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# Indirect Costs Related to Productivity Loss, Work-Related Quality of Life, and Resource Utilization in Workers with Multiple Sclerosis

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## Abstract

**Purpose** Multiple sclerosis (MS) often affects individuals during their most productive working years, resulting in reduced work capacity and quality of life. This study aimed to assess work productivity loss, work-related quality of life (WRQoL), and healthcare and social resource utilization among Italian workers with MS and to identify the predictors of productivity-related indirect costs.

**Methods** A cross-sectional study was conducted involving 160 employed people with MS (PwMS) in Italy. Work productivity and activity impairment were measured using the Work Productivity and Activity Impairment questionnaire for MS (WPAI:MS), while work-related difficulties were assessed with the MSQ-Job. WRQoL and healthcare and social support utilization were evaluated using validated instruments. Productivity losses were monetized using national wage data. Two-part regression models were applied to identify the predictors of annual indirect costs.

**Results** Overall, 79.4% of PwMS reported productivity loss, predominantly due to presenteeism (76.9%), with a mean overall work impairment of 40.3%. The mean annual cost of productivity loss was €12,580, 83% of which was attributable to presenteeism. Indirect costs were significantly higher among PwMS reporting work-related difficulties (€13,992 vs €7098; $p < 0.001$). Lower WRQoL, higher fatigue levels, and greater healthcare needs were associated with increased productivity losses, while higher WRQoL emerged as a protective factor.

**Conclusion** MS-related work impairment generates substantial indirect costs, largely driven by presenteeism. Interventions targeting workplace well-being, fatigue management, and vocational rehabilitation may help reduce productivity losses and improve quality of life among PwMS.

**Keywords** Multiple sclerosis · Lost productivity · Indirect costs · Healthcare resources · Work-related quality of life · Work-related difficulties

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## Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, and degenerative disease of the central nervous system, affecting an estimated 2.8 million people worldwide, including 1 million in Europe and over 144,000 in Italy [1, 2]. MS typically manifests in young adults between 20 and 40 years of age and follows a variable and often progressive clinical course. It remains the leading cause of non-traumatic neurological disability among young adults in Western countries [3]. The early onset of MS substantially affects both professional and personal life domains, with many individuals facing difficulties in maintaining employment [4, 5]. Indeed, only 20–40% of people with MS (PwMS) remain employed following diagnosis [6], and recent estimates indicate that 35.6% of PwMS are unemployed and 17.2% retire early due to disease-related limitations [7].

The socioeconomic impact of MS is considerable. In Italy, the mean annual cost per patient is estimated at €39,307, with direct healthcare costs (€21,069) representing the largest component, followed by indirect costs (€15,004) [8]. Both direct and indirect costs increase with disease progression, reflecting greater disability and higher healthcare utilization [9, 10]. Productivity losses are a major driver of the economic burden, accounting for nearly 30% of total costs in Italy [11]. Thus, reduced workforce participation represents a critical aspect of the disease's broader societal impact.

Workforce exclusion in MS arises from multiple factors. Unemployment and early retirement are common outcomes, while those who remain employed frequently experience work-related challenges such as absenteeism and presenteeism. Employees with MS have been shown to miss approximately four times more workdays annually than matched controls [12]. Furthermore, PwMS report 15–30% lower employment rates, reduced earnings, greater reliance on social benefits, and higher rates of work disability compared with the general population [13].

The most disabling symptoms, including fatigue, cognitive impairment, and motor dysfunction, play a central role in limiting work ability. Additional risk factors for job loss include male sex, progressive disease course, lower educational attainment, older age at diagnosis, and longer disease duration [14]. In Italy, regional disparities further influence employment status, with individuals living in Southern regions facing greater social and economic disadvantages compared to those in the North [11]. Exclusion from the workforce can aggravate financial hardship and social isolation, ultimately leading to poorer health outcomes [15].

Over the past two decades, the introduction of disease-modifying therapies (DMTs) has markedly improved disease control, reducing relapse rates and slowing disability progression [16]. These advances have enhanced the long-term prognosis of PwMS, allowing a larger proportion to remain employed. Nevertheless, the persistence of work-related difficulties continues to be a major determinant of job retention and employment participation [17].

Although the overall economic burden of MS has been extensively characterized [8, 9, 18], less attention has been paid to how specific work-related difficulties contribute to productivity losses and quality-of-life impairment. Work-related problems negatively affect both physical and psychological well-being, thereby influencing occupational outcome and overall quality of life (QoL). A better understanding of work-related factors associated with QoL is linked to higher satisfaction and perceived performance at work [17, 19].

Reduced QoL and productivity loss can further increase healthcare and social costs, underscoring the need for comprehensive interventions that address employment-related challenges. Job retention and participation are multifaceted issues requiring modern rehabilitation strategies focused on recovery of residual functions, enhancement of environmental interaction, and adoption of compensatory mechanisms. Such approaches may include workplace adaptation, assistive devices, task reorganization, and optimization of both home and work environments.

