Work-related problems in multiple sclerosis: a literature review on its associates and determinants

Alberto Raggi, Venusia Covelli, Silvia Schiavolin, Chiara Scaratti, Matilde Leonardi, and Michelle Willems

Neurology, Public Health and Disability Unit, Neurological Institute Carlo Besta IRCCS Foundation, Milan, Italy

Abstract

Purpose: To explore which variables are associated to or determinants of work-related difficulties or unemployment in persons with multiple sclerosis (MS).

Method: Papers published between 1993 and February 2015 were included. Quality was judged as poor, acceptable, good or excellent. Determinants were extracted from prospective and retrospective data, associated variables from cross-sectional data; variables were grouped by similarity. Evidence was judged as strong if there were at least two good studies reporting the same results; limited if there was only one good and some acceptable studies.

Results: Forty-two papers were selected, for a total of 31,192 patients (75% females). Work-related difficulties were referred as unemployment, lower amount of worked hours or job cessation. Strong evidence of impact over work-related difficulties was found for a core set of variables, i.e. expanded disability status scale, MS duration, patients' age, fatigue and walking problems. Little evidence exists on the impact of contextual factors.

Discussion: Most of the variables identified as associated to or determinants of work-related difficulties can be treated through rehabilitative interventions. It is important that future research addresses not only unemployment issues in MS, but also the amount and severity of problems affecting work-related tasks relying on specific assessment instruments.

Keywords

Employment, ICF classification, multiple sclerosis, review, work

Implications for Rehabilitation

- Multiple sclerosis (MS) affects young persons of working age and limitation in work activities is part of MS-related disability, but they are not consistently addressed in MS research: EDSS, MS duration, patients' age, fatigue, walking problems, cognitive and neuropsychological impairments were the factors most commonly found as associated to or determinant of difficulties with work.
- Evidence exists that rehabilitation interventions are effective for fatigue, cognitive impairment, mobility and walking difficulties. However, research did not address the impact of rehabilitation programmes on vocational outcomes.
- Rehabilitation researchers should include MS-specific assessment instruments for work-related difficulties to standardised clinical protocols, so that the benefits of rehabilitation on persons' ability to work can be demonstrated directly: in this way, cost-benefit balance analyses can be added to the evaluation of treatment effectiveness.

Introduction

Multiple sclerosis (MS) is a disorder of the central nervous system characterised by inflammatory demyelination, axonal loss and formation of sclerotic plaques on an autoimmune basis. Its incidence is 4.3/100,000 and prevalence is 54–232/100,000 and is higher in northern countries and among young adult females aged 20–40 years [1–3]. MS is characterised by a great variety of symptoms, involving motor, sensory, visual and autonomic systems [4], and therefore the kind of activities in which patients might experience limitations is extremely wide (e.g. walking or moving objects, communication, self-care): among them, difficulties in work-related activities are outstanding, in consideration of the young age of patients and of the chronic course of the diseases. Unemployment is in fact a relevant problem for MS patients: as a large cross-sectional study carried out in nine European countries has shown, only 35.8% of MS patients (40.9% among those aged below 65) are employed [5].

Despite this, unemployment issues in MS are only partially tackled. As concluded in a recent literature review [6], difficulties that people with MS can experience with employment are always secondary outcomes of research, thus it is quite difficult to
address which factors contribute to increased difficulties and determine reduced workforce participation. Fatigue, mobility impairments and cognitive impairments were reported as the main drivers of unemployment [6]. In an attempt to add information on specific work-related difficulties in MS patients, we performed a literature review, whose aims were to explore – beyond crude information on employment or unemployment rates – which variables are associated to presence of work-related difficulties or unemployment and which variables are determinant of work loss or increased work-related difficulties.

Methods

Search strategy

We performed a search on PubMed covering the period January 1993–February 2015 searching for peer-reviewed papers that reported issues on work-related problems in patients with MS. Search criteria in titles and/or abstracts were the following: Multiple Sclerosis AND (work* OR employ* OR job* OR jobless* OR occupation* OR vocation* OR unemployment*).

