Received: 23 July 2023 | Revised: 18 September 2023 | Accepted: 12 October 2023

DOI: 10.1111/jsr.14087

RESEARCH ARTICLE

Work productivity and activity impairment in patients with narcolepsy type 1

Chiara Bassi[1] | Francesco Biscarini[2,3] | Corrado Zenesini[2] | Marco Menchetti[3] | Luca Vignatelli[2] | Fabio Pizza[2,3] | Giuseppe Plazzi[2,4] | Francesca Ingravallo[1]

[1]Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Bologna, Italy

[2]IRCCS Istituto delle Scienze Neurologiche di Bologna (ISNB), Bologna, Italy

[3]Department of Biomedical and Neuromotor Sciences (DIBINEM), Alma Mater Studiorum, University of Bologna, Bologna, Italy

[4]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

Correspondence
Giuseppe Plazzi, IRCCS Istituto delle Scienze Neurologiche di Bologna (ISNB), Bologna, Italy.
Email: giuseppe.plazzi@isnb.it

Francesca Ingravallo, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Via Irnerio 49, 40126 Bologna, Italy.
Email: francesca.ingravallo@unibo.it

Summary

The aim of this study was to assess work productivity and activity impairments and to explore their association with excessive daytime sleepiness, body mass index (BMI), depression, and anxiety in patients with narcolepsy type 1. We carried out a cross-sectional study in which patients with narcolepsy type 1 and matched controls for sex, age, and education were assessed for occupational features, EDS (Epworth Sleepiness Scale), BMI, depression (Beck Depression Inventory), anxiety (State–Trait Anxiety Inventory), and Work Productivity and Activity Impairment (WPAI). Different statistical approaches were used to investigate differences between groups and correlations between WPAI scores and clinical features. The 127 patients with narcolepsy type 1 (mean age 38.2 ± 15.5, 91.3% taking drugs for narcolepsy) and 131 controls (mean age of 37.4 ± 14.3) included did not differ in terms of occupational features, except for hours worked/week (29.9 in patients vs. 34.9 in controls) and officially recognised disability (30.7% vs. 5.3%). Impairment in all WPAI scores was approximately three times greater in patients. Narcolepsy was associated with work time missed in 27.4% of patients, while 93.2% to 95.5% of them had some impairment while working or during daily activities (vs. 37.5–46.8% of controls). Correlations with WPAI scores were found for excessive daytime sleepiness only in patients, and for both depression and anxiety in patients and controls, with a stronger correlation for activity impairment in patients. These results suggest that, despite treatment, narcolepsy type 1 was associated with extensive impairment especially regarding job effectiveness and daily activities. Future studies should investigate risk factors and effects of interventions on these outcomes.

KEYWORDS
anxiety, depression, disability, sleep, sleepiness, work

Chiara Bassi and Francesco Biscarini contributed equally.

INTRODUCTION

Narcolepsy type 1 is a central disorder of hypersomnolence characterised by excessive daytime sleepiness, hypnagogic hallucinations, sleep paralysis, disrupted nocturnal sleep, and cataplexy (i.e., transient sudden loss of muscle tone triggered by emotions). Narcolepsy type 1 is associated with a deficiency of the hypothalamic neuropeptide hypocretin 1 in the cerebrospinal fluid, while normal levels of hypocretin and lack of cataplexy characterise the other form of narcolepsy, namely narcolepsy type 2 (NT2) (American Academy of Sleep Medicine, 2014). Metabolic and psychiatric comorbidities are often present and may worsen the patient's quality of life (QoL) (Bassetti et al., 2019): narcolepsy is associated with a higher body mass index (BMI) (Mohammadi et al., 2021), and the pooled prevalence of clinically significant depressive symptoms reaches up to 32% in patients with narcolepsy (Li et al., 2021), while anxiety rates reach up to 53% (Ohayon, 2013). Narcolepsy may also affect the working life of patients, possibly resulting in unemployment, and a diminished job satisfaction and chance of career advancement (Daniels et al., 2001; Dodel et al., 2007; Teixeira et al., 2004; White et al., 2020). Excessive daytime sleepiness, but not cataplexy, was found to be associated with work impairment (Dodel et al., 2004; Ingravallo et al., 2012; White et al., 2020), and a recent study found that a decrease in weight and a reduction in depressive feelings were positively correlated with an improved professional prognosis (White et al., 2020).

Unfortunately, the few studies that have examined the impairment in work and non-work activities of patients with narcolepsy through validated scales did not provide a comparison group (Emsellem et al., 2020; Thorpy et al., 2021) or were based on a self-reported diagnosis of narcolepsy (i.e., US National Health and Wellness Survey NHWS) (Flores et al., 2016). Overall, few studies have addressed the issue in cohorts of patients with an established diagnosis of narcolepsy type 1. The complexity of this disorder suggests the need to investigate the impact of narcolepsy type 1 on work and daily activities, and the association between impairment in these domains and measures of both excessive daytime sleepiness and the most common narcolepsy type 1 comorbidities, such as overweight, depression, and anxiety. This approach is in line with a bio-psycho-social perspective of narcolepsy that is increasingly being requested especially by, and for, younger patients (Graef et al., 2020; Ingram et al., 2021; Xiao et al., 2022), and concurs with increasing evidence that narcolepsy symptoms are not the only determinants that lead to impairment experienced by people with narcolepsy type 1 (D'Alterio et al., 2023; Maski et al., 2017).