Assessing the type and extent of work-related difficulties is essential for guiding vocational rehabilitation (VR), defined as the process through which individuals disadvantaged by illness or disability are supported to access, maintain, or return to employment [20, 21]. Effective VR interventions can inform personalized retention strategies and help mitigate the long-term socioeconomic burden of MS. Recent evidence highlights the complex interplay between job demands, resources, turnover intentions, and MS-specific work challenges [22].

Building upon this background, the present study aims to investigate the impact of MS on Italian workers experiencing work-related difficulties. The primary objective is to evaluate the cost of lost productivity, work-related quality of life (WRQoL), and healthcare and social resource utilization among PwMS with work-related difficulties. The secondary objective is to identify the predictors of productivity loss associated with MS.

## Method

### Study Design and Participants

This study is a cross-sectional online survey conducted among workers in Italy with a confirmed diagnosis of

multiple sclerosis (MS) according to the revised McDonald criteria [23].

Participants were recruited from the pool of MS patients in contact with the Rehabilitation Service of the Italian Multiple Sclerosis Society (AISM) in Liguria and the Santa Lucia Foundation IRCCS in Rome. This study is part of a broader research project funded by INAIL (Bando BRiC 2022, ID 31), titled "RiaL SM: The rehabilitation approach as a qualifying factor in the evaluation of reasonable accommodation in workers with Multiple Sclerosis." The cross-sectional survey presented here constitutes the initial exploratory phase of the RiaL SM project.

The subjects included were adults (>18 years) with a diagnosis of MS who were currently employed. After providing informed consent, participants were invited via email to complete an anonymous online self-assessment questionnaire. The questionnaire collected socio-demographic, clinical, and employment-related information, along with responses to several validated scales, as outlined below.

The survey was administered through the SurveyMonkey® is a widely used survey platform, and its mention refers only to the tool employed for data collection; therefore, a formal reference is not required platform, and participants typically required approximately 30 min to complete it.

## Measures

### Socio-Demographic, Clinical, and Work-Related Characteristics

Socio-demographic, clinical, and occupational data were collected, including the province of residence, age, sex, marital status, education level, disease type and duration, occurrence of relapses, use of disease-modifying drugs (DMDs), and disability level. Employment-related variables included years worked, type of employment contract, job role, and workplace characteristics.

### Fatigue

Fatigue severity was assessed using the Visual Analogue Scale for Fatigue (VAS-F). This is a single-item measure evaluating global fatigue intensity over the preceding 48 h. Participants were asked: "How would you rate your level of fatigue over the past 48 h?" Responses were recorded on a 10-cm horizontal line anchored by 0 = No fatigue and 10 = Extremely fatigued. Higher scores indicate greater fatigue severity.

### Work Difficulties

The work difficulties were assessed using the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job) [24]. The instrument comprises 42 items grouped into six subscales and an overall score ranging from 0 to 100, with higher scores indicating greater perceived work-related challenges. The MSQ-Job captures both MS-related (physical and cognitive) and organizational factors affecting work performance.

A total score exceeding 15.8 indicates the presence of severe work-related difficulties, distinguishing PwMS with substantial job-related challenges from those managing work demands effectively [25]. Exceeding this threshold reflects a meaningful impact of MS on occupational functioning and highlights the need for targeted interventions.

### Work Productivity Loss and Activity Impairment

Work productivity loss and activity impairment were measured using the Work Productivity and Activity Impairment Questionnaire for Multiple Sclerosis (WPAI: MS) [26, 27]. The WPAI:MS consists of six items assessing the impact of MS on work and daily activities during the previous seven days.

The instrument provides four independent domain scores (0–100 scale), with higher values indicating greater impairment:

- Absenteeism—percentage of work time missed due to MS;
- Presenteeism—percentage of impairment while working;
- Overall Work Productivity Loss—combined effect of absenteeism and presenteeism;
- Activity Impairment—percentage of impairment in regular daily activities.

### Indirect Cost

Indirect costs related to lost productivity were estimated based on WPAI:MS responses, incorporating both absenteeism (time missed from work) and presenteeism (reduced productivity while at work).

Gender-specific median daily wage rates for Italy (men: €104.9; women: €103.7 in 2024) were obtained from Eurostat [28], assuming a standard 8-h workday (40 h per week).

Absenteeism costs were calculated by multiplying the number of hours missed during the past week due to health problems by the corresponding hourly wage.

Presenteeism costs were estimated by applying the WPAI presenteeism percentage to total hours worked (full time: 160 h per month; part time: 80 h per month). The number of unproductive hours was then multiplied by the average hourly wage.

Total productivity loss was obtained by summing absenteeism and presenteeism costs. Weekly losses were annualized by multiplying by the average number of working weeks per year. Results were expressed as per-user and per-patient

annual costs to capture variations in productivity-related burden. "Per-user" costs refer to the average annual costs calculated only among individuals who actually reported productivity loss. "Per-patient" costs refer to the average annual costs calculated across the entire patient population, including those who did not experience productivity loss.

