Patient-Reported Outcomes

Work Productivity in Relapsing Multiple Sclerosis: Associations with Disability, Depression, Fatigue, Anxiety, Cognition, and Health-Related Quality of Life

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A B S T R A C T

Objectives: To characterize work productivity in relapsing multiple sclerosis (MS) by using a work productivity scale and to identify associations between work productivity and disability, depression, fatigue, anxiety, cognition, and health-related quality of life. **Methods:** Three hundred seventy-seven subjects with a clinically isolated syndrome or relapsing remitting MS participated in the study. Subjects underwent neurological examinations and completed patient-reported outcome and cognitive measures. Subjects also completed the Work Productivity and Activity Impairment Questionnaire: General Health to quantify absenteeism (missing work because of health problems), presenteeism (impairment while working), overall work impairment, and daily activity impairment attributable to health problems. Univariate correlations and multivariate models were used to determine the associations between each work productivity variable and clinical, patient-reported outcome, and cognitive measures. **Results:** Seventy-six percent of subjects were employed. Fourteen percent of working subjects reported absenteeism, and 47% reported presenteeism. The mean work time lost because of absenteeism was

4%, and the mean work time lost because of presenteeism was 12%. Absenteeism was not significantly associated with disease or patient-reported outcome measures. Statistically significant correlations (0.32–0.53) were found between presenteeism and increasing disability, fatigue, depression, anxiety, and reduced quality of life. No associations were observed between presenteeism and disease duration or cognitive function. **Conclusions:** Subjects with clinically isolated syndrome/relapsing remitting MS reported substantial work productivity losses due to presenteeism. Presenteeism was associated with increasing fatigue, depression, anxiety, and reduced quality of life. It is possible that the early identification and treatment of fatigue and mental health symptoms may improve productivity while working and extend employment for individuals with MS.
Keywords: depression, fatigue, multiple sclerosis, quality of life, work productivity.

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Introduction

Multiple sclerosis (MS) is a chronic demyelinating disease that affects the central nervous system. Approximately 400,000 individuals in the United States report having MS [1]. Common symptoms include numbness, problems with walking, balance, and coordination, bladder and bowel complaints, visual impairment, fatigue, depression, and cognitive dysfunction [2]. Most individuals have a first episode of demyelination or a clinically isolated syndrome (CIS) followed by a relapsing remitting disease course that is characterized by clearly defined attacks of worsening neurologic function with full or partial recovery. The majority of patients with relapsing remitting MS (RRMS) transition to a progressive phase known as secondary progressive MS. Fewer individuals present with primary progressive MS or progressive relapsing MS, which both have a slowly progressive course from onset [3]. MS is usually diagnosed between the ages of 20 and 50

years, significantly affecting education, career, and family life [4]. It also impacts employment. Unemployment rates among individuals with MS have been shown to be as high as 80% [5].

Numerous studies have examined factors related to employment status in MS. Increasing age [6,7], greater physical disability [4,6,8], a progressive disease course [9–11], and higher levels of fatigue [7,9] and anxiety [4] have all been associated with unemployment. Depression has been strongly related to unemployment in some [12] but not all studies in MS [6,9]. Similarly, gender [7,12], disease duration [4,12], and cognitive dysfunction [6,9,13] have been inconsistently associated with employment status.

Among working individuals with MS, research has traditionally focused on absenteeism or number of workdays missed. Individuals with MS have been shown to have significantly higher rates of medically related absenteeism and associated absenteeism days than employee controls. In a study by Ivanova et al. [14], employees with MS had four times more workdays lost than did

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controls over a 12-month period (37.7 vs. 8.8 day). Absenteeism in MS has been associated with the overall severity of illness [15]. Higher rates of comorbid diagnoses such as mental health disorders and other neurological disorders have been reported in MS [14] and may also impact time missed from work.

There is increasing evidence that presenteeism—reduced productivity while working—may be important in evaluating work productivity losses in individuals with chronic diseases. In arthritis, for example, it has been estimated that presenteeism accounts for 41% of total productivity losses while absenteeism accounts for only 10% [16]. In addition, presenteeism may correlate with health status better than absenteeism. Zhang et al. [17] reported stronger correlations between presenteeism and health status measures including functional disability, pain, fatigue, and disease activity than between absenteeism and the same health status measures in a group of subjects with rheumatoid arthritis.

In this report, our first goal was to characterize work productivity including absenteeism and presenteeism in individuals with a CIS or RRMS by using a work productivity scale. Given that the ability to work has been shown to vary across disease types, this study was limited to subjects with relapsing disease. Our second goal was to examine the associations between work productivity measures and demographic and disease characteristics, patient-reported outcomes (PROs) such as depression, fatigue, anxiety, and health-related quality of life, and cognitive function.

