. [63]	Informal care giving to more disabled people with multiple sclerosis	2008	US
Buchanan et al. [64]	A Pilot Study of Latinos With Multiple Sclerosis: Demographic, Disease, Mental Health, and Psychosocial Characteristics	2011	US
Bueno et al.[65]	Health-related quality of life in patients with longstanding 'benign multiple sclerosis'	2015	Canada
Buhse et al.[66]	Factors Associated with Health-Related Quality of Life Among Older People with Multiple Sclerosis	2014	US
Busche et al.[67]	Short term predictors of unemployment in multiple sclerosis patients.	2003	Canada
Butepage et al.[68]	Cost-of-illness trajectories among people with multiple sclerosis by comorbidity: A register-based prospective study in Sweden	2020	Sweden
Buzgova et al.[69]	Factors Influencing Health-Related Quality of Life of Patients with Multiple Sclerosis and Their Caregivers	2020	Czech Republic
Buzgova et al.[70]	Satisfaction of Patients With Severe Multiple Sclerosis and Their Family Members With Palliative Care: Interventional Study	2020	Czech Republic

Cadden et al.[71]	Factors associated with employment status in individuals with multiple sclerosis: Cognition, fatigue, and motor function	2015	US
Calabrese et al. [72]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Switzerland.	2017	Swizerland
Calandri et al.[73]	Improving the quality of life and psychological well-being of recently diagnosed multiple sclerosis patients: preliminary evaluation of a group-based cognitive behavioral intervention	2017	Italy
Calandri et al.[74]	Young adults' adjustment to a recent diagnosis of multiple sclerosis: The role of identity satisfaction and self-efficacy	2019	Italy
Cambier-Langrand et al. [75]	Impact socio professionnel précoce de la sclérose en plaques : une étude prospective d'une série de 24 patients	2016	France
Campbell et al.[76]	Cognitive impairment among patients with multiple sclerosis: associations with employment and quality of life	2016	UK
Campbell et al.[77]	Burden of multiple sclerosis on direct, indirect costs and quality of life: National US estimates.	2014	US
Carnero Contentti et al. [78]	Impact of multiple sclerosis on quality of life: Comparison with systemic lupus erythematosus	2017	Argentina
Carnero Contentti et al. [79]	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Carney et al.[80]	Societal costs of multiple sclerosis in Ireland.	2018	Ireland
Carrieri et al.[81]	Determinants of on-the-job-barriers in employed persons with multiple sclerosis: The role of disability severity and cognitive indices	2014	Italy
Casado et al. [82]	Direct costs of relapses in patients with relapsing-remitting multiple sclerosis	2021	Spain
Casado et al. [83]	Direct and indirect costs of Multiple Sclerosis in Baix Llobregat (Catalonia, Spain), according to disability	2006	Spain
Castelo-Branco et al. [84]	Clinical course of multiple sclerosis and labour-force absenteeism: a longitudinal population-based study.	2019	Sweden
Catanzaro et al.[85]	Economic status of families living with multiple sclerosis.	1992	USA
Cattaneo et al.[86]	Participation Restriction in People With Multiple Sclerosis: Prevalence and Correlations With Cognitive, Walking, Balance, and Upper Limb Impairments	2017	Italy/Belgium
Cervera-Deval et al.[87]	Social handicaps of multiple sclerosis and their relation to neurological alterations	1994	Spain

Chamot et al.[88]	Item response theory-based measure of global disability in multiple sclerosis derived from the Performance Scales and related items.	2014	USA
Chen et al. [89]	Risk factors of leaving employment due to multiple sclerosis and changes in risk over the past decades: survival analysis with competing risks	2019	Australia
Chen et al. [90]	Effects of multiple sclerosis disease-modifying therapies on employment measures using patient-reported data.	2018	Australia
Chen et al. [91]	Estimating MS-related work productivity loss and factors associated with work productivity loss in a representative Australian sample of people with multiple sclerosis.	2019	Australia
Chen et al.[92]	Impact of depression, fatigue and disability on quality of life in Chinese patients with multiple sclerosis.	2013	China
Chiu et al.[93]	Descriptive analysis of free-text comments on healthcare priorities and experiences in a national sample of people with multiple sclerosis.	2019	USA
Chiu et al.[94]	Effect of Rehabilitation Technology Services on Vocational Rehabilitation Outcomes of Individuals With Multiple Sclerosis	2015	USA
Chiu et al.[95]	Motivational and Volitional Variables Associated With Stages of Change for Exercise in Multiple Sclerosis: A Multiple Discriminant Analysis	2012	USA
Chiu et al.[96]	State vocational rehabilitation services and employment in multiple sclerosis.	2013	USA
Chiu et al.[97]	Employment as a health promotion intervention for persons with multiple sclerosis.	2016	USA
Chruzander et al.[98]	A 10-year follow-up of a population-based study of people with multiple sclerosis in Stockholm, Sweden: Changes in disability and the value of different factors in predicting disability and mortality	2013	Sweden
Chruzander et al.[99]	Longitudinal changes in sickness absence and disability pension, and associations between disability pension and disease-specific and contextual factors and functioning, in people with multiple sclerosis.	2016	Sweden
Chwastiak et al.[100]	Fatigue and psychiatric illness in a large community sample of persons with multiple sclerosis.	2005	USA
Cioncoloni et al.[101]	Individual factors enhance poor health-related quality of life outcome in multiple sclerosis patients. Significance of predictive determinants.	2014	Italy
Clingerman et al.[102]	The Influence of Resources on Perceived Functional Limitations Among Women with Multiple Sclerosis	2004	USA
Cofield et al.[103]	Shared Decision Making and Autonomy Among US Participants with Multiple Sclerosis in the NARCOMS Registry.	2017	USA

Coleman et al.[104]	Impact of mobility impairment on indirect costs and health-related quality of life in multiple sclerosis.	2013	USA
Concetta Incerti et al. [105]	Occupational stress and personality traits in multiple sclerosis: A preliminary study	2015	Italy
Conradsson et al.[106]	Changes in disability in people with multiple sclerosis: a 10-year prospective study.	2018	Sweden
Conradsson et al.[107]	Activity limitations and participation restrictions in people with multiple sclerosis: a detailed 10-year perspective.	2021	Sweden
Conradsson et al.[108]	Employment status of people with multiple sclerosis in relation to 10-year changes in functioning and perceived impact of the disease.	2020	Sweden
Contentti et al.[109]	Access and unmet needs to multiple sclerosis care in a cohort of Argentinean patients	2019	Argentina
Cores et al.[110]	Work status and cognitive performance in patients with relapsing remitting multiple sclerosis	2019	Argentina
Costa et al.[111]	Social support network and quality of life in multiple sclerosis patients.	2017	Portugal
Cowan et al.[112]	Psychosocial aspects of the lived experience of multiple sclerosis: personal perspectives	2018	Australia
da Silva et al.[113]	Cost analysis of multiple sclerosis in Brazil: a cross-sectional multicenter study	2016	Brazil
Dayapoglu et al.[114]	Quality of life in relapsing-remitting multiple sclerosis	2011	Pakistan
Dehghan et al.[115]	Occupational performance of individuals with Multiple Sclerosis based on disability level in Iran.	2019	Iran
Devins et al.[116]	Differences in illness intrusiveness across rheumatoid arthritis, end-stage renal disease, and multiple sclerosis	1993	Canada
D'hooghe et al.[117]	Self-reported levels of education and disability progression in multiple sclerosis.	2016	Belgium/The Netherlands
D'hooghe et al.[118]	Perceived neuropsychological impairment inversely related to self-reported health and employment in multiple sclerosis	2019	Belgium
Dorstyn et al.[119]	Piloting an email-based resource package for job seekers with multiple sclerosis.	2017	Australia
Dorstyn et al.[120]	Online Resource to Promote Vocational Interests Among Job Seekers With Multiple Sclerosis: A Randomized Controlled Trial in Australia.	2018	Australia
Dubois et al.[121]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Belgium.	2017	Belgium
Dusankova et al.[122]	Cost of multiple sclerosis in the Czech Republic: the COMS study.	2012	Czech Republic