The aim of this study was therefore to assess work productivity and activity impairments, and to explore their association with excessive daytime sleepiness, BMI, depression, and anxiety symptoms in patients with narcolepsy type 1 in comparison with people without sleep disorders.

METHODS

Study design

This was a cross-sectional study with a comparison group.

Setting and participants

Patients with a definitive diagnosis of narcolepsy type 1, according to the International Classification of Sleep Disorders-3 (American Academy of Sleep Medicine, 2014), and individuals without symptoms of sleep disorders (comparison group or controls) aged 18+ were invited to participate in the "Psychosocial Impact of Narcolepsy" study (D'Alterio et al., 2023). The study aimed to describe the psychosocial profile of patients with narcolepsy and that of sex- and age-matched people without sleep disorders through validated questionnaires, investigating the correlation between clinical features and social outcomes. Patients were recruited from those currently attending the outpatient clinic of the Narcolepsy Centre of Bologna, Italy. The centre is located in the Emilia Romagna region but most of the patients come from other Italian regions (Ingravallo et al., 2020). Controls were recruited from among parents, children, partners, or friends who accompany patients with narcolepsy or other neurological disorders (e.g., headache, neuromuscular disorders) in the tertiary neurological outpatient clinic of the IRCCS Institute of Neurological Sciences of Bologna.

Protocol approval and informed consent

The study was approved by the local Ethics Committee (Comitato Etico Interaziendale Bologna-Imola, protocol number: 16181). All participants provided written informed consent; confidentiality was assured.

Data collection

A semi-structured interview was conducted to obtain: (a) age at onset of symptoms, age at diagnosis, and current treatment (patients only); (b) height and weight, to calculate BMI; and (c) sociodemographic characteristics, including sex, age, education, sentimental status, occupational status, job characteristics, and official recognition of disability. In accordance with the Italian Social Security System non-contributory disability programme, citizens may benefit from non-economic and economic benefits according to the percentage of disability recognised (34–45% = prosthesis and aids; 46–73% = employment facilities for unemployed persons; 74%–99% = disablement benefit; 100% = disability pension) (Ingravallo et al., 2008). Disability status is ascertained by ad hoc appointed Medical Commissions that should establish the percentage of

disability proportionately to the "reduction of work capacity", regardless of the current occupational status of the applicant.

Questionnaires

Participants were asked to complete the following questionnaires.

The Epworth Sleepiness Scale (ESS) to assess sleepiness (total score range from 0 to 24).

The Beck Depression Inventory (BDI) to assess depressive symptoms (total score ranges from 0 to 63).

The State–Trait Anxiety Inventory (STAI) to assess the level of anxiety through two separate scales: the Trait anxiety scale, that assesses the respondents' typical anxiety level investigating how someone generally feels in various situations, and the State anxiety scale that assesses the respondents' feelings of anxiety "in the present moment"; for both scales the total score ranges from 20 to 80.

The Work Productivity and Activity Impairment Questionnaire – General Health (WPAI), a six-item instrument that provides four scores with reference to the past 7 days: (1) percentage of work time missed in the past 7 days due to health problems; (2) percentage of impairment while working during the past 7 days due to health problems; (3) percentage of overall work impairment due to health (combining the previous two scores); and (4) percentage of activity impairment (i.e., percentage of impairment in daily activities due to health problems) [http://www.reillyassociates.net/WPAI_Scoring.html]. The WPAI was adapted by replacing the word "problems" with "narcolepsy" for the group of patients. Work-related scores were obtained for participants who were currently employed, whereas activity (i.e., non-work) impairment was assessed in all participants.

Finally, patients were asked to complete a self-administered questionnaire on narcolepsy type 1 symptoms.

Statistical analysis

In the descriptive analysis we presented the continuous variables as the mean with standard deviation (SD) and median with interquartile range (IQR), while categorical variables were expressed as absolute (*n*) and relative frequency (%). We used the Kruskal-Wallis test variables and the Chi-square test for categorical variables between groups. Given the highly skewed distribution of WPAI scores, we also presented the scores according with three categories: 0% (i.e., no impairment), between 0% and 20%, and more than 20%. Spearman Rho correlations were estimated to evaluate the relationship between WPAI scores with ESS, BMI, BDI, and STAI trait and state anxiety scores. We evaluated the correlations by stratifying patients with narcolepsy type 1 and the control group. We considered a strong correlation to be a Rho >0.50, a moderate correlation between 0.30 to 0.50, and a weak one <0.30. A value of $p<0.05$ was considered as significant.

Statistical analyses were performed using STATA SE 14.

RESULTS

A total of 127 patients with narcolepsy type 1 completed all the questionnaires and were matched for sex, age, and educational level with 131 controls without sleep disorders. All patients except 11 (8.7%) took drugs for narcolepsy type 1 (clinical features of patients with narcolepsy type 1 are reported in Supplementary Table S1).

Socio-demographic and clinical characteristics

The sociodemographic characteristics of the two groups are shown in Table 1. The mean age was 38.2 ± 15.5 and 37.4 ± 14.3 for patients and controls, respectively, and 53.5% and 59.5% were female, respectively.

Patients and controls did not differ in age, sex, or education, but in the patient group 50.4% had a partner compared with 81.1% of the comparison group. Work status did not differ between groups, despite the higher unemployment rate reported by patients with narcolepsy type 1 (15.0% vs. 6.9%). Patients reported to work on average fewer hours/week (29.9 ± 12 vs 34.9 ± 14.2), while no significant differences were found between patients and controls with regard to work schedule or work shift.