Papers’ inclusion and exclusion criteria

Papers had to be written in English, have an abstract and be primary research articles, i.e. clinical trials and observational studies, either cross-sectional or longitudinal. Literature reviews, meta-analyses, commentaries, letters to the editors, editorials, case reports, qualitative studies, phase I and II studies were excluded.

The content of papers needed to enable the extraction of information on the impact of clinical or psychosocial variables on work performance or work participation in MS patients: therefore, papers had to report some information on employment or difficulties in work-related activities and this had to be connected to specific features measured in the study. Studies reporting employment rates only were excluded, as this would not enable to understand if the results were strictly connected to the specificity of the sample or not. Similarly, studies in which MS was not adequately defined (i.e. not diagnosed by a clinician) or in which MS was not the primary condition were excluded. Finally, studies in which employment issues (e.g. being a white or blue collar worker) were used as a predictor of other variables (e.g. disability, quality of life (QoL) or incidence of MS) were excluded too.

Paper selection and data extraction

Abstracts of papers that were selected from database searches were screened by an experienced researcher. To ensure quality and consistency of data extraction, 20% of the abstracts and of full-texts were randomly selected for a second check by another reviewer who was blind to the decision of the first one. If agreement rates were below 70%, each of double-checked abstract or manuscript was reviewed again by the two researchers to get to a final decision by consensus. An evaluation of the quality of each manuscript was performed using the guidelines of the National Institute for Health and Clinical Excellence (NICE) [7]: papers’ quality of the study was judged poor (1), acceptable (2), good (3) or excellent (4), and those with poor quality were excluded.

Extracted information was referred to the description of the variables that are associated or determinants of work-related problems. Determinants were extracted exclusively from prospective and retrospective studies, while variables associated with work-related problems were collected from cross-sectional studies or from cross-sectional analysis in longitudinal studies; for this reason, study design was classified as cross-sectional or prospective/retrospective. The main characteristics of the study population that were reported included sample size, percentage of female, age, MS duration, MS type – i.e. relapsing-remitting MS (RR), primary progressive or secondary progressive MS (PP or SP) – the Expanded Disability Status Scale (EDSS) [8] when available.

Two steps were followed to synthesise extracted information. First, variables referred to associates or determinants of work-related difficulties were grouped by similarity of content into overarching categories according to Popay’s guidelines on how to analyse narrative reviews [9]. Second, following a methodology recently used in some literature reviews on the difficulties experienced by patients with brain disorders [10–14], evidence was judged as strong if there were at least two good studies reporting the same results; limited if there was only one good and some acceptable studies reported the same result; controversial in case there were studies reporting contrasting results; in case the result was reported in one study only, or if no good study reported the result, the evidence was judged as inconsistent. Data were synthesised dividing associates and determinants of work-related difficulties, and only information on strong and on limited evidence are described. Information on inconsistent evidence is reported in the supplementary Table S1.

Results

As reported in Figure 1, a total of 771 records were identified, 155 abstracts were double-checked (89% of agreement): 172 records were retained for full-text analysis, but five were not found, thus leaving 167 full-texts candidate for data extraction. Double check was performed on 33 full-texts, with a low level of agreement (54.5%): the two reviewers (A. R. and V. C.) therefore discussed the full-texts with discordant decisions and, at the end of the process, data referred to 42 papers were extracted [15–56]. Table 1 reports the main descriptive data on selected studies: most of them were cross-sectional studies (30 of 42), eight were longitudinal prospective studies and four were retrospective studies. In total, data on 31 192 patients were reported of whom 75% were females, with an aggregate mean age of 48.7, MS duration 14.8 years, 58.7% with RR-MS. Aggregate mean employment rate was 51.6%, with six studies being carried out on a sample of employed persons only. Please refer to the supplementary material for information on data extracted from each single article.

Work-related difficulties were mostly referred as unemployment, in particular in cross-sectional studies, or as a lower amount of hours worked per week (i.e. part-time work). In prospective and retrospective studies, the concept was mostly referred to as job cessation, reduction in the amount of worked hours. Occasionally, limitations in work activities or reduction of work responsibilities (e.g. moving to a lower-level job duties) were used as outcomes of work-related difficulties.