Earnshaw et al.[123]	Cost effectiveness of glatiramer acetate and natalizumab in relapsing-remitting multiple sclerosis.	2009	USA
Esposito et al.[124]	Lifestyle and Mediterranean diet adherence in a cohort of Southern Italian patients with Multiple Sclerosis	2021	Italy
Estrutti et al.[125]	Employment status of people diagnosed with multiple sclerosis in Brazil.	2019	Brazil
Fantoni-Quinton et al.[126]	Impact of multiple sclerosis on employment and use of job-retention strategies: The situation in France in 2015.	2016	France
Farnoush et al.[127]	Educational, psycho mental and socio economical needs of an Iranian cohort with multiple sclerosis	2010	Iran
Farran et al.[128]	Quality of life and coping strategies in Lebanese Multiple Sclerosis patients: A pilot study	2016	Lebanon
Fernandez et al.[129]	Patient characteristics and determinants of quality of life in an international population with multiple sclerosis: Assessment using the MusiQoL and SF-36 questionnaires	2011	Europe
Fernandez-Jimenez et al.[130]	Quality of Life and Depressive Symptomatology in Multiple Sclerosis: A Cross-Sectional Study Between the USA and Spain	2021	USA/Spain
Fidao et al.[131]	Depression mediates the relationship between fatigue and mental health-related quality of life in multiple sclerosis	2021	Australia
Finlayson et al.[132]	Self-care, productivity and leisure limitations of people with multiple sclerosis in Manitoba	1998	Canada
Flachenecker et al.[133]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Germany.	2017	Germany
Flensner et al.[134]	Work capacity and health-related quality of life among individuals with multiple sclerosis reduced by fatigue: A cross-sectional study	2013	Sweden
Fogarty et al.[135]	Direct and indirect economic consequences of multiple sclerosis in Ireland.	2014	Ireland
Forbes et al.[136]	Health problems and health-related quality of life in people with multiple sclerosis.	2006	UK
Ford et al. [137]	Health status and quality of life of people with multiple sclerosis.	2001	UK
Forslin et al.[138]	Predictors for Employment Status in People With Multiple Sclerosis: A 10-Year Longitudinal Observational Study	2018	Sweden
Fragoso et al.[139]	The effect of multiple sclerosis on the professional life of a group of Brazilian patients.	2010	Brazil
Fraser et al.[140]	Vocational rehabilitation in multiple sclerosis (MS): a profile of clients seeking services.	2003	USA
Fraser et al.[141]	Predictors of vocational stability in multiple sclerosis	2009	USA

Freedman et al.[142]	Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: a case-control study based on death certificates.	2000	USA
Frndak et al.[143]	Negative work events reported online precede job loss in multiple sclerosis	2015	USA
Frndak et al.[144]	Disclosure of disease status among employed multiple sclerosis patients: association with negative work events and accommodations	2015	USA
Fuchs et al.[145]	Response heterogeneity to home-based restorative cognitive rehabilitation in multiple sclerosis: An exploratory study.	2019	USA
Garcia-Dominguez et al.[146]	Economic burden of multiple sclerosis in a population with low physical disability	2019	Spain
Genevie et al.[147]	Job Retention Among People with Multiple Sclerosis	1987	USA
Ghaffar et al.[148]	Occupational attainment as a marker of cognitive reserve in multiple sclerosis.	2012	Canada
Gil-Gonzàlez et al.[149]	Predicting improvement of quality of life and mental health over 18-months in multiple sclerosis patients	2021	Spain
Gill et al.[150]	Disclosing a Diagnosis in the Workplace: Perspective of People with Multiple Sclerosis	2021	Ireland
Gill et al.[151]	Depressive Symptoms Are Associated With More Negative Functional Outcomes Than Anxiety Symptoms in Persons With Multiple Sclerosis.	2019	Canada
Giordano et al.[152]	Low quality of life and psychological wellbeing contrast with moderate perceived burden in carers of people with severe multiple sclerosis.	2016	Italy
Giovannetti et al.[153]	Individualized quality of life of severely affected multiple sclerosis patients: practicability and value in comparison with standard inventories	2016	Italy
Giovannetti et al.[154]	Conversion to secondary progressive multiple sclerosis: Multi stakeholder experiences and needs in Italy	2020	Italy
Giovannetti et al.[155]	Cognitive function alone is a poor predictor of health-related quality of life in employed patients with MS: results from a cross-sectional study	2016	Italy
Glanz et al.[156]	Work productivity in relapsing multiple sclerosis: associations with disability, depression, fatigue, anxiety, cognition, and health-related quality of life.	2012	USA
Göksel Karatepe et al.[157]	Quality of life in patients with multiple sclerosis: the impact of depression, fatigue, and disability	2011	Spain
Gordon et al.[158]	Employment issues and knowledge regarding ADA of persons with multiple sclerosis	1997	USA
Gottberg et al.[159]	Health-related quality of life in a population-based sample of people with multiple sclerosis in Stockholm County.	2006	Sweden

Goverover et al.[160]	The relationship among performance of instrumental activities of daily living, self-report of quality of life, and self-awareness of functional status in individuals with multiple sclerosis.	2009	USA
Gracia et al.[161]	Costs of multiple sclerosis in Panama from societal, patient perspectives and health-related quality of life	2018	USA
Graham et al.[162]	Barriers and facilitators to employment as reported by people with physical disabilities: An across disability type analysis	2018	USA
Gregory et al.[163]	Employment and multiple sclerosis in New Zealand.	1993	New Zealand
Grima et al.[164]	Cost and health related quality of life consequences of multiple sderosis	2000	Canada
Gross et al.[165]	Characteristics, burden of illness, and physical functioning of patients with relapsing-remitting and secondary progressive multiple sclerosis: a cross-sectional US survey.	2017	USA
Grytten et al.[166]	The influence of coping styles on long-term employment in multiple sclerosis: A prospective study	2017	Norway
Gulick et al.[167]	Work performance by persons with multiple sclerosis: conditions that impede or enable the performance of work.	1989	USA
Gulick et al.[168]	Reliability and validity of the work assessment scale for persons with multiple sclerosis.	1991	USA
Gulick et al.[169]	Model for predicting work performance among persons with multiple sclerosis.	1992	USA
Gulick et al.[170]	Health status, work impediments, and coping related to work roles of women with multiple sclerosis.	1996	USA
Gustavsen et al.[171]	Shift work at young age is associated with increased risk of multiple sclerosis in a Danish population.	2016	Denmark
Gyllensten et al.[172]	How does work disability of patients with MS develop before and after diagnosis? A nationwide cohort study with a reference group.	2016	Sweden
Gyllensten et al.[173]	Comparing costs of illness of multiple sclerosis in three different years: A population-based study.	2018	Sweden
Gyllensten et al.[174]	Costs of illness of multiple sclerosis in Sweden: a population-based register study of people of working age.	2018	Sweden
Gyllensten et al.[175]	Costs of illness progression for different multiple sclerosis phenotypes: a population-based study in Sweden	2019	Sweden
Hadjigeorgiou et al. [176]	Observational study assessing demographic, economic and clinical factors associated with access and utilization of health care services of patients with multiple sclerosis under treatment with interferon beta-1b (EXTAVIA).	2014	Greece

Hakim et al.[177]	The social impact of multiple sclerosis-a study of 305 patients and their relatives.	2000	UK
Hamed et al.[178]	Environmental factors affecting the daily functioning of Jordanian individuals with multiple sclerosis.	2012	Jordan
Hategeka et al.[179]	Association of Unemployment and Informal Care with Stigma in Multiple Sclerosis: Evidence from the Survey on Living with Neurological Conditions in Canada.	2019	Canada
Heinonen et al.[180]	The retirement rate due to multiple sclerosis has decreased since 1995- A retrospective study in a Finnish central hospital.	2020	Finland
Heiznlef et al.[181]	Economic Burden of the Out-of-Pocket Expenses for People with Multiple Sclerosis in France	2020	France
Henriksson et al.[182]	Costs, quality of life and disease severity in multiple sclerosis: a cross-sectional study in Sweden.	2001	Sweden
Heredia-Torres et al.[183]	Occupational performance in multiple sclerosis and its relationship with quality of life and fatigue	2020	Spain
Hersch et al.[184]	The implications of suboptimal year-1 outcomes with disease-modifying therapy in employees with multiple sclerosis.	2021	USA
Honan et al.[185]	The Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ):development of a shortened scale	2014	Australia
Honarmand et al.[186]	Predicting employment status in multiple sclerosis patients: the utility of the MS functional composite	2010	Canada
Horwitz et al.[187]	Effect of occupation on risk of developing MS: an insurance cohort study.	2013	Denmark
Hyarat et al.[188]	Health Related Quality of Life Among Patients With Multiple Sclerosis: The Role of Psychosocial Adjustment to Illness	2019	Saudi Arabia/Jordan
Iezzoni et al.[189]	Health, disability, and life insurance experiences of working-age persons with multiple sclerosis.	2007	USA
Iezzoni et al.[190]	Experiences acquiring and using mobility aids among working-age persons with multiple sclerosis living in communities in the United States.	2010	USA
Imani et al.[191]	Economic costs incurred by the patients with multiple sclerosis at different levels of the disease: a cross-sectional study in Northwest Iran.	2020	Iran
Incerti et al.[192]	Adverse working events in patients with multiple sclerosis.	2017	Italy
Incerti et al.[193]	Can personality traits influence occupational stress in multiple sclerosis patients? A one-year longitudinal study.	2020	Italy