Patients were officially recognised as disabled persons more often than controls (30.7% vs. 5.3%). In particular, two patients (5.1%) were recognised with a percentage of disability of between 34% and 45%, 25 (64.2%) between 46% and 73%, 10 (25.6%) between 74% and 99%, and 2 (5.1%) were recognised with 100% disability (Figure 1). With regard to the occupational status of those officially recognised as disabled persons, 25.8% of the employed people and 26.7% of the students among the patients were recognised as disabled persons versus 6.6% of those in employment and 3.6% of the students among the controls ($p < 0.001$); the percentage of those recognised with disability was 43.7% and 42.1% among homemakers/retired and unemployed patients, respectively, while in the comparison group none included in these categories were recognised as disabled persons.

Regarding clinical aspects, patients had higher ESS scores and BMI than controls (12.1 ± 4.8 vs. 5.4 ± 3.2 and 27.1 ± 5.6 vs. 23.4 ± 4.2, respectively). BDI scores were also higher in patients with narcolepsy type 1 compared with controls (11.1 ± 10.1 vs. 6.5 ± 7.0) as well as STAI-Trait and State anxiety scores (42.9 ± 11.4 vs. 39.3 ± 10.2 and 39.4 ± 11.5 vs. 36.0 ± 11.1, respectively) (Table 1).

Work productivity and activity impairment

All the WPAI work-related scores were significantly higher in patients than in controls: the mean percentage of work time missed

TABLE 1 Sociodemographic and clinical characteristics of participants: comparisons between patients and controls.

		Patients with narcolepsy ($n = 127$)	Comparison group ($N = 131$)	p
Sex, women	*n* (%)	68 (53.5)	78 (59.5)	0.331
Age (years)	Mean (SD)	38.2 (15.5)	37.4 (14.3)	0.980
Education	*n* (%)			
	Middle school	29 (22.8)	24 (18.3)	0.081
	High school	76 (59.8)	69 (52.7)	
	>High school	22 (17.3)	38 (29.0)	
Had a partner	*n* (%)	57 (50.4)	106 (81.1)	<0.001
Occupational status	*n* (%)			
	In employment	62 (48.8)	77 (58.8)	0.156
	Student	30 (23.6)	28 (21.4)	
	Homemaker/retired	16 (12.6)	17 (12.9)	
	Unemployed	19 (15.0)	9 (6.9)	
Weekly work hours	*n* (%)	29.9 (12.4)	34.9 (14.2)	0.011
Work schedule	*n* (%)			
	Part-time	12 (19.4)	17 (22.1)	0.695
	Full-time	50 (80.6)	60 (77.9)	
Shift workers	*n* (%)	16 (25.0)	15 (19.0)	0.386
Recognised as disabled persons	*n* (%)	39 (30.7)	7 (5.3)	<0.001
Epworth Sleepiness Scale	Mean (SD)	12.1 (4.8)	5.4 (3.2)	<0.001
	Median (IQR)	11.0 (9.0–16.0)	5.0 (3.0–7.0)	
Body Mass Index	Mean (SD)	27.1 (5.6)	23.4 (4.2)	<0.001
	Median (IQR)	26.7 (22.8–30.5)	22.8 (20.3–25.4)	
Beck Depression Inventory	Mean (SD)	11.1 (10.1)	6.5 (7.0)	<0.001
	Median (IQR)	9.0 (3.0–18.0)	4.0 (1.0–10.0)	
STAI-Trait anxiety	Mean (SD)	42.9 (11.4)	39.3 (10.2)	0. 009
	Median (IQR)	43.0 (34.0–51.0)	37.0 (32.0–46.0)	
STAI-State anxiety	Mean (SD)	39.4 (11.5)	36.0 (11.1)	0.011
	Median (IQR)	37.0 (32.0–49.0)	34.0 (28.0–42.0)	

(5.4 ± 15.6 vs. 0.6 ± 4.3), the mean percentage of impairment while working (31.2 ± 25.8 vs. 12.6 ± 23.1), and the mean percentage of overall work impairment (32.9 ± 27.3 vs. 11.5 ± 22.4) (Table 2).

Patients with narcolepsy type 1 also had a greater mean activity impairment compared with controls (38.3 ± 24.7 vs. 12.4 ± 19.6) (Table 2). The subgroup analysis according to the participants' occupational status showed that non-working patients (i.e., those who were homemakers/retired or unemployed) had a higher level of activity impairment (46.7 ± 25.8 and 57.1 ± 26.4, respectively) than patients in employment and students (32.0 ± 23.8 and 35.2 ± 17.9, respectively); non-work activity impairment was significantly higher in patients in each category of occupational status (Table 2).

An assessment of the WPAI scores divided into categories showed large differences between patients and controls: particularly, for the 0% category, we observed that 72.6% of patients vs. 97.0% of controls reported no work time missed, 6.8% vs. 62.5% reported no impairment while working, 5.8% vs. 61.5% reported no overall work impairment, and 3.5% vs. 53.2% reported no activity impairment (Table 2).

Correlations between clinical features and work and activity impairment scores

Correlations between clinical features and WPAI scores are reported in Table 3. There was a positive significant correlation between ESS scores and all the WPAI scores in patients with narcolepsy type 1, with strong correlations (Rho>0.5) between ESS and percentage of impairment while working (Rho = 0.51), overall work impairment (Rho = 0.54), and activity impairment (Rho = 0.56), whereas no significant correlation was found between ESS and WPAI scores in the comparison group.

