

The Impact of Narcolepsy and Its Treatment – A European Study

a report by

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Narcolepsy with cataplexy affects approximately one in 2,000–3,000 people in most societies,¹ but about 80% of individuals are thought to remain undiagnosed despite recent refinements to diagnostic criteria.² The negative social impact of narcolepsy with cataplexy has been extensively studied, and includes impairment in driving skill, high prevalence of car, machine or domestic accidents and altered professional performance leading to unemployment, frequent changes of job, working disability and early retirement.^{3–5}

In the past, standard treatment has consisted of amphetamines for excessive daytime sleepiness (EDS) and antidepressants for cataplexy. However, over the past decade modafinil has become the first-line treatment for EDS,⁶ and sodium oxybate has been introduced to treat not only cataplexy, but also EDS and other symptoms of narcolepsy with cataplexy.^{7–9}

Few published studies have focused on the quality of life of patients with narcolepsy with cataplexy or pinpointed the persistent impact of symptoms on sufferers.¹² Previous studies have also ignored the impact of the disease on the patient's partner, friends or carers and the effect this has upon the family unit and/or social interactions. The impression from the physician's perspective has also been overlooked: no published data have examined the physician's perception of the patient's symptoms and quality of life and compared this with the patient's own assessment.

We decided to perform a European study on narcolepsy with cataplexy taking into account, for the first time, the perception of the three key facilitators in the management of the disease: patient, partner or friend and physician. The aims of this study were: to assess the frequency and severity of symptoms of narcolepsy with cataplexy in patients currently taking standard treatments; to assess the impact of the symptoms on the patient and those closest to them; and to compare this with the physician's impression of the symptom frequency and impact.

Methods

A total of 67 patients identified during routine consultations in specialist sleep centres were included in the study. Patients had previously been diagnosed with narcolepsy with clear-cut cataplexy following polysomnography and multiple sleep latency tests (MSLT): MSLT <8 minutes and at least two sleep-onset rhythmic eye movement periods. All patients were currently receiving treatment for their condition. Eighteen specialist sleep centres in four European countries – UK (four), France (five), Spain (five) and Germany (four) – participated in this study. The 67 patients with narcolepsy with cataplexy, together with their partner or friend and physician, were recruited from these centres: 11 from the UK, 25 from France, 23 from Spain and eight from Germany.

Physicians provided the patients with the contact details of a country-specific fieldwork agency and requested that the patients contact the agency to express their interest in participating in the study. Enrolment into the study took place after the completion of a structured telephone screening questionnaire, undertaken by the fieldwork agency. Entry criteria included a Ullanlinna Narcolepsy Scale (UNS) score of 10–44 and the identification of a partner or friend to participate in the research. The UNS is a simple 11-item questionnaire-based scale (range 0–44) addressing the two main features of narcolepsy: abnormal sleeping tendency and cataplexy.¹⁰

Patients enrolled into the study along with their partner or friend underwent a face-to-face interview with trained fieldwork agents who individually and privately administered the Patient or Partner/Friend Questionnaires. The patient's questionnaire included the Short Form 36 (SF-36), and patients were also asked to complete a seven-day diary form assessing their naps, cataplexy, drug usage, sleep latency and maintenance and ability to perform tasks. Interviewers provided instructions on how to complete this diary form. The physicians, who were expert in the management of narcolepsy, completed the Physician Questionnaire after the patient had agreed to participate in the study. The Physician Questionnaire included questions on symptom ratings, symptoms that required further improvement, treatments prescribed and the physician's view of the patient's commitment to and satisfaction with treatment.

Statistical Analysis

The SPSS statistics package was used to analyse the data from the respondents. Where comparisons were made, statistical significance was tested using the chi-squared test for categorical data and student's t-test for two-group comparisons of means. Descriptive statistics such as frequency analysis were reported in the form of percentages.