Ivanova et al.[194]	The cost of disability and medically related absenteeism among employees with multiple sclerosis in the US.	2009	USA
Iwanaga et al.[195]	Person-environment contextual factors as mediators for the relationship between symptom cluster and employment outcome in multiple sclerosis	2018	USA
Jacobsen et al.[196]	Brain atrophy and employment in multiple sclerosis patients: a 10-year follow-up study	2020	Norway
Jaracz et al.[197]	Quality of life and social support in patients with multiple sclerosis	2020	Poland
Jaworski et al.[198]	Conscientiousness and deterioration in employment status in multiple sclerosis over 3 years.	2021	USA
Jennum et al.[199]	The socioeconomic consequences of optic neuritis with and without multiple sclerosis: a controlled national study	2012	Denmark
Jennum et al.[200]	The socioeconomic consequences of multiple sclerosis: A controlled national study	2012	Denmark
Jiang et al.[201]	Stressful life events are associated with the risk of multiple sclerosis.	2020	Sweden
Jiménez-Lopez et al.[202]	Qualitative impact of cognitive impairment on daily life activities of patients with recently diagnosed multiple sclerosis	2012	Mexico
Johansson et al.[203]	Use of health services in people with multiple sclerosis with and without fatigue.	2009	Sweden
Johansson et al.[204]	The Swedish occupational fatigue inventory in people with multiple sclerosis.	2008	Sweden
Johansson et al.[205]	Participation in social/lifestyle activities in people with multiple sclerosis: Changes across 10 years and predictors of sustained participation.	2020	Sweden
Johansson et al.[206]	Associations between fatigue impact and lifestyle factors in people with multiple sclerosis - The Danish MS hospitals rehabilitation study.	2021	Denmark
Johnson et al.[207]	Social-services support for multiple sclerosis patients in West of Scotland.	1977	Scotland
Johnson et al.[208]	Disease and demographic characteristics associated with unemployment among working-age adults with multiple sclerosis	2013	USA
Johnson et al.[209]	The Cost and Benefits of Employment: A Qualitative Study of Experiences of Persons With Multiple Sclerosis	2004	USA
Johnson et al.[210]	Disability in multiple sclerosis and the provision of social and medical services: Findings in Wellington, New Zealand	1984	New Zealand
Jones et al.[211]	Quantifying the relationship between increased disability and health care resource utilization, quality of life, work productivity, health care costs in patients with multiple sclerosis in the US	2016	USA

Jongen et al.[212]	Relationship between working hours and power of attention, memory, fatigue, depression and self-efficacy one year after diagnosis of clinically isolated syndrome and relapsing remitting multiple sclerosis.	2014	The Netherlands
Jongen et al.[213]	Improved health-related quality of life, participation, and autonomy in patients with treatment-resistant chronic pain after an intensive social cognitive intervention with the participation of support partners.	2017	The Netherlands
Jønsson et al.[214]	Quality of life as a measure of rehabilitation outcome in patients with multiple sclerosis	1996	Denmark
Julian et al.[215]	Employment in multiple sclerosis. Exiting and re-entering the work force.	2008	USA
Kadrnozkova et al.[216]	Combining clinical and magnetic resonance imaging markers enhances prediction of 12-year employment status in multiple sclerosis patients.	2018	Czech Republic
Kahraman et al.[217]	Determinants of physical activity in minimally impaired people with multiple sclerosis.	2015	Turkey
Kahraman et al.[218]	Feasibility of a 6-Month Yoga Program to Improve the Physical and Psychosocial Status of Persons with Multiple Sclerosis and their Family Members	2018	Turkey
Kahraman et al.[219]	The multiple sclerosis work difficulties questionnaire: translation and cross-cultural adaptation to Turkish and assessment of validity and reliability.	2019	Turkey
Kalantari et al.[220]	Perceived Social Stigma in Patients with Multiple Sclerosis: A Study from Iran.	2018	Iran
Kallmann et al.[221]	Real-life outcomes of teriflunomide treatment in patients with relapsing multiple sclerosis: TAURUS-MS observational study.	2019	Germany
Kavaliunas et al.[222]	Earnings and Financial Compensation from Social Security Systems Correlate Strongly with Disability for Multiple Sclerosis Patients.	2015	Sweden
Kavaliunas et al.[223]	Cognitive function is a major determinant of income among multiple sclerosis patients in Sweden acting independently from physical disability.	2019	Sweden
Khader et al.[224]	Estimating the prevalence of cognition and mental health among multiple sclerosis patients: A population-based cross-sectional study	2019	Kuwait
Khan et al.[225]	Use of International Classification of Functioning, Disability and Health (ICF) to describe patient-reported disability in multiple sclerosis and identification of relevant environmental factors.	2007	Australia
Khan et al.[226]	Multiple sclerosis: disability profile and quality of life in an Australian community cohort.	2006	Australia
Kikuchi et al.[227]	Impact and characteristics of quality of life in Japanese patients with multiple sclerosis.	2011	Japan

Kirk-Brown et al.[228]	Disclosure of diagnosis of multiple sclerosis in the workplace positively affects employment status and job tenure	2014	Australia
Kleiter et al.[229]	Adherence, satisfaction and functional health status among patients with multiple sclerosis using the BETACONNECT® autoinjector: a prospective observational cohort study.	2017	Germany
Kobelt et al.[230]	Costs and quality[231] of life in multiple sclerosis. An observational study in Germany	2001	Germany
Kobelt et al.[232]	Costs and quality of life of multiple sclerosis in the United Kingdom.	2006	Europe
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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3, 4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	5
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5, 6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5, 6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA

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SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7, 8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	7, 8
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	8-12
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	8-12
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	12-15
Limitations	20	Discuss the limitations of the scoping review process.	15
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	1

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

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Occupational outcomes of people with Multiple Sclerosis: a scoping review

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Occupational outcomes of people with Multiple Sclerosis: a scoping review

Bruno Kusznir Vitturi[1], Alborz Rahmani[1,2], Guglielmo Dini[1,2], Alfredo Montecucco[1,2], Nicoletta Debarbieri[2], Elvira Sbragia[3,4], Paolo Bandiera[5], Michela Ponzio[6], Mario Alberto Battaglia[6,7], Tommaso Manacorda[5], Benedetta Persechino[8], Giuliana Buresti[8], Matilde Inglese[3,4], Paolo Durando[1,2]

1. Department of Health Sciences, University of Genoa, Italy
2. IRCCS Ospedale Policlinico San Martino, Occupational Medicine Unit, Genoa, Italy
3. Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI) and Center of Excellence for Biomedical Research (CEBR), University of Genoa, Genoa, Italy
4. IRCCS Ospedale Policlinico San Martino, Genoa, Italy
5. Italian Multiple Sclerosis Association (AISM)
6. Scientific Research Area, Italian Multiple Sclerosis Foundation (FISM), Italy
7. Department of Life Science, University of Siena, Siena, Italy
8. Italian Workers' Compensation Authority (INAIL)

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Corresponding author

Bruno Kusznir Vitturi, MD

Department of Health Sciences, University of Genoa, Italy

Building 3, L.go R. Benzi 10 - 16132 Genoa, Italy

E-mail: z_azul@hotmail.com

Abstract

Objectives. To update the knowledge on the occupational outcomes associated with Multiple Sclerosis (MS), systematically examine the extent, scope, and nature of the pre-existing literature, and identify research gaps in the existing literature.

Design. Scoping review.

Data sources. A comprehensive database search of PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science was performed. There were no time limits.

Eligibility criteria. We included any peer-reviewed original article reporting the occupational outcomes of people with MS between the ages of 18 and 65 years. We excluded those off-topic and with insufficient information.

Methods. This review was conducted following the Joanna Briggs Institute recommendations and the PRISMA-ScR checklist. Screening, reading of full-texts and data extraction was performed in a standardized way by expert reviewers from July 14, 2021, to October 31, 2021. We provided a narrative synthesis and an overview of findings.