BMI was not associated with WPAI outcomes in either patients or controls.

BDI scores significantly and directly correlated with all WPAI scores, except for the percentage of work time missed, in both

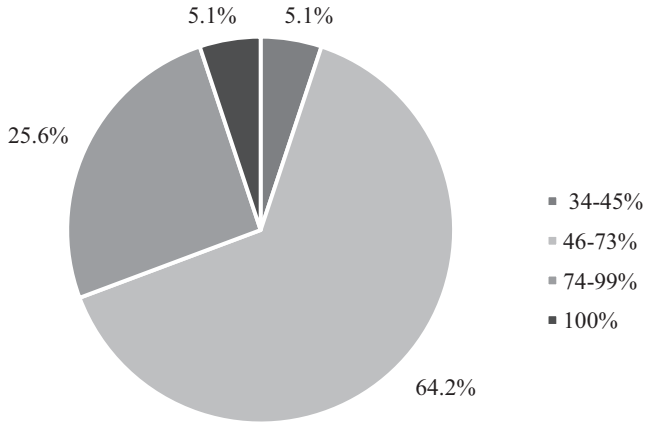

FIGURE 1 Degree of disability in the 39 patients officially recognised as having a disability: proportion of patients in the following disability ranges: 34%–45%, 46%–73%, 74%–99%, 100%.

patients and controls, with a strong correlation with activity impairment in patients with narcolepsy type 1 (Rho = 0.56).

STAI-Trait scores showed a significant direct weak correlation with all WPAI scores in controls, and with percentage of impairment while working and activity impairment in patients, the latter with a strong correlation (Rho = 0.59). Finally, STAI-State scores presented weak-to-moderate significantly positive correlations with all WPAI scores, except for the percentage of work time missed, in patients, and a weak positive correlation with impairment while working and activity impairment in controls.

DISCUSSION

The objective of this study was to assess work productivity and activity impairment in people with narcolepsy type 1 compared with those

TABLE 2 Work productivity and activity impairment scores according to ranges of responses in patient and comparison groups.

		Patients with narcolepsy ($n = 127$)	Comparison group ($n = 131$)	p
Percentage of work time missed[a]	Mean (SD)	5.4 (15.6)	0.6 (4.3)	0.026
	Median (IQR)	0 (0–3)	0 (0–0)	
Response range *N* (%)	0%	37 (72.6)	63 (97.0)	0.001
	0%–20%	10 (19.6)	1 (1.5)	
	>20%	4 (7.8)	1 (1.5)	
Percentage of impairment while working	Mean (SD)	31.2 (25.8)	12.6 (23.1)	<0.001
	Median (IQR)	20 (10–50)	0 (0–20)	
Response range *N* (%)	0%	4 (6.8)	45 (62.5)	<0.001
	0%–20%	31 (52.5)	16 (22.2)	
	>20%	24 (40.7)	11 (15.3)	
Percentage of overall work impairment	Mean (SD)	32.9 (27.3)	11.5 (22.4)	<0.001
	Median (IQR)	20 (10–50)	0 (0–10)	
Response range *N* (%)	0%	3 (5.8)	40 (61.5)	<0.001
	0–20%	24 (47.1)	16 (24.6)	
	>20%	24 (47.1)	9 (13.9)	
Percentage of activity impairment[b]	Mean (SD)	38.3 (24.7)	12.4 (19.6)	<0.001
	Median (IQR)	30 (20–60)	0 (0–20)	
Response range *N* (%)	0%	4 (3.5)	67 (53.2)	<0.001
	0%–20%	39 (33.6)	38 (30.1)	
	>20%	73 (62.9)	21 (16.7)	
In employment	Mean (SD)	32.1 (23.8)	12.1 (20.0)	<0.001
	Median (IQR)	20 (10–40)	0 (0–20)	
Student	Mean (SD)	35.2 (17.8)	10 (16.6)	<0.001
	Median (IQR)	30 (30–40)	0 (0–15)	
Homemaker/retired	Mean (SD)	46.7 (25.8)	19.4 (24.1)	0.003
	Median (IQR)	50 (20–70)	10 (0–30)	
Unemployed	Mean (SD)	57.1 (26.4)	13.3 (20)	0.001
	Median (IQR)	60 (50–70)	0 (0–20)	

[a]Only currently employed participants.
[b]All participants.

TABLE 3 Correlations between sleepiness, body mass index, depression and anxiety symptoms, and Work productivity and activity impairment scores in patient and comparison groups.

	Work time missed		Impairment while working		Overall work impairment		Activity impairment	
	Rho	*p*	Rho	*p*	Rho	*p*	Rho	*p*
Patients with narcolepsy								
Epworth Sleepiness Scale	0.35	0.012	**0.51**	<0.001	**0.54**	<0.001	**0.56**	<0.001
Body Mass Index	0.18	0.253	0.07	0.639	0.09	0.576	0.07	0.502
Beck Depression Inventory	0.23	0.110	0.36	0.005	0.32	0.020	**0.56**	<0.001
STAI- Trait	0.16	0.259	0.26	0.048	0.23	0.101	**0.59**	<0.001
STAI- State	0.15	0.305	0.32	0.012	0.29	0.038	0.48	<0.001
Comparison group								
Epworth Sleepiness Scale	−0.01	0.917	−0.12	0.305	−0.10	0.419	0.07	0.462
Body Mass Index	−0.12	0.339	0.18	0.138	0.08	0.526	0.08	0.389
Beck Depression Inventory	0.21	0.090	0.38	0.001	0.35	0.005	0.31	0.001
STAI- Trait	0.25	0.049	0.27	0.018	0.26	0.039	0.22	0.013
STAI- State	0.22	0.075	0.25	0.036	0.21	0.096	0.24	0.006

Note: Strong correlations (Rho>0.5) in bold.

without sleep disorders using the WPAI, and to investigate correlations between WPAI outcomes and excessive daytime sleepiness, the main disabling symptom of narcolepsy, BMI, depression, and anxiety, as frequently associated comorbid features.