Comparisons were also made between the views of patients and those of physicians and partners/friends on the impact of symptoms on quality of life. A difference of three on a 10-point weighting scale (equating to approximately 1 standard deviation [SD] for each of the



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Figure 1: Frequency of Narcolepsy with Cataplexy Symptoms as Reported by the Patient (Excludes 'Not Stated')

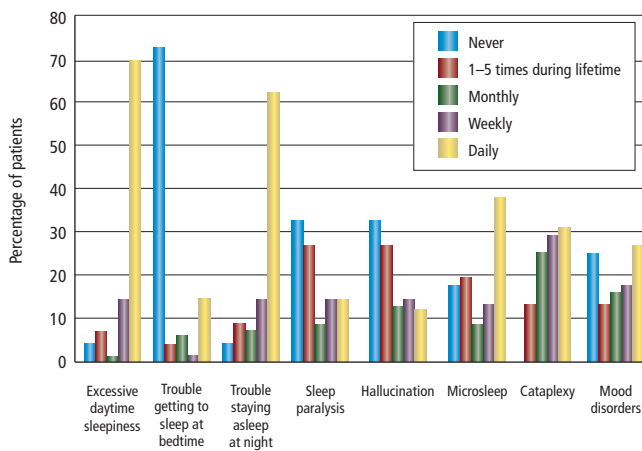


Figure 2: Short Form-36 Scores for Narcolepsy with Cataplexy in Patients Compared with US Norms

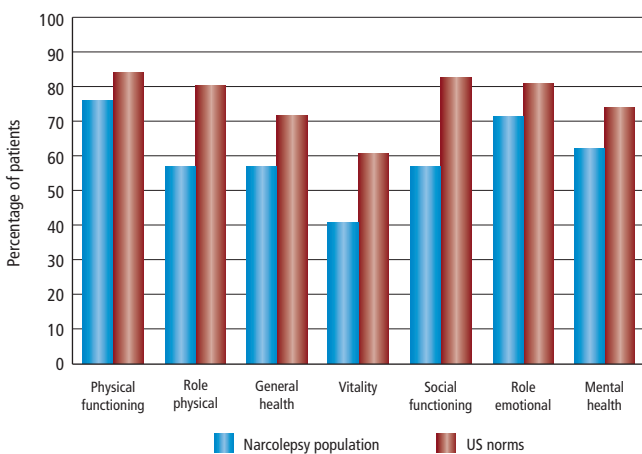
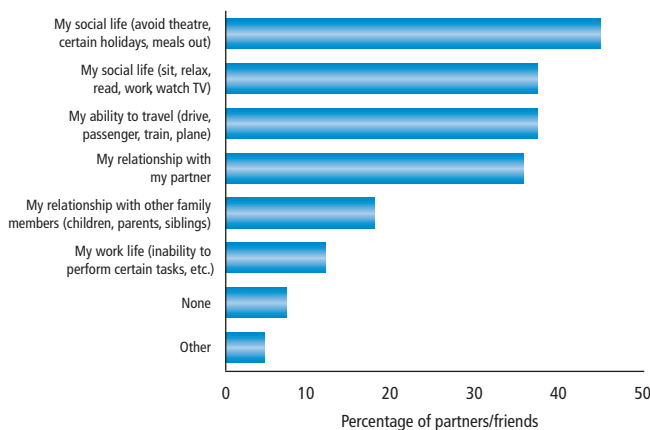


Figure 3: The Impact of Symptoms on Partner/Friend



symptoms) between the views of patients for each of the symptoms and those of physicians and/or partners/friends was deemed to be clinically relevant.

Results

Patient Characteristics

Of the 67 patients included in the study, 31 (46%) were men. Precise ages were not requested, but patients were categorised into seven age

groups ranging from 19 to >71 years (44.8% were aged ≤ 40 years; 55.2% were aged >40 years). Their UNS score ranged from 10 to 41 (mean \pm SD: 25.31 \pm 6.45). Body mass index (BMI) ranged from 17.3 to 44.6kg/m² (mean \pm SD: 27.49 \pm 5.89). Forty-one patients (61.2%) had a BMI >25kg/m².