Results. The initial systematic search yielded 104,228 results. After removing duplicates and applying the exclusion criteria, 403 articles were included in the review. In total, the studies evaluated 492,062 subjects with MS. One hundred fifty-four (38.2%) articles were published in the last 5 years, mostly from Europe and North America (50.9% and 33.0%, respectively). Concerning the occupational outcomes, studies mostly addressed unemployment (311, 77.2%), early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). The results were categorised into 7 subtopics: “Changes in work and occupational status due to MS”, “work-related socio-economic consequences of MS”, “risk factors for unfavourable occupational outcomes”, “reported barriers to employment”, “reported job accommodations and vocational rehabilitation strategies", "job satisfaction, stigma, and disclosing the diagnosis in the workplace" and "rating clinical scales".

Conclusions. There are several issues that deserve further in-depth study by the scientific community in order to improve the occupational outcomes of people with MS.

Keywords

Multiple sclerosis; occupational & industrial medicine; public health; health economics; epidemiology; neurology

Strengths and limitations of this study

- The scoping design allowed a summary of the diverse/heterogeneous range of terms and conceptualisations or even the multidimensional relationship of work and MS.
- All original peer-reviewed articles included were reviewed by our research group.
- As we respected the scoping review approach, we did not formally assess the quality of included studies.
- We could have missed some data for not including results from the grey literature.

1. Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disease that causes demyelination and neurodegeneration in the central nervous system. It mainly affects young people between 20 and 40 years of age and it is the main cause of non-traumatic disability among young adults in the Western world [1]. MS is a global disease, affects 2.5 million people worldwide, the incidence and prevalence are known to be increasing in both developed and developing countries [2]. The symptoms are extremely varied and the clinical course is within a spectrum that extends from relapsing-remitting to progressive [1-3].

In addition to the inherent clinical complexity of MS, the age of onset of the disease brings inevitable repercussions to work activity, as it often coincides with the moment in which patients find themselves managing the already expected difficulties of the job market and the beginning of the professional career [4]. As long as MS symptoms remain 'invisible', people with MS (PwMS) are reluctant to inform their employer about their disease out of fear of losing their job [4]. Concerns about disclosing the diagnosis in the workplace stem from a range of issues involving the fear of appearing vulnerable, suffering discrimination and losing their jobs. [5]. PwMS often require essential accommodations in the work environment to continue providing satisfactory work. Often limiting and disabling, symptoms such as fatigue, neuropsychiatric impairment, and motor disturbances constantly threaten the full performance at work and the search for new professional skills. PwMS are more vulnerable to unemployment and early retirement and the influence of MS on professional life is known to be directly associated with quality of life (QoL) [6].

The impact of MS on work activities has already been evaluated in many studies carried out in different parts of the world [7–10]. Calabrese et al. demonstrated that workforce participation can decline from 82% to 8% and employment rates vary between 31% and 65% [7], being influenced by

factors such as the degree of disability, the duration of disease, the level of education and the type of work activity. Another study outlined the complexity of the association between employment and MS and revealed that 56.2% of PwMS are unemployed and face great difficulty in returning to the workforce [8].

Besides the potential consequences of MS for people's working life, it is also important to recognize the impact of the disease at the community level. Long-term absence, invalidity, and early retirement may demand an annual expense of 17,945€ per patient in the late stages of MS [11]. Loss of productivity at work and occupation change due to MS account for an annual cost of $2,691 and $2,982 for each patient, respectively [12]. Indeed, the impact of MS on occupational outcomes is responsible for a significant economic burden and represents a matter of public health all around the world.

There is an eminent need for further scientific research on the occupational outcomes of PwMS. Furthermore, research in this area is highly encouraged as it contributes to address the eighth Sustainable Development Goal set up by the United Nations. Although it is relatively easy to find information on MS and work in the literature, being diagnosed with MS still increases the risk of unemployment, early retirement, loss of working capacity, reduced monthly income, job dissatisfaction and impaired QoL. Recent advances in the treatment of MS and the emergence of new types and modalities of work also call for new studies investigating the role of MS on work. Moreover, previous reviews were focused on specific occupational outcomes that do not reflect the totality of possible outcomes, contributing only partially to the holistic understanding of the relationship between MS and work [13–17]. Due to the large number and heterogeneity of articles already published, there is a significant difficulty in detecting gaps in the pre-existing literature and consolidating evidence on the subject. This scenario favours unnecessary investments in redundant studies that could be reallocated to research with potential to truly influence patients' lives. In this context, we decided to conduct the first scoping review related to the occupational outcomes of PwMS, as it can provide a broad map of the existing evidence and identify gaps for potential future studies.

2. Objectives

The objectives of the present scoping review are related to occupational outcomes associated with MS: the primary objective is to update the knowledge on the occupational outcomes of PwMS compared with people without MS, and among PwMS by clinical characteristics. Our secondary objectives were to systematically examine the extent, scope, and nature of the pre-existent literature, to summarize and disseminate the research results deriving from the already published articles, to identify research gaps in the existing literature and to provide an accurate rationale to develop further relevant research in the area.

3. Methods

We performed this scoping review following the guidelines outlined by Arksey and O'Malley, the Joanna Briggs Institute recommendations, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for scoping review (PRISMA-ScR) guidelines [18–20]. As this was a literature review, it analysed data from already published original articles and did not involve the recruitment of subjects and, therefore, the ethical approval was not necessary.

3.1. Study selection/search strategy

From July 14, 2021, to July 31, 2021, we systematically searched on PubMed/MEDLINE, Scopus, SciVerse ScienceDirect, and Web of Science the following keywords (employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "work resumption" OR workplace* OR "return to work" OR "work force" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "disseminated sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating"). The details of the search strategy used are reported in Table 1. We decided not to include specific terms due to the expected diversity in concepts and terms related to the central argument of the study. Furthermore, this choice is supported by the traditional scoping review methodology. After the preliminary identification, the articles were exported and managed in Mendeley 1.19.8 (Elsevier, New York, USA).

PubMed	(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")
Scopus	TITLE-ABS KEY [(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR "job retention" OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune Diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")]
SciVerse Science Direct	("employ" OR "occupation" OR "work" OR "vocation" OR "labour" OR "Job" OR "retire" OR "disability pension") AND "multiple sclerosis"
Web of Science	(employ* OR unemploy* OR occupation* OR "work" OR vocation* OR "workplace" OR "workforce" OR "labour force" OR "labor force" OR career* OR job* OR retire* OR "disability pension" OR "worker" OR "fitness for work") AND ("multiple sclerosis" OR "demyelinating autoimmune diseases" OR "demyelinating autoimmune disorders" OR "clinically isolated syndrome" OR "demyelinating")

Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

3.2. Inclusion and exclusion criteria

A priori, we chose a broad search methodology to be able to form an accurate and comprehensive picture of the relationship between the occupational outcomes and MS. The PCC (Population/Concept/Context) framework was used to define inclusion criteria. We included any peer-reviewed original article reporting the occupational outcomes of PwMS between the ages of 18 and 65 years (population). MS must have been diagnosed according to accepted international criteria at the time of the study. No time limits were set for the search. The context was broad and we accepted articles published in English, Italian, Spanish, French, and Portuguese, as these are the languages spoken in our research group (context). The term "occupational outcomes" was defined as direct and indirect work-related characteristics/consequences potentially associated with MS (concept).

After removing duplicate entries, we performed an initial screening of titles and abstracts to assess potential relevance and excluded those not directly or indirectly focused on the topic of interest. Screening of titles, abstracts, and full texts for each article was conducted by two experienced and trained investigators (BKV and AR), each blinded to the other's ratings. In case of discrepancy, a final decision was made by a consensus after a debate with a senior researcher (GD). Afterward, we obtained relevant full-text articles, read all of them, evaluated their eligibility, and determined their final inclusion or exclusion.

Studies written in languages other than the five pre-specified above and studies designed as reviews, letters to the editor, conference abstracts, expert opinions, commentaries, case reports, case series, editorials were excluded. Studies that did not address any aspect of an occupational outcome or that eventually only mentioned it as part of the arguments presented in the introduction or discussion (off-topic articles) were excluded. In case of lack of essential information or full-text not being available, we tried to contact the corresponding author twice to obtain the information by email. Whenever our contact attempt failed, the study was excluded. We did not accept studies where MS was not the primary condition or the subjects had other chronic diseases that could potentially influence the occupational outcomes (e.g. a study that included patients with MS and migraine). Some authors published more than one article with the same study population and reporting the same occupational outcomes. In these cases, we included the most recent one and excluded the others. Figure 1 provides the PRISMA flowchart overview of the search and screening strategy performed.