A total of 48 variables were found to be associated to work-related difficulties in MS patients: these were reported on 141 occasions from 36 papers. For 19 of them there was a strong evidence of impact, for 7 a limited evidence, and for the remaining 22 the evidence was inconsistent. A total of 18 variables were found to be determinants of change in the course of work-related difficulties in MS patients: these were reported on 41 occasions from 11 papers. For six of them there was a strong evidence of impact, for four a limited evidence, and for the remaining eight the evidence was inconsistent. Most of the determinants were determinants of negative course: the exception to this was for Natalizumab. For no variables, either associated or determinant, a contrasting evidence was found. Table 2 reports information on associated variables and determinants.
Strong evidence exists that males have lower workforce participation compared to female counterparts, with employment rates that were 4–25.8% lower [15–17] and up to 4.8 the odds of being unemployed [18,19].

There was strong evidence that older age is associated to lower workforce participation [15,16,20]. Higher age was also found, with strong evidence, as a determinant of work-related problems, defined as reduction in amount of hours worked per week [21–23], unemployment [23–25] or loss of employment [16,26].

There was a strong evidence that education level is associated to work-related difficulties. Patients with lower education levels had 0.21–0.52 the odds of being able to work or employed [18,27,28], and between 16.2% and 39.8% lower employment rates [15]. In another study, worker respondents showed higher levels of education [29]. Limited evidence was found that low-education level is a predictor of work loss and unemployment [23,26].

**Table 1. Main features of selected studies.**

|                      | Cross-sectional \((N = 30)\) | Prospective or retrospective \((N = 12)\) | Total \((N = 42)\) |
|----------------------|------------------------------|------------------------------------------|-------------------|
| Sample size          |                              |                                          |                   |
| Total                | 19 985                       | 11 207                                   | 31 192            |
| Mean (min–max)       | 666 (33–8180)                | 934 (50–8867)                            | 742 (33–8867)     |
| Females % (min–max)  | 73.9 (60.8–90.7%)            | 74.4 (56.3–87.4%)                       | 74.1 (56.3–90.7%) |
| Aggregate mean age   | 49.6 (37–57.5)               | 46.9 (37.5–54.9)                        | 48.7 (37–57.5)    |
| Percentage employed  | 52.7 (14–100%)               | 49.7 (34.4–100%)                        | 51.6 (14–100%)    |
| Full-time (%)        | 45.8                         | 55.5                                     | 50.4              |
| Part-time (%)        | 54.2                         | 44.5                                     | 49.6              |
| Unemployed (%)       | 47.3                         | 50.3                                     | 48.4              |
| Disability pension (%) | 74                           | 89.6                                     | 74.8              |
| Relapsing-remitting MS (%) | 53.8                      | 79.5                                     | 58.7              |
| Progressive MS (%)   | 41.3                         | 24.4                                     | 40.6              |
| Primary progressive (%) | 25.3                        | 35.2                                     | 25.6              |
| Secondary progressive (%) | 67.9                        | 61.5                                     | 67.7              |
| MS duration, mean (Min–max) | 13.4 (1.1–22.2)        | 17.4 (2.6–27.2)                         | 14.8 (1.1–27.2)   |
| EDSS                 | 3.8 (1.5–6.4)                | 3 (1.5–4.6)                              | 3.7 (1.5–6.4)     |
| Average quality (mean ± SD) | 2.5 ± 0.6                   | 2.7 ± 0.6                                | 2.6 ± 0.6         |

Percentages are calculated for valid categories, thus the sum does not always correspond to 100%. In particular, 0.7% of patients were not diagnosed with relapsing-remitting or progressive MS, but either with clinically isolated syndrome or with relapsing-progressive MS.