#### Work-Related Quality of Life

Work-related quality of life was evaluated using the Work-Related Quality of Life Scale (WRQoL) [29, 30]. The Italian version of this multidimensional scale consists of 25 items rated on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree) and measures seven domains [31]:

- Job and Career Satisfaction (JCS): It reflects employees' satisfaction with their job, career opportunities, and the extent to which work provides achievement, recognition, and personal growth—4 items (q6, q8, q14, q16);
- General Wellbeing (GWB): It captures overall psychological and physical well-being, which both affects and is affected by work—5 items (q2, q7, q11, q13, q17);
- Home–Work Interface (HWI): It assesses how well the organization supports employees in balancing work demands with personal and family responsibilities– 3 items (q3, q4, q20);
- Stress at Work (SAW): It assesses whether work demands are perceived as reasonable and manageable rather than excessive or overwhelming—2 items (q5, q15);
- Control at Work (CAW): It measures the degree to which employees feel involved in decisions and able to exercise control over their work environment—4 items (q1, q9, q19, q24);
- Working Conditions (WCS): It evaluates satisfaction with the physical work environment, resources, safety, and overall conditions needed to perform effectively—4 items (q10, q12, q18, q25);
- Employee Engagement (EEN)—3 items (q21, q22, q23).

Items q5 and q15 are reverse-coded. Subscale scores were calculated as the mean of their items, and the overall WRQoL score was obtained as the mean of all subscale scores. Higher scores indicate better WRQoL.

#### Healthcare and Social Resource Utilization

Healthcare and social resource utilization were assessed using the Needs and Provision Complexity Scale—Gets (NPCS-Gets), a component of the NPCS specifically designed to measure services received by individuals with long-term neurological conditions [32].

The NPCS consists of 15 items across six subscales within two domains—Health and Personal Care and Social Care and Support (total score range: 0–50; domain scores: 0–25). The subscales include the following: healthcare (0–6), personal care (0–10), rehabilitation (0–9), social support (0–13), equipment (0–3), and accommodation (0–9).

The NPCS was translated into Italian following standard forward–backward translation procedures. Native speakers first translated the instrument from English to Italian, after which a back-translation was performed. The final version was reviewed by expert clinicians and researchers in healthcare, social services, and MS to ensure linguistic and conceptual equivalence.

### Statistical Analysis

Descriptive statistics were applied to summarize all study measures. The distribution of quantitative variables was assessed for normality using the Kolmogorov–Smirnov test. Continuous variables are presented as means and standard deviations (SD), whereas categorical variables are expressed as frequencies and percentages.

Comparisons between participants with and without work-related difficulties were performed to identify group differences. For categorical variables, the Chi-square test or Fisher's exact test was applied as appropriate. For continuous variables, independent samples *t*-tests or Mann–Whitney U tests were used, depending on data distribution.

Given the zero-inflated and right-skewed nature of productivity loss data, two-part (two-stage) models were employed to estimate productivity loss outcomes in relation to selected independent variables. In the first stage, a logit model (logistic regression) was used to estimate the probability of observing a positive versus zero productivity loss. In the second stage, a generalized linear model (GLM) with a log link and gamma distribution was applied to estimate the magnitude of productivity loss among participants with non-zero values. Model fit was assessed separately for each part of the two-part model. For the first part (logit), we report the pseudo-$R$-squared, while for the second part (GLM with gamma distribution and log link), model fit is evaluated using AIC, BIC, and deviance-based measures. To account for potential intra-center correlation, all models incorporated robust (sandwich-type) variance estimators. Marginal (incremental) effects were computed to facilitate interpretation of the two-part model coefficients, providing estimates of the expected change in productivity loss associated with each covariate [33].

To identify independent predictors of productivity loss, variables that were statistically significant ($p < 0.05$) in univariate two-part analyses were subsequently entered into a multivariate two-part model.

All statistical tests were two-tailed, and a $p$-value $< 0.05$ was considered statistically significant. Analyses were

performed using Stata (version 17, StataCorp, College Station, TX, USA).

## Results

A total of 225 workers with MS consented to participate in the study. Of these, 40 (17.8%) were excluded for not meeting the inclusion criteria, and 25 (11.1%) were excluded due to incomplete questionnaires. The 25 excluded participants did not differ significantly from the 160 individuals included in the final analysis in terms of gender ($p = 0.730$), mean age ($p = 0.803$), or educational level ($p = 0.229$).

The analysis was thus restricted to 160 subjects. The 73.8% showed work difficulties based on the cut-off score of the MSQ-Job questionnaire.

The characteristics of the sample are reported in Table 1. In particular, the subjects with work-related difficulties had a higher educational level ($p = 0.0016$), EDSS score ($p = 0.016$), and fatigue level ($p < 0.0001$).