3.3. Data extraction

Data were extracted in a standardized way by an expert reviewer (BKV) and they were double-checked after two months in order to minimise the intrapersonal variability. We determined the information to extract *a priori*. Among the basic characteristics, we gathered information about the authors' names, the title of the study, the year of publication, the country of origin of the study, the study design, the number of subjects with and without MS, the subtype of the disease, the prevalence of each clinical symptom, the duration of the disease, the distribution by age and sex, the level of education, the marital status, the description of any neuroradiological finding, treatment data, assessment of the QoL and disability, prevalence of fatigue, psychiatric symptoms, and cognitive symptoms. Regarding the occupational outcomes, the following data were collected: the description of the profession, the prevalence of unemployment and early retirement, the influence of the disease on monthly income, the need for disability pension, the indirect cost of MS, the stigma and prejudice faced in the workplace, job characteristics, strategies of vocational rehabilitation and job accommodations, patient opinion on work and working life in general, barriers to employment, degree of job satisfaction, need for a change of employment due to MS, the prevalence of work handicap and information on the disclosure of the diagnosis in the workplace. Job accommodations were defined as any reasonable adjustment to a job or work environment that enables PwMS to perform their job duties. Barriers to employment were defined as any challenge or difficulty that may prevent PwMS from getting or keeping a job or advancing in their career. The definitions of sick leave and absenteeism vary in the literature. We considered sick leave when the absence is granted because of illness. Usually, it takes many days and are due to a specific necessity provoked by the illness. In contrast, we considered absenteeism the habitual non-presence of an employee at their job that is not formally justified to the employer or linked to the illness. Usually, it takes just a couple of days but may be more frequent [21, 22].

3.4. Data synthesis

Following data extraction, due to the range of outcomes assessed and different study designs included in the review, we used a narrative synthesis to report data. This process was carried out after reading the full-text of all the articles included in the review in order to summarize the results as clearly and accurately as possible and cover all the outcomes found. One expert reviewer (BKV) performed a thematic categorization of the findings, which was verified by two other reviewers (AR and AM). The results were categorised into 7 subtopics: “Changes in work and occupational status due to MS”, “work-related socio-economic consequences of MS”, “risk factors for unfavourable occupational outcomes”, “reported barriers to employment”, “reported job accommodations and vocational rehabilitation strategies”, “job satisfaction, stigma, and disclosing the diagnosis in the workplace” and “rating clinical scales”. These subgroups were created to guide the synthesis of the main results reported in the pre-existing literature. We generated a set of statements to adequately represent each subtopic, based on their relevance and degree of evidence.

3.5. Patient and public involvement

No patients or public were involved in the study.

4. Results

Overview of the literature search

The initial systematic search yielded 104,228 results, of which 7,486 were from PubMed, 8,346 were from Scopus, 63,731 were from SciVerse Science Direct 24,665 were from Web of Science. Removing duplicates and applying the eligibility criteria resulted in a total of 1,136 articles. At the end of the study selection, 403 articles were included in the review, and information about the baseline clinical-epidemiological characteristics and the occupational outcomes was properly extracted (Table S1). Figure 1 describes the entire PRISMA-ScR flowchart.

Characteristics of the included literature

The number of studies published on the topic has increased over time, as 154 (38.2%) of the included studies were published in the last 5 years. Most of the studies were conducted in Europe and North America (50.9% and 33.0%, respectively). Asia and Oceania produced 32 (7.9%) and 24 (6.0%) of the studies on the subject, respectively. There were no published data on the association between MS and work from the African continent. Italy, with less than 1% of the world population, promoted the publication of 29 (7.2%) articles on the subject of our study. Regarding the study design, 314 (77.9%) were cross-sectional, 12 (3.0%) were interventional, and 77 (19.1%) were longitudinal. Only 63 (15.6%) studies included a control group in their analysis. In total, the 403 studies evaluated 492,062 subjects with MS. Among the explored characteristics of MS, the assessment of disability and QoL, the type of MS, and the prevalence of fatigue, psychiatric and cognitive symptoms were the most mentioned variables (Table 2). Neuroimaging data and the use of disease-modifying drugs (DMDs) were explored in 10 (2.5%) and 117 (29.0%) studies, respectively.

Clinical and demographic characteristics			**Occupational outcomes**		
	n	%		n	%
Age	394	97.8	Job description	55	13.6
Sex	389	96.5	Work performance	57	14.1
Educational level	288	71.5	Vocational rehabilitation	19	4.7
Civil status	180	44.7	Unemployment	311	77.2
Socioeconomic conditions	47	11.7	Early retirement	120	29.8
EDSS	212	52.6	Disability pension	117	29.3
Disease duration	274	68.0	Sick leave	77	19.1
Type of MS	258	64.0	Impact on monthly income	52	12.9

Neuroimaging findings	10	2.4	Indirect cost of MS	85	21.1
Description of symptoms	59	14.6	Work characteristics	57	14.1
Quality of Life	139	34.4	Barriers to employment	65	16.1
Disability assessment	234	58.1	Job accommodations	45	11.2
Fatigue	169	41.9	Stigma and prejudice	23	5.7
Psychiatric symptoms	209	51.9	Job satisfaction	19	4.7
Cognitive symptoms	160	39.7	Disclosure of the diagnosis in the workplace	17	4.2
Motor symptoms	84	20.8	Professional absenteeism	74	18.4
Treatment (DMDs)	117	29.0	Patients' opinion about work	85	21.9
			Occupational change	78	19.3
			Work disability	38	9.4

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Work was considered as a dependent variable in 285 (70.7%) articles. Eighty-two (28.8%) studies dealt with the description of employment outcomes, 85 (29.8%) aimed to assess the economic impact of MS, 14 (4.9%) described any strategy of vocational rehabilitation, 17 (6.0%) evaluated the QoL in MS in general, 81 (28.4%) determined possible risk factors associated with occupational outcomes and 6 (2.1%) aimed to develop a possible assessment scale of occupational outcomes. The prevalence of unemployment was the most explored variable (311, 77.2%). Other addressed issues were early retirement (120, 29.8%), disability pension (117, 29.0%), sick leave (77, 19.1%), the influence of MS on monthly income (52, 12.9%), the indirect cost of MS (74, 18.4%) and work characteristics (57, 14.1%). Barriers to employment were reported in 65 (16.1%) studies and job accommodations in 45 (11.2%) studies. Perceived stigma in the workplace, job satisfaction, and knowledge of colleagues about MS were less commonly explored aspects in the studies (5.7%, 4.7%, and 4.2%, respectively). Finally, 59 (14.6%) articles examined occupational absenteeism, 85 (21.1%) aimed to understand the patient's opinion on aspects of his professional life, and 19 (4.7%) evaluated strategies of occupational rehabilitation. The definition of each outcome is extremely diverse across studies in order to suit the particularities of the study design and the research context.

Changes in work and occupational status due to MS

MS is a disease that directly influences the patient's professional life [23–26]. PwMS are vulnerable to a spectrum of several negative consequences at work, ranging from reduction of working hours to unemployment. In a Swedish cohort, only 28% and 23% of PwMS were working full- and part-time after a follow-up of 10 years, respectively [27]. A Norwegian study demonstrated that after 19 years of disease, only 45% of patients were still employed [10]. Even for those who remain employed, more than a quarter show some deterioration in employment status and 56% observe a work performance loss in the short term after the diagnosis [28,29]. Moreover, once unemployed, it is difficult for workers with MS to return to the workforce [8]. Pfleger et al. found that the probability of remaining without early pension at 20 years was 22% for patients and 86% for controls [30].

Work-related socio-economic consequences of MS

MS is a debilitating disease that poses a substantial burden in terms of absenteeism, presenteeism, disability pension, and sick leave costs [31–34]. Both employees and employers bear the socio-economic consequences of MS. Employees with MS are significantly more likely to have disability days compared to employees without MS (21.4% vs 5.2%) [35]. Overall, employees with MS had lost over 4 times more workdays compared to their controls (37.7 vs 8.8 days) [36]. In a cohort of 8350 PwMS, two-thirds received a form of benefit [37]. Increased disability as measured on the Expanded Disability Status Scale (EDSS) is strongly associated with reduced earnings and increased benefits [23,37,38] but it is noteworthy that even mild disability can pose a significant economic burden at the expense of premature retirement, premature work disability, and time lost from work [23,31,38,39]. Interestingly, Jennun et al. demonstrated that negative effects on employment and health costs have been shown up to 8 years prior to MS diagnosis [40]. Neusser et al. reported an estimated total expenditure of 4.3 billion euros annually when considering all interventions enabling work-life integration [41]. Studies on the economic impact of MS come from different countries and continents [7,9,42–44], so the interpretation of their findings must necessarily take into account the specific social security systems of different countries.