**Demographic variables**

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Table 2. Variables associated and determinants of work-related difficulties in MS patients.

| Overarching category | Variables                              | Associated variables | Determinants |
|----------------------|----------------------------------------|----------------------|--------------|
| Demographic issues   | Male gender                            | 5*                   | –            |
|                      | Age                                    | 3*                   | 7*           |
|                      | Low education                          | 5*                   | 2            |
| MS features          | EDSS score                             | 12*                  | 6*           |
|                      | Older age at onset                     | 2*                   | –            |
|                      | MS duration                            | 9*                   | 3*           |
|                      | Progressive course                     | 4*                   | –            |
| Neurological symptoms| Fatigue                                | 11*                  | 5*           |
|                      | Pain                                   | 3                    | –            |
|                      | Brainstem symptoms (onset)             | 2                    | –            |
|                      | Cerebellar symptoms (onset)            | 2                    | –            |
| Psychological and neuropsychological symptoms | Information processing speed | 5*                   | 2            |
|                      | Cognitive dysfunction                  | 4*                   | 2            |
|                      | Working memory                         | 7*                   | –            |
|                      | Memory                                 | 5*                   | –            |
|                      | Attention                              | 7*                   | –            |
|                      | Low mood                               | 6*                   | 2            |
|                      | Anxiety                                | 3                    | –            |
| Mobility             | Mobility problems                      | 6*                   | –            |
| Daily activities     | Walking problems                       | 3*                   | 2*           |
|                      | ADL difficulties                       | 3*                   | –            |
|                      | Problems with physical activities      | 2*                   | –            |
| Treatment            | Natalizumab                            | –                    | 3*           |
| Contextual factors   | Negative environment                   | 2                    | –            |
|                      | Interpersonal difficulties             | 2*                   | –            |
| Other issues         | Quality of life                        | 4                    | –            |
|                      | MS Impact on daily life (MSIS-29)      | 2                    | –            |

Items marked with * are indicative of strong evidence.

**MS features**

We found strong evidence that higher EDSS score is associated to reduced work capacity [30], more problems at work [31], more frequent short-term and long-term work absence [32] and higher unemployment rates [15–17,20,33], with those with EDSS > 6.5 having up to 12.3 the odds of being unable to work [18,27,34], and having less than 3% of the probability of being employed [28]. We found strong evidence that higher EDSS is a determinant of work-related problems, defined as reduction in amount of hours worked per week [21,22], loss of employment [16,23,35] or unemployment [23,24].

There was strong evidence that older age at onset was associated to worse employment outcomes. For each year of age at onset there was 8% of increased risk of being unemployed [19] and, in another study, employed patients were found to have MS onset approximately 3 years before compared to unemployed ones [28].

There was strong evidence that increased MS duration is associated to and determinant of higher unemployment rates, with unemployed patients having between 3.2 and 7 years of MS duration more than employed ones [15–17,20,28,30,33,36] and more limitations in work activities [37]. Higher disease duration was also found as a determinant of reduction in amount of hours worked per week [21,22] and unemployment [23].

Finally, there was strong evidence that patients with progressive MS course, irrespectively of disease duration, are more likely to be unemployed: patients with a progressive MS course had unemployment rates 27–44.3% higher compared to those with relapsing course [23,28,38], with 4.2 the odds of being unemployed [34].

**Neurological symptoms**

There was a strong evidence that fatigue is associated to work-related problems. Unemployed MS patients had higher scores at fatigue measures [17,28,34,39–41], and fatigue measures were correlated to capacity to work and work limitations, likelihood of reducing the amount of work, changing work type and leaving work [25,27,37,39,42,43]. The evidence of a negative impact of fatigue as a determinant of work-related problems was strong as well. Improvement in fatigue was found as determinant of improvement in work-related ability and increase in the amount of hours worked [21] and in reduction of sick leave [44], while worsening of fatigue was found to be a determinant of work loss [23,26,29].

Limited evidence was found for the association between pain, brainstem and cerebellar symptoms at onset and work-related problems. Presence of pain was associated to higher likelihood of reducing the amount of work, changing work type, leaving work [42], and unemployment status [40,45]. Patients with brainstem and cerebellar symptoms at onset had up to 8.5 the odds of being unemployed compared to those with visual or sensory symptoms [19], and up to 36 the odds of being unemployed in the early stages of MS course (i.e. with EDSS scores below 2.0) [18].

**Psychological and neuropsychological symptoms**

In this area, the level of evidence referred to neuropsychological symptoms, i.e. impairment in working memory, information processing speed, cognitive dysfunction, attention and memory, was much more frequently reported than that referred to psychological ones (low mood and anxiety).