### Work Productivity Loss and Indirect Cost

Among working people, 79.4% ($n = 127$) reported any absenteeism or presenteeism in the last week, of which 1.7 times more reported presenteeism compared to absenteeism

**Table 1** Socio-demographic, clinical and work-related variables

| Variables | All participants ($N = 160$) | Without work difficulties ($N = 42$)* | With work difficulties ($N = 118$)* | P value |
|---|---|---|---|---|
| *Socio-demographic variables* | | | | |
| Age in years, mean (SD) | 48.2 (9.5) | 49.7 (7.6) | 47.7 (10.1) | 0.239 |
| Gender, *n* (%) | | | | |
| Female | 106 (66.3%) | 28 (66.7%) | 78 (66.1%) | 0.836 |
| Male | 53 (33.1%) | 14 (33.3%) | 39 (33.1%) | |
| Non-binary | 1 (0.6%) | 0 (0.0%) | 1 (0.8%) | |
| Level of education, n (%) | | | | |
| Primary/High school | 85 (53.1%) | 29 (69.0%) | 56 (47.5%) | 0.016 |
| University | 75 (46.9%) | 13 (31.0%) | 62 (52.5%) | |
| Civil status, *n* (%) | | | | |
| Living alone | 26 (16.2%) | 3 (7.1%) | 23 (19.5%) | 0.062 |
| Married/cohabitant | 134 (83.8%) | 39 (92.9%) | 95 (80.5%) | |
| Province of residence, *n* (%) | | | | |
| Genoa | 104 (65.0%) | 25 (59.5%) | 79 (67.0%) | 0.386 |
| Rome | 56 (35.0%) | 17 (40.5%) | 39 (33.0%) | |
| *Clinical variables* | | | | |
| Duration of illness in years, mean (SD) | 15.6 (10.2) | 16.6 (10.4) | 15.3 (10.2) | 0.438 |
| Disease course, *n* (%) | | | | |
| RR | 104 (65.0%) | 30 (71.4%) | 74 (62.7%) | 0.309 |
| SP/PP | 56 (35.0%) | 12 (28.6%) | 44 (37.3%) | |
| EDSS score, mean (SD) | 3.2 (2.3) | 2.4 (2.2) | 3.4 (2.3) | 0.016 |
| Fatigue (VAS), mean (SD) | 6.3 (2.3) | 4.9 (2.6) | 6.8 (2.0) | < 0.0001 |
| Currently treated with DMD, *n* (%) | 137 (85.6%) | 35 (83.3%) | 102 (86.4%) | 0.622 |
| Relapse in the last three months, *n* (%) | 23 (14.4%) | 6 (14.3%) | 17 (14.4%) | 0.985 |
| *Work-related variables* | | | | |
| Total years worked, mean (SD) | 22.4 (10.6) | 23.5 (9.0) | 22.0 (11.1) | 0.336 |
| Years worked in the current position, mean (SD) | 14.8 (10.5) | 16.5 (9.5) | 14.2 (10.8) | 0.138 |
| Employment contract, *n* (%) | | | | |
| Fixed term | 18 (11.2%) | 5 (11.9%) | 13 (11.0%) | 1.000 |
| Open-ended | 142 (88.8%) | 37 (88.1%) | 105 (89.0%) | |
| Employment type, *n* (%) | | | | |
| Full time | 117 (73.1%) | 30 (71.4%) | 87 (73.7%) | 0.773 |
| Part time | 43 (26.9%) | 12 (28.6%) | 31 (26.3%) | |

*The presence of work difficulties according to the MSQ-Job cut-off (> 15.8)

(76.9 vs 44.5%). In our sample, the mean percentage of work time lost because of absenteeism was 7.9%, while the mean percentage of impairment while working was 36.6% (presenteeism). The proportion of subjects who reported any overall work impairment was 79.4% (127 out of 160), and the mean percentage of overall working impairment was 40.3%. The proportion of subjects who reported any activity impairment was 88.8% (142 of 160) and the mean percentage of activity impairment was 48.2% (Fig. 1).

Overall, all WPAI:MS outcomes were higher in participants with work difficulties than those without, and the differences were statistically significant (Fig. 1).

The MS-related mean annual cost of lost productivity was € 12,580 when calculated in subjects with any work productivity loss. Approximately 83% of these costs were due to presenteeism (Table 2).

The MS-related mean annual cost of lost productivity (in the total working sample) was significantly higher among participants with work difficulties than those without one (€13,992 vs € 7098 per year). Also, in this case, the largest component was due to the presenteeism cost (Table 2).

## Work-Related Quality of Life

Considering the entire sample, the mean subscale score of the "Stress at Work" (2.7 ± 1.1), a factor that evaluates work-related stress and excessive pressure, was found to be the lowest, highlighting a negative impact of stress on WRQoL. In contrast, the highest mean rating WRQoLwas observed in the domains of "Working Conditions" (WCS, 3.4 ± 0.9), "Home Work Interface" (HWI, 3.3 ± 1.0), and "Employee Engagement" (EEN, 3.3 ± 0.9).