Daytime medications taken during the study period were modafinil (62.7%), methylphenidate (19.4%) and antidepressants, including venlafaxine (11.9%), clomipramine (11.9%), fluoxetine (7.5%), paroxetine (4.5%) and dextroamphetamine (3.0%). Sodium oxybate was taken at night by 26.9% of the patients. Overall, 7.5% of the patients were extremely satisfied with their current treatment, 22.4% were very satisfied, 35.8% were satisfied, 26.9% were less than satisfied and 6% were unsatisfied, and in 1.5% no view was stated.

Symptom Frequency

The frequency with which patients experienced the various symptoms of narcolepsy is shown in Figure 1. Despite standard treatments, 70% of patients reported EDS every day and 31% had daily cataplexy. Of note, 63% reported nightly problems of staying asleep and 15% had trouble getting to sleep each night, highlighting the night-time sleep abnormalities.

Quality of Life

The impact of the patient's symptoms on his/her quality of life as estimated by the SF-36 is shown in Figure 2. These values have been compared with norms for the general US population.¹¹ Patients had significantly lower scores than US norms in all domains ($p < 0.001$; $p < 0.05$ for role emotional) except bodily pain. The statistically significant differences were greater in patients with a UNS score >25 compared with those with a score ≤ 25 .

The influence of individual symptoms on the patient's SF-36 domains was assessed. This analysis is not able to demonstrate the influence of EDS and cataplexy on the individual SF-36 domains because they occurred so frequently. Statistically significant influences were observed for the following symptoms across individual SF-36 domains: trouble getting to sleep influenced bodily pain ($p < 0.01$) and physical functioning ($p < 0.05$); mood disorders influenced mental health ($p < 0.01$), vitality ($p < 0.01$) and role emotional ($p < 0.05$).

Day-to-day Activities and Accidents

A range of day-to-day activities were affected by the patient's narcolepsy: 56.7% of patients did not visit the cinema or theatre due to their narcolepsy, while relationships with others were affected in 28.4% of patients. Other activities affected included playing sports and general household chores, with only 16.4% of patients reporting that their narcolepsy had no effect on their day-to-day activities.

Narcolepsy had caused at least one accident at home or at work in 32.9% of patients during the previous year. Of those patients who held a driving licence, 24% had had a road traffic accident due to sleepiness in the previous year.

Response of Partner/Friend

Of the partners/friends who entered the study, 48% provided day-to-day care for the patient with narcolepsy and cataplexy, and 59.4% of these carers provided help for more than one hour per day. The impact of the patient's symptoms on the life of his or her partner/friend is shown in Figure 3. For the partner/friend, there was a negative impact on social life

(44.8%), personal time (37.3%), ability to travel (37.3%) and relationship with partner (35.8%).

The partners/friends recognised the problems of daytime sleepiness, concentration and mood/morale experienced by the patient (see *Table 1*). The partners/friends did not experience these symptoms themselves to the same degree, although 46.3% stated that they experienced negative mood/morale, 31.3% reported increased feelings of daytime sleepiness and 28.4% reported a loss of concentration (see *Table 1*).

Patient, Partner/Friend and Physician Comparative Assessment

The frequency of the symptoms experienced by patients with narcolepsy was assessed independently by the patient, partner/friend and physician (see *Figure 4*). Significant differences in the frequency of symptoms observed were reported between: the patient and partner/friend for cataplexy ($p < 0.01$); the patient and physician for cataplexy ($p < 0.05$), mood disorders ($p < 0.01$) and sleep paralysis ($p < 0.01$); and the partner/friend and physician for mood disorder ($p < 0.05$), microsleep ($p < 0.05$) and trouble getting to sleep ($p < 0.05$).