There was a strong evidence that information processing speed was associated to and determinant of work-related difficulties. Unemployed patients had worse scores at neuropsychological evaluation [17,18,33,36] and increased impairments in these measures were also associated to likelihood of having higher limitations in work activities [37]. Limited evidence was found that worsening of scores at neuropsychological testing are determinants of work cessation [24] and reduction of work responsibilities [46].
In six papers [24,26,27,36,42,47], a generic statement on the presence of some kind of cognitive dysfunction was made. Strong evidence was found on the association between such a kind of neuropsychological impairment and presence of work-related difficulties, defined as likelihood of reducing the amount of work, changing work type and leaving work [37,42], and working less days per week [48]. In three papers, a generic assessment of memory function was performed, and there is strong evidence that memory impairment is associated to higher unemployment rates [40,41,47], likelihood to leave job [25] and higher odds of absenteeism and work impairment [49].

There was a strong evidence that impairment of working memory is associated to work-related problems, defined as unemployment [17,18,33,47], having limitations in work activities or higher likelihood of reducing the amount of work, changing work type and leaving work [37,42], and working less days per week [48]. In three papers, a generic assessment of memory function was performed, and there is strong evidence that memory impairment is associated to higher unemployment rates [40,41,47], likelihood to leave job [25] and higher odds of absenteeism and work impairment [49].

Strong evidence was found that attention problems were associated to higher unemployment rates [18,36,47], higher odds of absenteeism and work impairment [49], and reduced amount of days worked per week [48]. Moreover, unemployed patients had worse scores at attention tests [33] and those with attention impairments were more likely to leave job [25].

There was a strong evidence on the association between work-related difficulties and reduced mood levels. Patients with low mood were more likely to work less days per week [48], had between 17% and 40% higher odds of being unemployed [18,19], and unemployed patients had higher scores at depression tests [15,29,33]. Limited evidence was also found that depression was a predictor of a higher probability of quit working [23,29]. With regard to anxiety, limited evidence exists that unemployed patients had higher scores at anxiety tests [15,50], and were more likely to have limitations in work-related activities [37].

Mobility

There was a strong evidence that problems with mobility are associated to work-related difficulties, in terms of higher likelihood of reducing the amount of work, changing work type and leaving work [42], working part-time or not working at all [29,40,47,51]. Mobility problems were associated also to more severe difficulties in work-related activities [52].

More specifically, strong evidence was found that walking difficulties were both associated to and determinant of work-related problems. Reduced walking capacity was associated to unemployment [47], presence of problems in the workplace [31], and frequency of sick leave [44]. Increase in walking difficulties and use of ambulatory aids was a predictor of job cessation [29], while improvement in walking capacity predicted the reduction of sick leave [44].

Daily activities

There was a strong evidence that unemployed patients had higher difficulties in activities of daily living (ADL) and personal independence [20] and that patients with good scores at ADL measures had 15% the possibility of being unemployed (i.e. those with scores had 6.7 the odds of being unemployed) [53]. Patients self-declaring needs for support in performing daily activities also had more difficulties in work-related activities [52].

Strong evidence on the association between problems in physical activities and employment was also found: unemployed patients had more problems in physical activities than those employed [41], and having problems in physical activities was associated to unemployment [53].

Treatment

Strong evidence was found that treatment with Natalizumab predicted an improvement in work-related problems [21,22] in terms of the amount of worked hours that increased by 3.3 hours/week, as well as in terms of reduction of sick leave period, that was reduced by 33% [44].

Contextual factors

Limited evidence exists that negative work environment, defined as non-supportive workplace and workplace inaccessibility, was associated to higher odds of reducing the proportion of worked hours [42] or increasing the likelihood of having left work [40,42].

Strong evidence exists that difficulties with interpersonal relationships are associated to work-related problems, which were found to be correlated to difficulties with participation in social situations and with personal interactions [52]. In another study, unemployed patients had in fact more problems with interpersonal relationships [42].

Other issues

There was a limited evidence on the association between QoL and work-related problems. Patients who had no capacity to work reported worse QoL scores than those that had capacity to work [27], and presence of more and more severe problems at work was associated with worse QoL scores [54]. In two studies, correlation analyses were used: QoL scores were correlated to a measure of difficulties in work-related activities, so that worse QoL was associated to more and more severe difficulties [52], and a moderate association between employment status and higher QoL was found in another study [30].