We found that, despite treatment, patients with narcolepsy type 1 were more likely to have an official recognition of disability and had three times greater impairments in productivity and activity than people without narcolepsy. The subjective sleepiness level was associated with work and activity impairments in patients with narcolepsy type 1 but not in the comparison group, while depression and anxiety, but not BMI, were associated with work and non-work impairment in both patients and controls, with a stronger association with non-work activities in patients with narcolepsy type 1.

Even though patients with narcolepsy type 1 reported a higher unemployment rate, in line with other European studies, we did not find significant differences between patients and controls in terms of employment status (Jennum et al., 2009; White et al., 2020); on average, however, patients with narcolepsy type 1 worked fewer hours than the controls. This finding has rarely been reported by previous studies and deserves further investigation, since reducing weekly working hours may be a strategy that patients adopt in order to cope with their work impairment due to narcolepsy. On the other hand, 30.7% of patients were officially recognised as disabled persons versus 5.3% of controls. This result is in line with studies carried out in other European Countries (Jennum et al., 2009; White et al., 2020), but shows a higher percentage than that previously reported in the USA (Flores et al., 2016), probably due to welfare differences among the different countries that should be considered when planning international surveys or making transnational comparisons.

It is worth noting that, in almost all patients, the degree of disability was greater than 45%, the minimum rate required for employment facilities to be offered to unemployed persons in Italy. This result may suggest either that the Medical Commissions that assess disability have a clear understanding of the impact of narcolepsy on work activities or that only patients with relevant impairment apply for disability benefits. Some patients, despite a relevant work impairment, may not apply for disability benefits for fear of being reported to the driving licensing authority and losing their driving licence (Ingravallo et al., 2008). Indeed, previous studies have indicated that the Medical Commissions assessing disability were willing to report between 67% and 100% of patients with narcolepsy to the driving licensing authority (Ingravallo et al., 2008).

Comparisons between patients and controls regarding the WPAI scores showed the extensive impact of narcolepsy type 1 on work and non-work activities despite almost all patients being under treatment. The WPAI is a validated tool for assessing work productivity loss and activity impairment, and its psychometric properties have been extensively tested in various populations (Prasad et al., 2004; Reilly et al., 1993). This is the first study that has examined patients with narcolepsy type 1 and controls who were matched for sex, age, education, and the first that has used WPAI in non-pharmacological studies in order to understand the impact of narcolepsy on WPAI outcomes.

Interestingly, while narcolepsy was associated with missed work time in a quarter of patients, almost all of them had problems while working. Similar findings have been found in untreated patients with narcolepsy type 1, confirming previous observations that narcolepsy and other chronic neurological disorders such as epilepsy are associated with minimal absenteeism (Thorpy et al., 2021) but have a greater impact on job effectiveness, suggesting that investigations into the work impact of narcolepsy should look beyond the measure of missed workdays. Ad hoc designed studies are needed to better investigate the reasons for these findings. However, we can speculate

that the reduced job effectiveness may contribute to the diminished chance of promotion and job satisfaction reported by patients with narcolepsy.

In accordance with previous studies (Flores et al., 2016; Thorpy et al., 2021), patients with narcolepsy reported a greater impairment in non-work activities than in overall work activities. In our study, the subgroup analysis according to patients' occupational status showed that this result was mainly due to answers from non-working patients (i.e., homemakers, retired, and unemployed patients), while patients who had an occupation reported a comparable impairment in both work and non-work activities. Since in our study half of non-working patients were officially recognised as disabled persons compared with a quarter of occupied patients, we hypothesised that this result may be due to the higher severity of narcolepsy in many non-working patients, who were probably outside the labour market due to narcolepsy, instead of a different impact of narcolepsy on work and non-work activities.

Regarding clinical features associated with functional impairment, we confirmed the direct relationship between WPAI scores and the severity of sleepiness in accordance with the ESS found in patients with narcolepsy and obstructive sleep apnea (Jennum et al., 2021; Stepnowsky et al., 2019; Weaver et al., 2021). Interestingly, no correlation was found in the control group, suggesting that sleepiness needs to reach a pathological threshold before it impairs work productivity and non-work activities. Moreover, while symptoms of depression and anxiety also had some correlation with work and activity impairment in people without sleep disorders (Erickson et al., 2009; Khansa et al., 2020), we found a strong correlation with activity impairment only in patients with narcolepsy type 1. Symptoms of narcolepsy type 1 can have notable effects on patients' social interactions (Daniels et al., 2001; Teixeira et al., 2004) and may lead to withdrawal behaviours (Raggi et al., 2019) and feelings of loss of control (Fortuyn et al., 2010) that may cause psychological distress and reactive anxiety-depressive symptoms that may, in turn, worsen the activity impairment. As an alternative explanation, the impact of depression and anxiety may be greater because they add a burden to the already impaired activity functioning in patients with narcolepsy type 1. The understanding of this mechanism has a clinical relevance: reducing sleepiness may be effective in reducing the impairment due to narcolepsy (Emsellem et al., 2020; Thorpy et al., 2021; Weaver et al., 2021), but further management of depressive and anxiety symptoms could be necessary, thus calling for future longitudinal/interventional studies investigating the relation between mood, anxiety, excessive daytime sleepiness, and work/productivity impairments. Furthermore, since narcolepsy type 1 remains a rare disorder and several new medications have only become available in the past few years, future multicentre, and possibly international, studies are needed to assess the potential impact of medications on the personal and socio-economic burden of narcolepsy.