Risk factors for unfavourable occupational outcomes

Multiple studies have addressed the risk factors associated with worse professional outcomes. The progressive phenotype of the disease is certainly a negative predictor of occupational outcomes in PwMS compared to the relapsing-remitting form [10,39,45]. Older age, longer disease duration, and high EDSS are also associated with a higher risk of unemployment [46–49]. Recently, the link between neuroimaging findings and occupational status has been demonstrated. Tauhid et al. showed that the T1 lesion load, the ratio between the T1 and T2 burden, and the overall brain volume are significantly different between employed and non-employed PwMS [50]. In a cohort of 145 patients followed up to 12 years, severe brain atrophy, T1 and T2 injury load were the best predictors of deterioration of the occupational status [51]. Cognitive impairment, neuropsychiatric symptoms, and fatigue are also well-described risk factors for labor force withdrawal and work productivity loss [28,52,53]. The main reasons reported by people with MS for their loss of employment involved the ineffective management of symptoms of MS in the workplace, rather than workplace-related factors including insufficient flexibility of employment conditions or being dismissed.

Reported barriers to employment

Some studies described the main barriers to employment for PwMS, which may result from the disease itself or circumstances related to the workplace. Cognitive symptoms, pain, fatigue, psychiatric disorders, disease severity, mobility/gait impairment are illness-related factors considered as major barriers to employment [54–57]. In addition, jobs requiring long-distance travel, overly stressful work, limited feedback on performance, hostile supervisors, high-temperature level and inflexible work schedules are some working conditions considered difficult for PwMS [57–59]. Moreover, negative work events have been reported as an important barrier. Workers with MS may be particularly vulnerable to verbal reprimands, decrease in scheduled work hours, reduction of job responsibilities, and mandatory additional retraining [29,60–62]. Kordovski et al. and Frindak et al both demonstrated that negative work events may act as an indicator of an increased risk of unemployment in the short and medium term [61,63].

Reported job accommodations and vocational rehabilitation strategies

Job accommodations are associated with greater chances of retaining occupation. The studies considered work accommodations as reasonable adjustments in the workplace or strategies related to professional re-training and vocational rehabilitation. In a study with 746 workers with MS, participants with a progressive course of the disease, cognitive impairment, a higher number of MS symptoms, and greater symptom severity were more likely to use job accommodations [64]. More than 60% of PwMS who kept their jobs described any type of accommodation and adopting flexible hours as the most frequently reported accommodation [29,65,66]. Other common accommodations are the possibility of working from home and availability of memory aids, additional time to complete tasks, preferential parking, written job instructions, and air conditioning [29,60]. Rumrill Jr. et al. listed the use of equipment/assistive technological resources as being of great importance [66].

Dorstyn et al. verified that sending a standardized, mail-delivered, resource-based package to job seekers with MS improved their vocational self-efficacy, optimism, and identity [67]. Chiu et al. examined the effect of rehabilitation technology interventions on job retention and concluded that this kind of technological tool may ensure better occupational outcomes [68]. Vocational rehabilitation is a topic that interests PwMS, a group of people receptive to this type of initiative [69]. According to these subjects, a program of vocational rehabilitation must address two main points: managing work performance and expectations [70].

Job satisfaction, stigma, and disclosing the diagnosis in the workplace

Almost one-third of patients who remain employed are dissatisfied at work [54] and 20% to 30% of workers do not feel comfortable disclosing their diagnosis in the work environment [29,59,63,71]. Approximately 40% of these patients did not inform the occupational physician about their diagnosis [72]. More often, patients with increased disease severity and longer work experience disclosed their diagnosis [63]. In parallel, PwMS with "invisible" symptoms tend not to disclose. A quarter of PwMS report feelings of stigmatization at work. Stigma is directly associated with poorer QoL, work handicap, and depression [45,55,73].

Rating clinical scales

The EDSS and the Multiple Sclerosis Functional Composite (MSFC) scale have both been associated with employability [74]. Andries et al. designed the Work and Handicap Questionnaire (WHQ) aiming to estimate the degree of work handicap in PwMS, neuromuscular diseases, and asthma based on the association of daily life disabilities and job demands [75]. Although it was not specifically created for PwMS, it showed good reliability. Honan et al. developed a shortened version of the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ) that consists of a 23-item measure of self-reported perceived workplace difficulties in PwMS [76]. Schiavolin et al. designed and validated the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job), which demonstrated to be a useful tool for measuring the work-related difficulties in PwMS [77]. Both MSWDQ and MSQ-Job proved to be comprehensive tools for tracking subjective work-related problems, but they could not be compared with objective occupational outcomes in a longitudinal perspective and were not validated as a predictive tool of unemployment. McFadden et al. created a 22-item, self-administered scale that indicates if PwMS are at low, medium or high risk of work instability [78]. It was further used in a 3-year longitudinal study aimed at assessing the psychological determinants of job retention [79]. Table 3 summarizes all scales associated with occupational outcomes.

Study	**Name**	**Specific for MS**	**Specific for work**	**Longitudinally validated**	**Usefulness**
Andries et al. [75]	Work and Handicap Questionnaire (WHQ)	No	Yes	No	The WHQ makes an inventory of possibly harmful working conditions and of possible strategies to counter health-related work problems by means of the work adjustments.
Gulick et al.[80]	Work Assessment Scale (WAS)	No	Yes	Yes	The WAS evaluates work-impeding and work-enhancing situations and conditions.
Honan et al.[76]	The Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ)	Yes	Yes	No	The MSWDQ measures the workplace difficulties that can predict the necessity of reducing working hours, work withdrawal and expectations in PwMS.
McFadden et al.[78]	MS-specific Work Instability Scale (MS-WIS)	Yes	Yes	No	The MS-WIS indicates low, medium, and high risk of work instability (job retention).
Raggi et al.[77]	Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job)	Yes	Yes	No	The MSQ-Job measures difficulties in work-related tasks.
Honarmand et al.[74]	Multiple Sclerosis Functional Composite (MSFC)	Yes	No	No	The MSFC predicts unemployment.
Busche et al.[48]	EDSS	Yes	No	Yes	The EDSS predicts unemployment.

Table 3. Identified scales described in the literature associated with occupational outcomes.

5. Discussion

The scientific literature on occupational outcomes and MS is vast. Nevertheless, it is possible to identify some important gaps on this subject. The quality of the scientific evidence in this field is still limited due to a significant lack of longitudinal and interventional studies. Few studies have analyzed the evolution of occupational outcomes of PwMS over time, much less the factors that led to an eventual change: there is no scientific evidence that any improvement has occurred in the prevalence of unfavourable occupational outcomes. Indeed, there is no study supporting the hypothesis that a worker with MS in 2022 is not susceptible to the same occupational consequences caused by the disease as 40 years ago. In contrast, over the past 20 years, there have been notable advances in the treatment of MS due to a significant increase in the availability and effectiveness of disease-modifying drugs (DMDs) that, in theory, may have influenced various occupational outcomes [81]. In this scenario, a study that assesses the specific role of DMDs on occupational outcomes is highly encouraged. Likewise, there is a lack of studies that compare the variables related to work based on a geographical perspective (e.g. countries, continents). Furthermore, there is little evidence on the biopsychosocial context related to work disability, as most articles focus only on the relationship between work trajectories and morbidity.

Data about occupational outcomes come from different contexts and study designs. In most cases, occupational outcomes are part of the primary objectives of the studies. The geographical distribution of the origin of the studies is uneven and creates a bias in the interpretation of the results. No article defined the term "occupational outcomes" and the definitions of each variable differed substantially. Our scoping review brings an evidence-based description about the several possibilities of occupational outcomes and shows that it comprises of several possible variables, most of them easily evaluated objectively - such as unemployment or salary reduction. The variables described in the literature comprise potentially reversible outcomes present at the beginning of the illness and outcomes that are generally irreversible and are associated with the end of the professional career.

The literature is unanimous regarding the MS burden on the economy and public health; indeed, the economic impact of the influence of MS on work has driven several research projects. However, the cost-effectiveness of the new DMDs has not been thoroughly studied, considering both the occupational items and the feasible strategies of professional integration concerning their potential benefit in promoting better occupational outcomes with consequent decrease of the economic impact of MS.