Two studies addressed the impact of MS on physical and psychological domains, showing a limited evidence of the association of MS impact and work-related problems. In a first study, presence of moderate to severe problems with employment was associated to higher MS impact and, vice versa, no or minimal problems with employment were associated to lower MS impact [54]. In a second study, higher MS impact was correlated with less working hours per week, and with lower amount of daily worked hours [48].

Discussion

With this review, we aimed to assess the level of evidence on the clinical, social and personal variables that are either associated to or determinants of work-related difficulties, unemployment or work loss in persons with MS. Our results show that a core set of variables, namely EDSS score, MS duration, patients’ age, presence of fatigue and walking difficulties, are associated to and determinants of increased work-related difficulties. A strong evidence of the association between the mental impairment and work-related difficulties was found: the only exception to this concerns anxiety. Other factors associated to work-related difficulties were male gender, older age at onset and progressive course, presence of mobility problems, problems with ADL, general difficulties with physical activities and, finally, presence of interpersonal difficulties. The only determinant of improvement in work-related difficulties was therapy with Natalizumab. Most of the studies conceptualised work-related difficulties as unemployment and the average employment rate was 51.6%, well-balanced between full-time and part-time workers: such a figure is higher than that reported in previous reports, indicating employment rates between 36% and 41% [5,6].

Three of the five most relevant associates and determinants are strictly connected one to the other: although the course of MS is
difficult to predict and some patients may keep on having low EDSS after several years (i.e. the controversial benign MS [57]), it is clear that longer disease duration, higher EDSS scores and older patients’ age are largely overlapping concepts, with a relatively limited possibility for a clinical impact. New emerging treatments, e.g. Fingolimod [58] or Natalizumab [59], are expected to reduce relapse rates and disability progression in patients with RR-MS: evidence was found in two studies that Natalizumab also had effect reduction of work-related difficulties. Our results show that longer disease duration, higher EDSS and older age are associated to reduced workforce participation and higher difficulties in work-related activities. The same was found for disease progression: it has to be noted that patients with progressive MS generally have longer disease duration, older age and later age at onset [28,60], and therefore it is little surprising that they were more likely to be unemployed.

The other two main issues are related to presence of fatigue and walking difficulties. Treatment of fatigue can be based on pharmacotherapy [61,62] or on rehabilitation programmes [63–66]. Walking ability is also susceptible of treatment through rehabilitation [67,68], with possibility to plan also pharmacological and robot-assisted interventions. In brief, literature shows that both fatigue and walking ability are associated to and determinants of work-related difficulties, and can be improved through rehabilitative programmes. Therefore, rehabilitation treatments specifically addressing the impact over vocational abilities of the reduction of fatigue and improvement of walking abilities should be pursued.

The reduction in relapse rates and disability progression are among the main aims of medical therapy of MS and there is good evidence that new treatments are likely to limit disease progression [58,59]. It is therefore expected that, with these treatments, patients will be able to keep on working for a longer period. Other symptoms can be treated, with a possible impact on increased employability and vocational outcomes: examples of this include pain [69,70], reduced mood or anxiety [71–74] and other neuropsychological impairments, e.g. information processing speed, executive functions, memory and attention that are among the most relevant mental health symptoms of MS [75,76]. Our results provided strong evidence that impairments in cognitive functions were associated to lower employment rates and more difficulties with work tasks: however, the evidence that cognitive dysfunction in general, and information processing speed impairment in particular, were determinants of work-related problems was limited. In our opinion, the reason for this limited evidence mostly lies in the lack of longitudinal studies that systematically address such a relationship. The body of evidence on the effect of cognitive rehabilitation in MS is controversial. A recent review found that cognitive training, also in combination with other neuropsychological rehabilitation methods, improves attention, memory span, working memory, immediate verbal memory and delayed memory [77]. Previous reviews found benefit of neuropsychological rehabilitation approaches for attention, executive functions, learning and, again, memory [78,79]. The possibility to impact on cognitive functions with rehabilitation programmes has a profound relevance for rehabilitation professionals, as these programmes are likely to impact on patients’ ability to keep on working and participating to daily life situations [80].