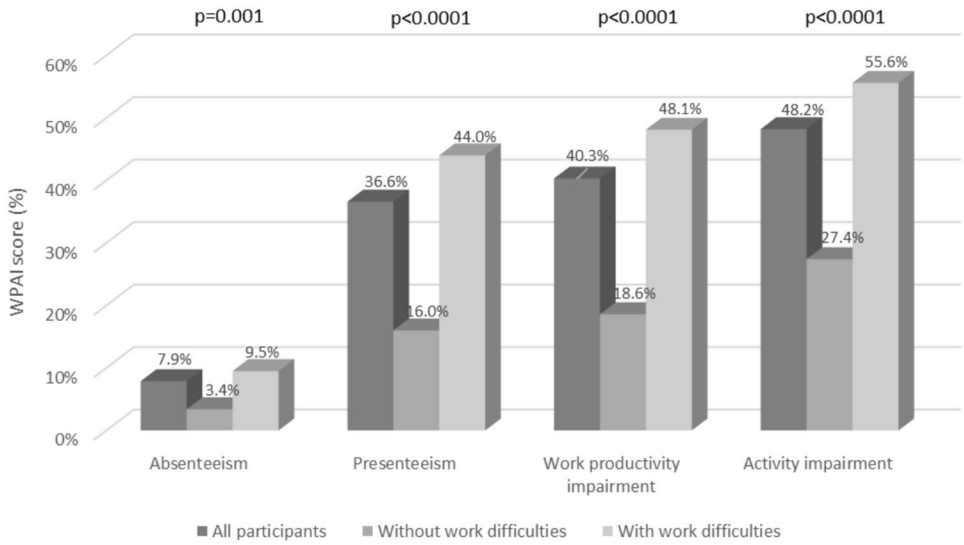


**Fig. 1** The work productivity and activity impairment (WPAI:MS score, %). The WPAI:MS outcomes were calculated on the total sample to provide an overall estimate of the effect

**Table 2** Costs of MS-related absenteeism, presenteeism, and total work productivity loss

| | All participants | Without work difficulties | With work difficulties |
|---|---|---|---|
| | Mean annual costs (SD) per worker with any work productivity loss (€) | | |
| Absenteeism | | | |
| Cost per user | 4492 (4209) | 3349 (1987) | 4680 (4452) |
| Cost per patient | 1993 (3579) | 798 (1718) | 2419 (3960) |
| Presenteeism | | | |
| Cost per user | 10397 (5818) | 6294 (4646) | 11391 (5653) |
| Cost per patient | 7992 (6731) | 3596 (4695) | 9557 (6667) |
| Total work productivity loss* | | | |
| Cost per user | 12,580 (7982) | 7098 (5057) | 13,992 (8004) |
| Cost per patient | 9986 (8750) | 4394 (5269) | 11,976 (8894) |

**Note:** "Per-user" costs are calculated among individuals with productivity loss only; "per-patient" costs are calculated across the entire sample, including those without productivity loss

*Total work productivity loss = absenteeism + presenteeism

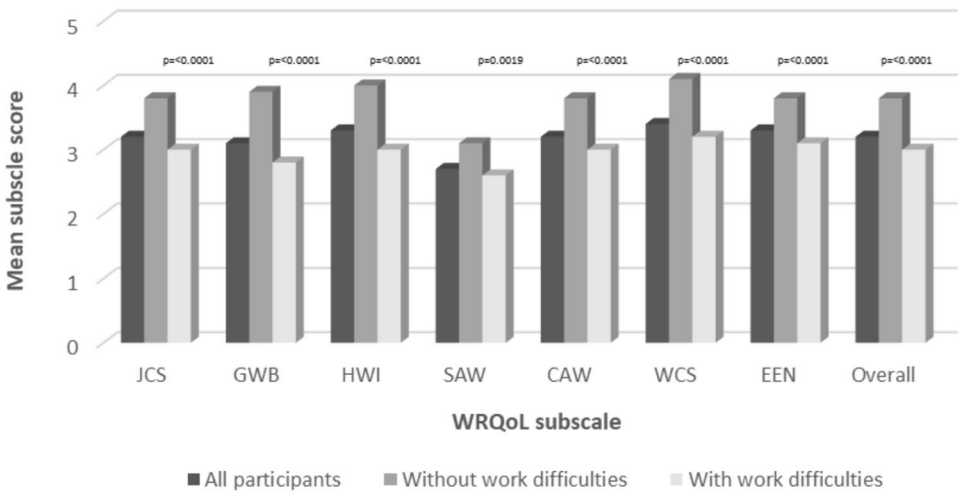


**Fig. 2** Work-related quality of life subscale scores. *CAW* control at work, *GWB* general well-being, *HWI* home work interface, *JCS* job career satisfaction, *PMS* premenstrual syndrome, *SAW* stress at work, *WCS* working conditions, *EEN* employee engagement. The *p*-value refers to the comparison of the different subscales between subjects with and without work-related difficulties

In general, all WRQoL subscales and overall scores in subjects without work difficulties were significantly lower than those in subjects with work difficulties (Fig. 2).