We acknowledge some limitations of this study. Clinical evaluation was based on a self-reported questionnaire, and sleepiness was evaluated only with the ESS, without the implementation of other scales (such as the Narcolepsy Severity Scale (Dauvilliers et al., 2017), that was not available when the study was designed). We did not explore in detail whether working patients had some job accommodations, a topic worthy of attention in order to better understand how people with narcolepsy cope with narcolepsy in the workplace. Another possible limitation concerns the recruitment of controls among family members or partners of patients with narcolepsy or other neurological disorders. Regrettably, since we did not collect this information, we were unable to determine the proportion of relatives of patients with narcolepsy type 1 in the comparison group. Nevertheless, since the sociodemographic characteristics of the comparison group mirrored that of the Italian population, we were confident that our recruitment strategy probably had minimal to no impact on the primary study outcomes. Finally, the cross-sectional nature of our study prevented us from establishing causal relationships between the investigated variables.

The strengths of the study include the involvement of a sizeable cohort of patients with a definitive diagnosis of narcolepsy type 1, considering the rarity of the disease, a comprehensive assessment of work productivity and activity impairment through the WPAI questionnaire, and the involvement of a comparison group, ensuring the assessment of the impact of narcolepsy type 1 on various outcomes.

CONCLUSION

This study indicates that, despite treatment, narcolepsy type 1 was associated with an extensive impairment especially of job effectiveness and daily activities correlated with sleepiness, anxiety, and depression, and emphasises the importance of collecting a comprehensive work history and of monitoring these outcomes in both clinical and research settings. Future studies, possibly longitudinal, are needed to identify risk factors for functional impairment and disability in patients with narcolepsy type 1, to investigate countermeasures adopted by patients to cope with narcolepsy symptoms in the workplace, and to assess the effect of specific psychological interventions (counselling, behavioural activation, interpersonally oriented techniques, etc.) on these important patient-reported outcomes.

AUTHOR CONTRIBUTIONS

Chiara Bassi: Writing – original draft; writing – review and editing; formal analysis; data curation; visualization. **Francesco Biscarini:** Writing – original draft; writing – review and editing; visualization. **Corrado Zenesini:** Conceptualization; writing – review and editing; formal analysis; data curation; methodology; validation. **Marco Menchetti:** Conceptualization; methodology; writing – review and editing; supervision. **Luca Vignatelli:** Conceptualization; methodology; writing – review and editing. **Fabio Pizza:** Conceptualization; writing – review and editing; methodology; supervision; resources. **Giuseppe Plazzi:** Conceptualization; methodology; writing – review and editing; supervision; resources. **Francesca Ingravallo:** Conceptualization; investigation; writing – original draft; methodology; writing – review and editing; supervision; data curation; project administration; validation.

ACKNOWLEDGEMENTS

The authors thank Alessandra D'Alterio, Andrea Rossetti, Chiara Cichetti, Matteo Comes Franchini, Lucia Lambertucci, and Chiara Laposata for their valuable help in data collection. The authors are indebted to all participants in the study and to the Associazione Italiana Narcolettici e ipersonni (AIN onlus, www.narcolessia.org), which supported the study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Francesco Biscarini https://orcid.org/0000-0001-9756-6470
Corrado Zenesini https://orcid.org/0000-0002-9855-8197
Marco Menchetti https://orcid.org/0000-0003-0553-539X
Luca Vignatelli https://orcid.org/0000-0002-9051-7091
Fabio Pizza https://orcid.org/0000-0003-2294-9551
Giuseppe Plazzi https://orcid.org/0000-0002-1051-0472
Francesca Ingravallo https://orcid.org/0000-0002-5194-375X

REFERENCES

American Academy of Sleep Medicine (Ed.). (2014). *International classification of sleep disorders* (3rd ed.). American Academy of Sleep Medicine.

Bassetti, C. L. A., Adamantidis, A., Burdakov, D., Han, F., Gay, S., Kallweit, U., Khatami, R., Koning, F., Kornum, B. R., Lammers, G. J., Liblau, R. S., Luppi, P. H., Mayer, G., Pollmächer, T., Sakurai, T., Sallusto, F., Scammell, T. E., Tafti, M., & Dauvilliers, Y. (2019). Narcolepsy – clinical spectrum, aetiopathophysiology, diagnosis and treatment. *Nature Reviews. Neurology*, *15*(9), 519–539. https://doi.org/10.1038/s41582-019-0226-9

D'Alterio, A., Menchetti, M., Zenesini, C., Rossetti, A., Vignatelli, L., Franceschini, C., Varallo, G., Pizza, F., Plazzi, G., & Ingravallo, F. (2023). Resilience and its correlates in patients with narcolepsy type 1. *Journal of Clinical Sleep Medicine*, *19*(4), 719–726. https://doi.org/10.5664/jcsm.10418