Finally, limited evidence was found on the most outstanding issues that might be positively tackled to increase workforce participation, namely the presence of a negative work environment, which was addressed in two studies only. Inflexible work schedules, financial insecurity, employers’ failure to provide support and reasonable accommodation or hostility have been previously found as correlates of perceived discrimination by MS patients in the workplace [81,82]. Despite this theme is of clear importance, it is poorly addressed: the fact that the search was carried out on PubMed only might be an explanation for this and could be ascertained in future studies. Strong evidence was found that difficulties with interpersonal relationships negatively act on patients’ ability to work, while no evidence was found on the ability to determine longitudinal changes in vocational status, which drives to relevant implications for vocational rehabilitation. The need for a connection with workplaces has been reported in several papers in terms of education of employers and colleagues, workplace support, counselling and guidance to mediate with the needs of employers, as well as supporting people to adapt, adjust, and resolve daily difficulties in work tasks [83–85]. This implies that vocational rehabilitation should be planned as a bridge between the inpatient or outpatient settings and the workplace.

The generalised underuse of measures of work-related difficulties among the studies herein included is likely to be the main reason for the partial conceptualisation of work-related difficulties. To our knowledge, three instruments exist that are focused on work issue in MS patients, the MS Work Difficulties Questionnaire (MSWDQ) [42,86], the MS-specific Work Instability Scale (MS-WIS) [87] and the MS Questionnaire for Job Difficulties (MSQ-Job) [52]. The first questionnaire measures dimensions connected to subjective workplace difficulties, but it does not consider negative attitudes of the workplace. This aspect is instead captured by the MS-WIS which, however, does not measure the specific limitations due to MS. The MSQ-Job measures difficulties due to MS-related symptoms as well as difficulties due to features of the workplace, and provides information on the impact of MS on the amount and severity of difficulties in work activities. By using one of these instruments, it is possible to evaluate the degree to which rehabilitation programmes, acting on the variables identified in the present review, impact over patients’ ability to work: this will provide additional evidence on the effect of rehabilitation interventions.

Some limitations need to be acknowledged. First, although the corresponding authors were contacted by e-mail, some papers could not be found and, more in general, despite the quality control measures aimed to reduce the possibility that relevant papers are excluded, we cannot be sure that all relevant articles were included. Second, the search was carried out on PubMed only: this might have hampered the results, in particular those connected to the social aspects of working with MS. However, we preferred to rely on a medical search engine to reduce the number of records in which clinical descriptions of participants to studies are based on self-reported diagnoses: in the case of MS, this would have created a lot of possible confusion with MS-like conditions such as other demyelinating diseases, clinically isolated syndrome, neuromyelitis optica or optic neuritis. Third, studies were heterogeneous in terms of sample size (33–8867), percentage of females (56.3–90.7%), percentage of employed persons (14–100%), MS duration (1.1–27.2 years) and average EDSS (1.5–6.4).

Conclusions

Most of the available evidence on variables that are associated to or determinant of work-related difficulties deals with known demographic variables (e.g. male gender and higher age), MS duration, age at onset and disability (EDSS score), progressive course, fatigue, cognitive functions, mobility, walking and ADL difficulties. Few evidence exist on the impact of contextual factors, with the exclusion of interpersonal difficulties, which is a relevant research gap.

Most of the problems herein identified, e.g. fatigue, cognitive impairment or walking difficulties, can be positively treated with
rehabilitation interventions. As clinicians and researchers, we must make an effort to connect these issues to vocational outcomes, otherwise we will not demonstrate what can be done to increase patients’ ability to work, but just produce updates on unemployment rates.

Future research should address work-related difficulties not only in terms of unemployment, that might be subject also to factors not related to MS, but also in terms of how MS impacts on work-related difficulties: to get to this point, existing MS-specific assessment instruments [42,52,87] or other fit-for-purpose measures, should be regularly used. In this way, it will be possible to show how much of an improvement in vocational outcomes can be due to rehabilitation interventions, thus also opening to the issue of cost-benefit balance.

Declaration of interest

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Supplementary material available online