## Healthcare and Social Resource Utilization

Table 3 reports the distribution of healthcare and social resources used.

In our sample, medical care, rehabilitation therapy, and advocacy support were the services more frequently received in the last 6 months. In particular, advocacy support was found to be a need most demanded by those with employment difficulties ($p < 0.001$). In addition, the same subgroup received a higher percentage of aids and equipment ($p = 0.018$) and adapted accommodation ($p = 0.045$) than subjects without work-related difficulties.

**Table 3** Distribution of healthcare and social resources used

| | All participants | Without work difficulties | With work difficulties | P value |
|---|---|---|---|---|
| Health | | | | |
| Medical care | 145 (90.6%) | 38 (90.5%) | 107 (90.7%) | 1.00 |
| Nursing care | 25 (15.6%) | 9 (21.4%) | 16 (13.6%) | 0.228 |
| Personal care | | | | |
| Help with basic self-care at home | 20 (12.5%) | 3 (7.1%) | 17 (14.4%) | 0.222 |
| Help with social activities in the local community | 24 (15.0%) | 3 (7.1%) | 21 (17.8%) | 0.097 |
| Rehabilitation | | | | |
| Rehabilitation therapy | 102 (63.8%) | 22 (52.4%) | 80 (67.8%) | 0.074 |
| Support to return to work (vocational) | 4 (2.5%) | 0 (0.0%) | 4 (3.4%) | 0.574 |
| Social support | | | | |
| Social worker and case manager | 20 (12.5%) | 2 (4.8%) | 18 (15.3%) | 0.077 |
| Family support | 9 (5.6%) | 3 (7.1%) | 6 (5.1%) | 0.699 |
| Respire care | | | | |
| Residential setting | 4 (2.5%) | 0 (0.0%) | 4 (3.4%) | 0.574 |
| Day care setting | 7 (4.4%) | 0 (0.0%) | 7 (5.9%) | 0.191 |
| Advocacy | 54 (33.8%) | 1 (2.4%) | 53 (44.9%) | < 0.001 |
| Equipment | 37 (23.1%) | 4 (9.5%) | 33 (28.0%) | 0.018 |
| Accommodation | | | | |
| Adapted accommodation | 17 (10.6%) | 1 (2.4%) | 16 (13.6%) | 0.045 |
| Supported accommodation or residential care | 4 (2.5%) | 2 (4.9%) | 2 (1.7%) | 0.277 |

We used the Chi-square test to assess associations between categorical variables and applied Fisher's exact test when the conditions for the Chi-square test were not met

Considering the subscales and domain scores of the NPCS provision scale, we observed significant differences for both domain scores (health personal care and social care and support) between the two subgroups of workers. Overall, we observed mean scores higher in the PwMS with work-related difficulties than those without ones. The differences were significant for personal care ($p=0.048$), rehabilitation (0.045), social support ($p<0.0001$), and equipment ($p=0.012$) (Table 4).

### Factors Associated with MS-Related Work Productivity Loss

We observed an incremental cost for work productivity loss associated with the following: the presence of work-related difficulties (3831€, $p<0.001$); each additional point of the fatigue subscale (1141€, $p=0.011$); having a full-time contract than part-time one (5810€, $p<0.001$); and each additional point of the health domain of the scale on health services received (274€, $p=0.001$).

We observed a decremented cost for each additional year of age (− 109€, $p=0.007$) and for each additional point of work-related quality of life (− 2119€, $p<0.001$) (Table 5).

## Discussion

This study provides a comprehensive assessment of the impact of MS on productivity, work-related quality of life, and healthcare and social resource utilization using data from an online survey conducted in Italy in 2024 among Italian workers with MS. The results revealed that approximately 74% of workers with MS reported experiencing work-related difficulties, as measured by the MSQ-Job questionnaire. This indicates that roughly 3 out of 4 workers in our sample faced significant challenges in their jobs. The

**Table 4** NPCS provision reported during the last 6 months: subscales and domain scores

| NPC subscales | All participants | Without work difficulties | With work difficulties | *p*-value* |
|---|---|---|---|---|
| | Mean (SD), range* | | | |
| | *Health and Personal Care domain* | | | |
| Health | 2.5 (1.1), 0–6 | 2.5 (1.1), 0–5 | 2.5 (1.1), 0–6 | 0.935 |
| Personal care | 0.6 (1.6), 0–8 | 0.4 (1.5), 0–8 | 0.7 (1.6), 0–8 | 0.048 |
| Rehabilitation | 2.7 (2.2), 0–6 | 2.1 (2.2), 0–6 | 2.9 (2.2), 0–6 | 0.045 |
| Total Health Personal Care | 5.8 (3.1), 0–15 | 5.0 (3.0), 0–15 | 6.1 (3.1), 0–15 | 0.039 |
| | *Social care and Support domain* | | | |
| Social support | 1.1 (1.3), 0–5 | 0.3 (0.7), 0–3 | 1.3 (1.4), 0–5 | < 0.0001 |
| Equipment | 0.3 (0.6), 0–3 | 0.1 (0.3), 0–1 | 0.4 (0.7), 0–3 | 0.012 |
| Accommodation | 0.3 (1.0), 0–6 | 0.3 (1.3), 0–6 | 0.3 (0.9), 0–6 | 0.107 |
| Total Social care and Support | 1.7 (1.9), 0–9 | 0.7 (1.9), 0–9 | 2.0 (1.8), 0–7 | < 0.0001 |