Daniels, E., King, M. A., Smith, I. E., & Shneerson, J. M. (2001). Health-related quality of life in narcolepsy. *Journal of Sleep Research*, *10*(1), 75–81. https://doi.org/10.1046/j.1365-2869.2001.00234.x

Dauvilliers, Y., Beziat, S., Pesenti, C., Lopez, R., Barateau, L., Carlander, B., Luca, G., Tafti, M., Morin, C. M., Billiard, M., & Jaussent, I. (2017). Measurement of narcolepsy symptoms: The narcolepsy severity scale. *Neurology*, *88*(14), 1358–1365. https://doi.org/10.1212/WNL.0000000000003787

Dodel, R., Peter, H., Spottke, A., Noelker, C., Althaus, A., Siebert, U., Walbert, T., Kesper, K., Becker, H. F., & Mayer, G. (2007). Health-related quality of life in patients with narcolepsy. *Sleep Medicine*, *8*(7–8), 733–741. https://doi.org/10.1016/j.sleep.2006.10.010

Dodel, R., Peter, H., Walbert, T., Spottke, A., Noelker, C., Berger, K., Siebert, U., Oertel, W. H., Kesper, K., Becker, H. F., & Mayer, G. (2004). The socioeconomic impact of narcolepsy. *Sleep*, *27*(6), 1123–1128. https://doi.org/10.1093/sleep/27.6.1123

Emsellem, H. A., Thorpy, M. J., Lammers, G. J., Shapiro, C. M., Mayer, G., Plazzi, G., Chen, D., Carter, L. P., Villa, K. F., Lee, L., Menno, D., Black, J., & Dauvilliers, Y. (2020). Measures of functional outcomes, work productivity, and quality of life from a randomized, phase 3 study of solriamfetol in participants with narcolepsy. *Sleep Medicine*, *67*, 128–136. https://doi.org/10.1016/j.sleep.2019.11.1250

Erickson, S. R., Guthrie, S., Vanetten-Lee, M., Himle, J., Hoffman, J., Santos, S. F., Janeck, A. S., Zivin, K., & Abelson, J. L. (2009). Severity of anxiety and work-related outcomes of patients with anxiety disorders. *Depression and Anxiety*, *26*(12), 1165–1171. https://doi.org/10.1002/da.20624 PMID: 19842165.

Flores, N. M., Villa, K. F., Black, J., Chervin, R. D., & Witt, E. A. (2016). The humanistic and economic burden of narcolepsy. *Journal of Clinical Sleep Medicine*, *12*(3), 401–407. https://doi.org/10.5664/jcsm.5594

Fortuyn, H. A., Lappenschaar, M. A., Furer, J. W., Hodiamont, P. P., Rijnders, C. A., Renier, W. O., Buitelaar, J. K., & Overeem, S. (2010). Anxiety and mood disorders in narcolepsy: A case-control study. *General Hospital Psychiatry*, *32*(1), 49–56. https://doi.org/10.1016/j.genhosppsych.2009.08.007

Graef, D. M., Byars, K. C., Simakajornboon, N., & Dye, T. J. (2020). Topical review: A biopsychosocial framework for pediatric narcolepsy and idiopathic hypersomnia. *Journal of Pediatric Psychology*, *45*(1), 34–39. https://doi.org/10.1093/jpepsy/jsz085

Ingram, D. G., Jesteadt, L., Crisp, C., & Simon, S. L. (2021). Perceived challenges in pediatric narcolepsy: A survey of parents, youth, and sleep physicians. *Journal of Clinical Sleep Medicine*, *17*(1), 13–22. https://doi.org/10.5664/jcsm.8774

Ingravallo, F., Gnucci, V., Pizza, F., Vignatelli, L., Govi, A., Dormi, A., Pelotti, S., Cicognani, A., Dauvilliers, Y., & Plazzi, G. (2012). The burden of narcolepsy with cataplexy: How disease history and clinical features influence socio-economic outcomes. *Sleep Medicine*, *13*(10), 1293–1300. https://doi.org/10.1016/j.sleep.2012.08.002

Ingravallo, F., Vignatelli, L., Brini, M., Brugaletta, C., Franceschini, C., Lugaresi, F., Manca, M. C., Garbarino, S., Montagna, P., Cicognani, A., & Plazzi, G. (2008). Medico-legal assessment of disability in narcolepsy: An interobserver reliability study. *Journal of Sleep Research*, *17*(1), 111–119. https://doi.org/10.1111/j.1365-2869.2008.00630.x

Ingravallo, F., Vignatelli, L., Pagotto, U., Vandi, S., Moresco, M., Mangiaruga, A., Oriolo, C., Zenesini, C., Pizza, F., & Plazzi, G. (2020). Protocols of a diagnostic study and a randomized controlled non-inferiority trial comparing televisits vs standard in-person outpatient visits for narcolepsy diagnosis and care: TElemedicine for NARcolepsy (TENAR). *BMC Neurol*, *20*(1), 176. https://doi.org/10.1186/s12883-020-01762-9

Jennum, P., Coaquira Castro, J., Mettam, S., Kharkevitch, T., & Cambron-Mellott, M. J. (2021). Socioeconomic and humanistic burden of illness of excessive daytime sleepiness severity associated with obstructive sleep apnoea in the European Union 5. *Sleep Medicine*, *84*, 46–55. https://doi.org/10.1016/j.sleep.2021.05.010

Jennum, P., Knudsen, S., & Kjellberg, J. (2009). The economic consequences of narcolepsy. *Journal of Clinical Sleep Medicine*, *5*(3), 240–245.