Moreover, despite the literature provides a wide description of possible risk factors and work accommodations for PwMS, little evidence exists concerning the possible protective factors associated with occupational outcomes. Most studies are focused on the aspects related to the disease, and few are dedicated to work-related risk factors. Furthermore, the real role of each type of accommodation in promoting favourable occupational outcomes is still unclear due to a lack of studies providing strong evidence (longitudinal and interventional studies).

Our scoping review identified gaps between the patient's interest in receiving technical guidance on how to improve the occupational outcomes and the degree of evidence on this topic. Few studies were dedicated to identifying strategies capable of promoting job retention, work performance, and even return to work. Moreover, most of the strategies of vocational rehabilitation were studied in small samples of subjects and did not consider the particular characteristics of PwMS. Given the still unsatisfactory unemployment rates among PwMS, vocational rehabilitation may be a valuable complementary resource that deserves further research.

There is also extremely limited evidence related to job satisfaction, stigma, and prejudice in the workplace; in this view, it is important to study these outcomes to gauge an individual's overall level of work adjustment. More studies are needed to understand the reasons for not communicating the diagnosis of MS, including to the occupational physician, since the disclosure may be the first step to promote the worker's full integration.

Only few studies tried to develop a scale associated with the occupational outcomes of PwMS. All the proposed scales described the work handicap or job difficulties in restricted samples and mostly in a cross-sectional design. Most of them revealed to be excessively extensive and complex, which represents a limitation for their wide use in clinical practice. The EDSS is the only scale that has already been associated with occupational outcomes as it generally reflects the severity and progression of the disease. However, this evidence comes from secondary analysis of studies and, despite being simple, the EDSS does not include several other factors already proven to specifically influence the professional outcomes, which can also raise concerns about its sensitivity. The development of a simple and validated scale should be the subject of future studies, as it may represent an easy-to-use tool capable of supporting a more objective and uniform assessment of PwMS by physicians with different backgrounds.

Finally, no study addressed how the new ways of working in the 21st century interfered with the occupational outcomes of PwMS. The nature and the pattern of work have undoubtedly changed in the last 20 years [82] and it is reasonable to imagine that PwMS may find more alternatives and resources to ensure a fruitful professional life. Possibly, technological advances in the workplace may even relativize the concept of work disability. PwMS with the same clinical characteristics can be classified with different degrees of work disability depending on the technological adjustments that help them perform their work. It is reasonable to imagine that a few decades ago, a worker with MS could easily be considered unfit for work, while today's modernisation of types of work and the provision of various technological resources may contribute to delay the definitive endpoint of inability to work.

This is the first scoping review dedicated to the occupational outcomes of PwMS. We highlight that a broad and rigorous search strategy was used to properly include all relevant studies describing the occupational outcomes of MS and promote reliable and accurate results. We applied a range of outcome possibilities that allowed us to accurately understand the evidence related to the impact of MS in the occupational setting. The wide variability of aspects, outcomes, and measures identified motivated the breadth of our methods. This review highlighted several opportunities for new research on the topic. Among the limitations of the study, we did not formally assess the quality of included studies, as we respected the scoping review approach. We could also have missed some data for not including results from the grey literature. Notwithstanding, we intended to disclose the current reality regarding the highest scientific evidence in the field of MS and work and, therefore, the selection of peer-reviewed articles seemed more appropriate. We decided not to use specific terms in our search strategy which may have excluded some articles from our review. Nevertheless, there is an infinite number of possible specific words and synonyms that could be characterised as occupational outcomes so that it would be impossible to cover all the possibilities. Finally, the definitions of each variable changed significantly according to the study, so that, as usually happens with systematic reviews, it was not possible to standardise a definition for each one of them.

6. Conclusions

This is the first scoping review dedicated to the occupational outcomes of PwMS. MS is a chronic neurological disorder that is often associated with disabilities and significant impairment of professional life. Many studies have already been published on the subject and several outcomes have been described. Nevertheless, there are still several issues that deserve further in-depth study by the scientific community in order to match the quality of scientific evidence to the undeniable complexity inherent in this topic.

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Legends

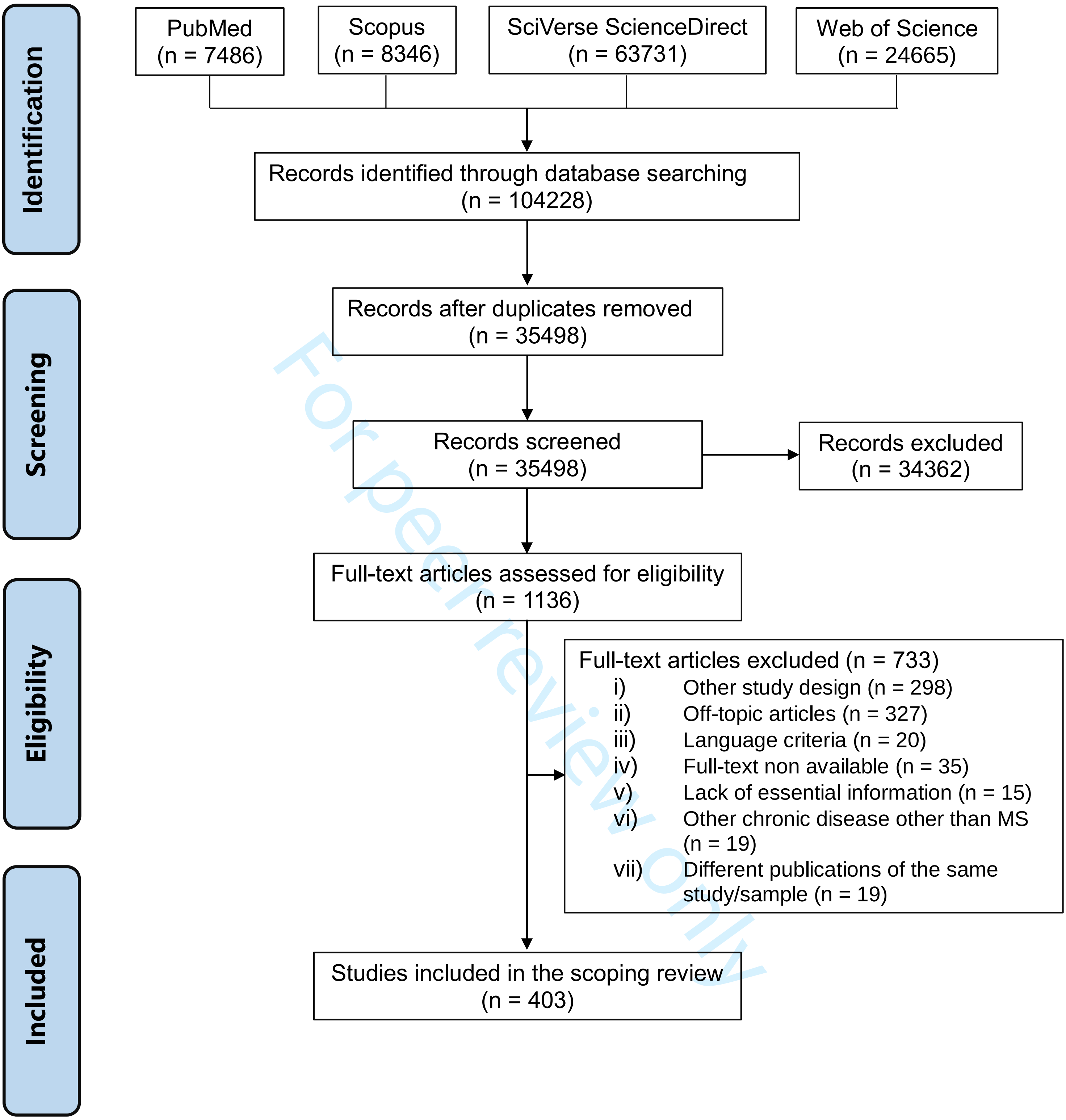
Table 1. Detailed search strategy in PubMed, Scopus, SciVerse Science Direct and Web of Science.

Table 2. Clinical, epidemiological and occupational variables reported in the 403 studies.

Table 3. Identified scales described in the literature associated with occupational outcomes.

Figure 1. PRISMA flowchart.

Table S1. Complete list of all articles included in the scoping review.