*Reported ranges refer to the observed values in the study sample and subsamples, not to the full theoretical range of the scale

**Table 5** Multivariate analysis to determine variables associated with workers' productivity losses

| Variables | Workers' productivity losses, incremental effect (€) (95% CI) | p-value |
|---|---|---|
| With work-related difficulties (without) | 3831 (2560–5103) | < 0.001 |
| Age | − 109 (− 189 to − 30) | 0.007 |
| Living along (cohabitant) | 1678 (− 118 to 3475) | 0.067 |
| EDSS score | 217 (− 45 to 480) | 0.105 |
| Fatigue | 1141 (259 to 2024) | 0.011 |
| Years worked in current position | − 46 (− 1118 to 26) | 0.211 |
| Full time (part time) | 5810 (4584–7036) | < 0.001 |
| WRQoL | − 2119 (− 2485 to − 1753) | < 0.001 |
| Health NPC domain | 274 (117 to 431) | 0.001 |
| Pseudo-$R^2=0.286$ | | |
| AIC = 20.7, BIC = − 545.5, Deviance/df = 0.296 | | |

The model using clustered sandwich estimator of the variance to take account of the nested effect of living in two geographical areas (i.e., Genoa and Rome) where the participating MS centers are located

findings highlighted a substantial burden of disease-related work impairment, with nearly 80% of participants reporting some degree of productivity loss due to MS.

Consistent with previous research, presenteeism, defined as reduced effectiveness while working, was the major contributor to productivity loss, reported 1.7 times more frequently than absenteeism (76.9% vs 44.5%). The literature indicates a pronounced difference between MS patients and the general population, with higher proportions of absenteeism and presenteeism [13, 34]. On average, participants lost 7.9% of work time due to absenteeism and experienced a 36.6% impairment while working (presenteeism), resulting in an overall work productivity loss of 40.3%. This predominance of presenteeism aligns with evidence from other European studies showing that productivity loss among PwMS is often driven by reduced performance rather than absence from work [8, 9, 17]. It also underscores the hidden yet pervasive effects of MS on day-to-day functioning, particularly among individuals striving to maintain employment despite physical and cognitive challenges.

The mean annual cost of productivity loss was estimated at €12,580, with approximately 83% attributable to presenteeism. Costs were nearly doubled among those with self-reported work difficulties (€13,992 vs €7098), confirming that perceived job-related challenges are a strong indicator of reduced work capacity and increased economic burden. This finding reinforces the importance of early identification and management of work difficulties to mitigate productivity losses. Despite the differences observed between groups, presenteeism consistently emerged as the largest contributor to productive time loss and the primary driver of productivity-related costs [11, 34]. Moreover, a recent Italian study on the economic burden of MS, in agreement with our results, observed an association between productivity loss and the presence of work-related difficulties [17].

The analysis of Work-Related Quality of Life (WRQoL) revealed that employees faced the greatest challenges in managing work-related pressures, reflecting a marked sense of overload and strain. In contrast, participants generally reported positive perceptions of their work environment, felt supported in balancing professional and personal demands, and expressed good levels of engagement in their roles. Nevertheless, the presence of work-related difficulties was associated with a deterioration across all WRQoL subscales, reflected in significantly lower scores. This pattern aligns with previous evidence indicating that poorer perceived quality of work life is closely linked to greater fatigue, disability, and psychological distress [17, 19].

Our findings further showed that WRQoL acted as a protective factor in the cost model: each additional point on the WRQoL scale was associated with a €2119 reduction in productivity loss. These results suggest that improving workplace well-being and satisfaction may directly reduce the indirect costs of MS. Recent studies have demonstrated that workplace interventions aimed at enhancing well-being—such as flexible work arrangements, psychological support, and accommodations for physical or cognitive symptoms—can help retain PwMS in the workforce and reduce indirect costs [35–37].

In terms of healthcare and social resource use, medical care, rehabilitation therapy, and advocacy support were the most frequently received services in the previous six months. Notably, PwMS with work-related difficulties showed a greater need for advocacy support, as well as higher use of aids, equipment, and adapted accommodation. Differences between the two subgroups were also significant across several subscales of the NPCS, particularly personal care, rehabilitation, social support, and equipment, indicating that those with employment difficulties require more comprehensive multidisciplinary support. These findings are consistent with previous research indicating that people with MS who encounter work-related challenges have an increased need for advocacy services, workplace accommodations, and adaptive equipment or modified environments [38, 39].