Methods

Subjects

Subjects with CIS/RRMS were selected from the Comprehensive Longitudinal Investigation of Multiple Sclerosis at the Brigham and Women's Hospital, Partner's MS Center (CLIMB) study, an ongoing prospective observational cohort study that began enrolling subjects in 2000 [18]. Inclusion criteria for the CLIMB study are age 18 years or older and CIS with a positive magnetic resonance imaging (MRI) scan with two or more lesions characteristic of MS or a diagnosis of MS according to the revised McDonald criteria [19]. Patients are approached about possible study participation by their physicians during their routine visits to the Partner's MS Center. To date, 1879 subjects have been enrolled. This represents nearly half of the patients with MS followed at our center.

CLIMB subjects have clinical visits every 6 months that include complete neurological examinations. Current levels of disability are determined by using the Expanded Disability Severity Scale (EDSS) [20], an ordinal clinical rating scale with total scores ranging from 0 (normal neurologic examination) to 10 (death due to MS), in increments of 0.5. A subset of subjects also completes PRO and cognitive measures annually. The original battery included depression, fatigue, health-related quality of life, and working memory tests using the measures described in detail below. Beginning in July 2010, subjects began completing additional questionnaires to assess work productivity and anxiety. For each subject, the last clinical visit with associated questionnaire data was used. Because only a subset of the CIS/RRMS CLIMB subjects has completed the new questionnaires, our final sample size was 377 subjects. Fig. 1 summarizes how the overall study population was reduced to the final cohort. Demographic and clinical characteristics of subjects are provided in Table 1.

PRO and Cognitive Measures

PRO and cognitive measures include the Multiple Sclerosis Quality of Life-54 [21], Center for Epidemiologic Studies Depression Scale [22], Modified Fatigue Impact Scale (MFIS) [23], State-Trait Anxiety Inventory for Adults (STAI) [24], and Symbol
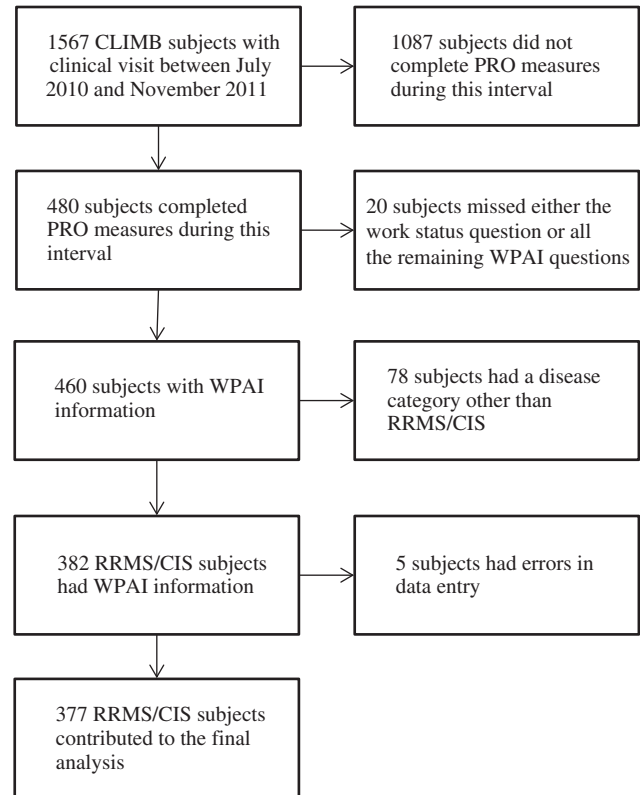
Fig. 1 – Flow diagram summarizing how the overall study population was reduced to the final cohort.

Digit Modalities Test (SDMT) [25,26]. The Multiple Sclerosis Quality of Life-54 is a 54-item questionnaire that includes the Medical Outcomes Study Short-Form 36 Health Survey (SF-36) [27] and 18 MS-specific items. The SF-36 items were combined by

Table 1 – Demographic characteristics of study subjects.	
N	377
Age (y), mean ± SD	45.4 ± 10.6
Disease duration (y), mean ± SD	12.4 ± 7.8
% of males	23.9
Race (%)	
Asian	0.8
Black or African American	2.1
More than one race	1.1
Unknown or not reported	1.1
White	95.0
Ethnicity (%)	
Hispanic or Latino	4.0
Non-Hispanic or Latino	95.5
Unknown	0.5
Disease category (%)	
RRMS	94.7
CIS	5.3
EDSS, median (IQR)	1.5 (0–2.5)
% treated	71.7
SDMT score, mean ± SD	56.7 ± 12.5
% working	75.6

CIS, clinically isolated syndrome; EDSS, Expanded Disability Status Scale; IQR, interquartile range; RRMS, relapsing remitting multiple sclerosis; SDMT, Symbol Digit Modalities Test.