Identification
Screening
Eligibility
Included
PubMed (n = 7486)
Scopus (n = 8346)
SciVerse ScienceDirect (n = 63731)
Web of Science (n = 24665)
Records identified through database searching (n = 104228)
Records after duplicates removed (n = 35498)
Records screened (n = 35498)
Records excluded (n = 34362)
Full-text articles assessed for eligibility (n = 1136)
Full-text articles excluded (n = 733)
i) Other study design (n = 298)
ii) Off-topic articles (n = 327)
iii) Language criteria (n = 20)
iv) Full-text non available (n = 35)
v) Lack of essential information (n = 15)
vi) Other chronic disease other than MS (n = 19)
vii) Different publications of the same study/sample (n = 19)
Studies included in the scoping review (n = 403)

AUTHOR	**TITLE**	**YEAR**	**COUNTRY**
Abbas et al. [1]	Caractéristiques des personnes atteintes d'une sclérose en plaques selon la situation professionnelle	2008	France
Abbasi et al.[2]	Risk factors of Multiple sclerosis and their Relation with Disease Severity: A Cross-sectional Study from Iran	2016	Iran
Abdulla et al.[3]	Factors that influence quality of life in patients with multiple sclerosis in Saudi Arabia	2021	Saudi Arabia
Abdullah et al.[4]	MS People's Performance and Satisfaction With Daily Occupations: Implications for Occupational Therapy	2017	Kuwait
Abolhassani et al. [5]	Social aspects of multiple sclerosis for Iranian individuals	2014	Iran
Ahmad et al.[6]	The increasing economic burden of multiple sclerosis by disability severity in Australia in 2017: Results from updated and detailed data on types of costs	2020	Australia
Ahmadi et al.[7]	Relationship Between Anxiety and Depression with Disability Over Multiple Sclerosis Patients in Rafsanjan, Iran	2018	Iran
Akbar et al.[8]	A mixed-methods study of cognitive performance in persons with multiple sclerosis: Association between neuropsychological test performance and interviews about daily cognitive functioning	2021	Canada
Al-Asmi et al. [9]	Magnitude and concurrence of anxiety and depression among attendees with multiple sclerosis at a tertiary care Hospital in Oman	2015	Oman
Alhussain et al. [10]	Multiple Sclerosis Patients in Saudi Arabia: Prevalence of Depression and its Extent of Severity.	2020	Saudi Arabia
Alosaimi et al. [11]	Psychosocial predictors of patient adherence to disease-modifying therapies for multiple sclerosis	2017	Saudi Arabia
Alsharie et al. [12]	Stressful life events and the risk of primary progressive multiple sclerosis: A population-based case-control study	2021	Iran
Alshubaili et al. [13]	Relationship of depression, disability, and family caregiver attitudes to the quality of life of Kuwaiti persons with multiple sclerosis: a controlled study	2007	Kuwait
AlZahrani et al. [14]	Association of acute stress with multiple sclerosis onset and relapse in Saudi Arabia	2019	Saudi Arabia
Amaducci et al.[15]	Multiple sclerosis among shoe and leather workers: an epidemiological survey in Florence.	1982	Italy
Amato et al.[16]	Cognitive impairment in early-onset multiple sclerosis. Pattern, predictors, and impact on everyday life in a 4-year follow-up.	1995	Italy
Amato et al.[17]	Cognitive Dysfunction in Early-Onset Multiple Sclerosis	2001	Italy

Andries et al.[18]	Working with a chronic disorder--the development of the Work and Handicap Questionnaire.	2004	The Netherlands
Archibald et al. [19]	Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients	1994	Canada
Aronson et al.[20]	Quality of life among persons with multiple sclerosis and their caregivers	1997	Canada
Arroyo et al.[21]	Correlation between spasticity and quality of life in patients with multiple sclerosis: the CANDLE study	2013	Spain
Artemiadis et al.[22]	Structural MRI correlates of cognitive function in multiple sclerosis	2018	Greece
Babamohamadi et al. [23]	Dimensions of Adaptation, General Health, and life Satisfaction in Multiple Sclerosis	2016	Iran
Bamer et al.[24]	Validation study of prevalence and correlates of depressive symptomatology in multiple sclerosis.	2008	United States
Barin et al.[25]	Patterns of care for Multiple Sclerosis in a setting of universal care access: A cross-sectional study	2019	Switzerland
Baroin et al.[26]	Validation of a new quality of life scale related to multiple sclerosis and relapses.	2013	France
Barzegar et al.[27]	Comparative study of quality of life, anxiety, depression, and fatigue among patients with neuromyelitis optica spectrum disorder and multiple sclerosis: The first report from Iran	2018	Iran
Bass et al.[28]	Effect of Multiple Sclerosis on Daily Activities, Emotional Well-being, and Relationships: The Global vsMS Survey.	2020	Europe
Battaglia et al. [29]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Italy	2017	Italy
Baughman et al. [30]	Staying on the job: The relationship between work performance and cognition in individuals diagnosed with multiple sclerosis	2015	US
Baumstarck et al. [31]	Health-related quality of life as an independent predictor of long-term disability for patients with relapsing–remitting multiplesclerosis-remittingmultiplesclerosis:A2-yearlongitudinalstudy	2013	France
Baumstarck et al. [32]	Is the Concept of Quality of Life Relevant for Multiple Sclerosis Patients with Cognitive Impairment? Preliminary Results of a Cross-Sectional Study	2012	France
Bayas et al.[33]	Combination treatment of fingolimod with antidepressants in relapsing–remitting multiple sclerosis patients with depression: a multicentre, open-label study – REGAIN	2016	Germany
Beatty et al.[34]	Demographic, Clinical, and Cognitive Characteristics of Multiple Sclerosis Patients Who Continue to Work	1995	US
Beatty et al.[35]	Changes in neuropsychological test performance over the workday in multiple sclerosis	2003	US/Italy

Becker et al.[36]	Patient satisfaction and healthcare services in specialized multiple sclerosis centres in Germany	2018	Germany
Beier et al.[37]	Relationship of perceived stress and employment status in individuals with multiple sclerosis.	2019	US
Benedict et al.[38]	Predicting neuropsychological abnormalities in multiple sclerosis	2006	US
Benedict et al.[39]	Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change	2005	US
Benedict et al.[40]	Negative work events and accommodations in employed multiple sclerosis patients.	2013	US
Berg et al.[41]	Costs and quality of life of multiple sclerosis in Sweden.	2006	Sweden
Bessing et al.[42]	Changes in multiple sclerosis symptoms are associated with changes in work productivity of people living with multiple sclerosis	2021	Australia
Birnbaum et al.[43]	Economic impact of multiple sclerosis disease-modifying drugs in an employed population: direct and indirect costs	2008	US
Bishop et al. [44]	The relationship between housing accessibility variables and employment status among adults with multiple sclerosis	2013	US
Bishop et al. [45]	Employment Among Working-Age Adults With Multiple Sclerosis: A Data-Mining Approach to Identifying Employment Interventions	2015	US
Bishop et al. [46]	Life domains that are important to quality of life for people with multiple sclerosis: A population-based qualitative analysis	2019	US
Bishop et al. [47]	Sources of information about multiple sclerosis: Information seeking and personal, demographic, and MS variables	2009	US
Bishop et al. [48]	The relationship of self-management and disease modifying therapy use to employment status among adults with multiple sclerosis	2009	US
Bishop et al. [49]	Quality of life among people with multiple sclerosis: Replication of a three-factor prediction model	2015	US
Björkenstam et al.[50]	Heterogeneity of sickness absence and disability pension trajectories among individuals with MS	2015	Sweden
Björkenstam et al.[51]	Is disability pension a risk indicator for future need of psychiatric healthcare or suicidal behavior among MS patients- a nationwide register study in Sweden?	2015	Sweden
Blinkenberg et al.[52]	Increased socioeconomic burden in patients with primary progressive multiple sclerosis: A Danish nationwide population-based study	2020	Denmark

Bo et al.[53]	Access to social security benefits among multiple sclerosis patients in Italy: A cross-sectional study.	2018	Italy
Bøe Lunde et al.[54]	Employment among Patients with Multiple Sclerosis-A Population Study	2014	Norway
Bonafede et al. [55]	Productivity Loss and Associated Costs Among Employed Patients Receiving Disease-Modifying Treatment for Multiple Sclerosis	2021	US
Boyko et al.[56]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Russia	2017	Russia
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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3, 4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	5
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5, 6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5, 6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7, 8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	7, 8
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	8-12
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	8-12
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	12-15
Limitations	20	Discuss the limitations of the scoping review process.	15
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	1

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.