Khansa, W., Haddad, C., Hallit, R., Akel, M., Obeid, S., Haddad, G., Soufia, M., & Kheir, N. (2020). Abi Elias Hallit C, Khoury R, Salameh P, Hallit S. Interaction between anxiety and depression on suicidal ideation, quality of life, and work productivity impairment: Results from a representative sample of the Lebanese population. *Perspectives in Psychiatric Care*, *56*(2), 270–279. https://doi.org/10.1111/ppc.12423

Li, X., Sanford, L. D., Zong, Q., Zhang, Y., Tan, L., Li, T., Ren, R., Zhou, J., Han, F., & Tang, X. (2021). Prevalence of depression or depressive symptoms in patients with narcolepsy: A systematic review and meta-analysis. *Neuropsychology Review*, *31*(1), 89–102. https://doi.org/10.1007/s11065-020-09443-7

Maski, K., Steinhart, E., Williams, D., Scammell, T., Flygare, J., McCleary, K., & Gow, M. (2017). Listening to the patient voice in narcolepsy: Diagnostic delay, disease burden, and treatment efficacy.

Journal of Clinical Sleep Medicine, *13*(3), 419–425. https://doi.org/10.5664/jcsm.6494

Mohammadi, S., Moosaie, F., Saghazadeh, A., Mahmoudi, M., & Rezaei, N. (2021). Metabolic profile in patients with narcolepsy: A systematic review and meta-analysis. *Sleep Medicine*, *81*, 268–284. https://doi.org/10.1016/j.sleep.2021.02.040

Ohayon, M. M. (2013). Narcolepsy is complicated by high medical and psychiatric comorbidities: A comparison with the general population. *Sleep Medicine*, *14*(6), 488–492. https://doi.org/10.1016/j.sleep.2013.03.002

Prasad, M., Wahlqvist, P., Shikiar, R., & Shih, Y. C. (2004). A review of self-report instruments measuring health-related work productivity: A patient-reported outcomes perspective. *PharmacoEconomics*, *22*(4), 225–244. https://doi.org/10.2165/00019053-200422040-00002

Raggi, A., Plazzi, G., & Ferri, R. (2019). Health-related quality of life in patients with narcolepsy: A review of the literature. *The Journal of Nervous and Mental Disease*, *207*(2), 84–99. https://doi.org/10.1097/NMD.0000000000000918

Reilly, M. C., Zbrozek, A. S., & Dukes, E. M. (1993). The validity and reproducibility of a work productivity and activity impairment instrument. *PharmacoEconomics*, *4*(5), 353–365. https://doi.org/10.2165/00019053-199304050-00006

Stepnowsky, C., Sarmiento, K. F., Bujanover, S., Villa, K. F., Li, V. W., & Flores, N. M. (2019). Comorbidities, health-related quality of life, and work productivity among people with obstructive sleep apnea with excessive sleepiness: Findings from the 2016 US National Health and wellness survey. *Journal of Clinical Sleep Medicine*, *15*(2), 235–243. https://doi.org/10.5664/jcsm.7624

Teixeira, V. G., Faccenda, J. F., & Douglas, N. J. (2004). Functional status in patients with narcolepsy. *Sleep Medicine*, *5*(5), 477–483. https://doi.org/10.1016/j.sleep.2004.07.001

Thorpy, M. J., Ohayon, M. M., Carls, G., Black, J., Pasta, D. J., Hyman, D. L., & Villa, K. F. (2021). Assessing the impact of sodium oxybate treatment on functioning, productivity, and health-related quality of life in patients with narcolepsy: Findings from the nexus narcolepsy registry (waves 1-4). *Sleep Medicine*, *84*, 380–388. https://doi.org/10.1016/j.sleep.2021.06.010

Weaver, T. E., Mathias, S. D., Crosby, R. D., Bron, M., Bujanover, S., Menno, D., Villa, K. F., & Drake, C. (2021). Relationship between sleep efficacy endpoints and measures of functional status and health-related quality of life in participants with narcolepsy or obstructive sleep apnea treated for excessive daytime sleepiness. *Journal of Sleep Research*, *30*(3), e13210. https://doi.org/10.1111/jsr.13210

White, M., Charbotel, B., Fort, E., Bastuji, H., Franco, P., Putois, B., Mazza, S., & Peter-Derex, L. (2020). Academic and professional paths of narcoleptic patients: The Narcowork study. *Sleep Medicine*, *65*, 96–104. https://doi.org/10.1016/j.sleep.2019.07.020

Xiao, L., Chen, A., Parmar, A., Frankel, L., Toulany, A., Murray, B. J., & Narang, I. (2022). Narcolepsy treatment: Voices of adolescents. *Behavioral Sleep Medicine*, *20*(2), 260–268. https://doi.org/10.1080/15402002.2021.1916496

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Bassi, C., Biscarini, F., Zenesini, C., Menchetti, M., Vignatelli, L., Pizza, F., Plazzi, G., & Ingravallo, F. (2023). Work productivity and activity impairment in patients with narcolepsy type 1. *Journal of Sleep Research*, e14087. https://doi.org/10.1111/jsr.14087