These findings highlight the interdependence between employment status, quality of life, and healthcare needs. The increased demand for social and rehabilitation resources among individuals with work difficulties may reflect both greater functional limitations and the need for interventions aimed at maintaining independence and employability.

Our regression analysis identified several key predictors of productivity loss, shedding light on the complex interplay between individual characteristics, work conditions, and health status. Higher productivity costs were associated with the presence of work-related difficulties, greater fatigue severity, full-time employment, and more intensive use of health services. Conversely, older age and higher work-related quality of life emerged as protective factors, predicting lower productivity losses. Disability level (EDSS score), living situation, and years worked in the current position were not significantly associated with productivity loss.

These results, consistent with previous literature, highlight that fatigue management and workplace well-being are critical and potentially modifiable determinants of economic outcomes in PwMS [40]. Fatigue, a pervasive symptom in MS, appears to compromise both work efficiency and the ability to sustain stable participation in the workforce, reinforcing the need for early identification and targeted interventions [41].

The association between full-time employment and higher productivity costs likely reflects increased exposure to job demands and pressure, which may exacerbate symptoms and lead to longer or more frequent periods of work impairment. This finding underscores the importance of adopting flexible work arrangements and individualized job accommodations, not simply to reduce burden, but to

enable sustainable employment trajectories [42]. Moreover, the protective role of work-related quality of life suggests that a supportive, well-structured work environment may buffer the negative impact of MS-related symptoms on productivity. Enhancing organizational support, fostering autonomy, and ensuring reasonable adjustments may therefore contribute not only to improved well-being but also to reduced indirect societal costs [35].

Overall, these findings illustrate how clinical, demographic, and occupational factors jointly shape productivity outcomes, and they point to clear targets for intervention at both the individual and workplace levels.

### Limitation

This study has several limitations. First, its cross-sectional design prevents causal inferences and does not allow observation of changes over time, making it difficult to establish the temporal relationship between predictor variables and productivity loss. The sample, drawn from two rehabilitation centers, may not be representative of all workers with MS in Italy, introducing potential selection bias. A limitation of this study is the geographic restriction of the sample to Northern and Central Italy, excluding Southern regions; given known socioeconomic disparities, this may limit generalizability and potentially underestimate indirect costs at the national level. Participation in an online survey may also have favored individuals who are more motivated, digitally literate, or less severely impaired. Moreover, all information was self-reported, increasing the risk of recall and reporting biases, and clinical data were not objectively verified, limiting the accuracy of disease-related variables. Restricting the sample to currently employed individuals excludes those who may have left the workforce due to MS, potentially underestimating the true impact of the disease on employment.

In addition, the method used to estimate indirect costs has its own limitations. Productivity losses were derived from self-reported WPAI:MS data, which are subject to recall bias and subjective interpretation—particularly for presenteeism—and may not reflect typical work patterns when based on a single reference week. The use of standardized national median wages and fixed assumptions about working hours may not correspond to actual salaries or schedules, leading to possible over- or underestimation of costs. This method also assumes a linear relationship between reported impairment and productivity loss and annualizes short-term data, which may amplify temporary fluctuations. Finally, it does not account for workplace accommodations or compensatory strategies that could mitigate the real economic impact of MS on productivity.

## Conclusion

Overall, this study demonstrates that the economic burden of MS extends beyond direct healthcare costs, with presenteeism and work-related difficulties emerging as the dominant sources of productivity loss among employed individuals. The estimated annual indirect cost (€12,580) specifically refers to the active workforce and should not be interpreted as representing the total productivity loss associated with MS at the population level. Moreover, these estimates rely on standardized assumptions (e.g., a 40-h work week and median wages), which may not fully capture individual work patterns. The finding suggests that interventions promoting vocational rehabilitation, fatigue management, and workplace adaptation may substantially reduce the indirect cost of MS. In addition, enhancing work-related quality of life could serve as a protective factor, improving both well-being and economic sustainability.

Future studies should adopt longitudinal designs to explore how changes in clinical status, treatment, and workplace conditions influence productivity trajectories over time. Evaluating the cost-effectiveness of targeted rehabilitation and job retention programs would further inform policies aimed at preserving employment and reducing the societal burden of MS.

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**Data Availability** The data that support the findings of this study are available on reasonable request from the corresponding author.

### Declarations

**Conflict of interest** The authors declare no competing interests.

**Ethical Approval** The study was approved by the Liguria Regional Ethics Committee (P.R. 8/2024-DB id 13621; 11/03/2024) and by the Local Ethics Committee Lazio Area 5 (P.R. n.139/SL/24; 7/05/2024).

**Consent to Participate** Through Survey Monkey software, before filling in the questionnaire, the patients were asked to give their informed consent to their anonymous participation in the study.

**Consent for Publication** Not applicable.



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