The impact of the symptoms on the patient’s quality of life was also reported separately by the patient, partner/friend and physician. Significant differences were identified between: the patient and partner/friend for mood disorders ($p < 0.05$), microsleep ($p < 0.01$), trouble getting to sleep ($p < 0.01$), trouble staying asleep ($p < 0.01$), cataplexy ($p < 0.01$) and hallucination ($p < 0.05$); the patient and physician for EDS ($p < 0.05$), mood disorders ($p < 0.001$), microsleep ($p < 0.05$), trouble getting to sleep ($p < 0.01$), trouble staying asleep ($p < 0.001$), cataplexy ($p < 0.01$), sleep paralysis ($p < 0.001$) and hallucination ($p < 0.001$); and the partner/friend and physician for mood disorders ($p < 0.01$) and sleep paralysis ($p < 0.01$).

A three-point difference in the 10-point weighting scale used in this questionnaire was taken as clinically important, allowing for up to 1 SD. The percentage of physicians and partners/friends who ranked the symptom impact on the patient’s quality of life differently from the patient is shown in *Table 2*.

For every symptom the physicians were more likely to underestimate than overestimate the impact on the patient’s quality of life, particularly for trouble getting to sleep, trouble staying asleep and mood disorder. The differences between the partner and the patient were statistically smaller than the differences between the physician and the patient, but for every symptom the partners also underestimated the impact relative to the patient.

Discussion

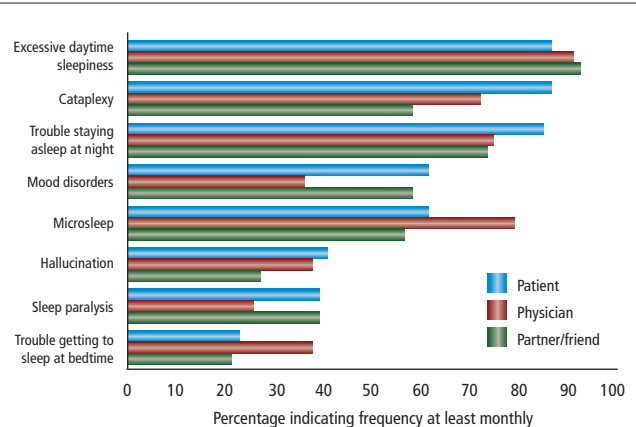
This study was designed to assess how effectively patients suffering from narcolepsy with cataplexy are managed with currently available treatments and to determine the continuing impact of the symptoms on the patients and those closest to them. The views of patients were also compared with those of their partner or close friend and their treating physician to understand ways in which care might be further improved.

The 18 participating European sleep centres identified 67 patients using agreed diagnostic criteria, all of whom were receiving standard

Table 1: Perception by Partner/Friend of the Impact of Symptoms on the Patient and Him/Herself

Narcolepsy Symptoms	Perceived Impact on Patient’s Day (%)	Impact on Partner’s/ Friend’s Day (%)
Increased feeling of daytime sleepiness	76.1	31.3
Have difficulty concentrating or focusing on details/tasks or problems with memory	64.2	28.4
Negative impact on mood/morale	59.7	46.3
Ability or willingness to undertake physical tasks	50.7	13.4
Negative impact on work	26.9	7.5
Does not affect the day	4.5	13.4
Other	7.5	1.5

Figure 4: Frequency of Narcolepsy with Cataplexy Symptoms Reported by the Patient, Partner/Friend and Physician



treatment. No control group was included. Although 66% of patients were at least satisfied with their current medication, EDS continued to cause frequent symptoms, impaired quality of life with significant impact on day-to-day activities and frequent accidents, particularly road traffic accidents.

The least well-controlled symptoms were EDS and cataplexy, which are the main targets of current treatments, with other conventionally recognised symptoms occurring frequently, including difficulties with sleep and mood disorders.^{12–14} These high frequencies of EDS and cataplexy contrast with the high level of satisfaction recorded by patients for their treatments.¹³ These findings raise the possibility that the patient’s satisfaction with his/her treatment may reflect his/her overall experience of the broad range of symptoms rather than a judgement relating to EDS and cataplexy. They also indicate that a substantial unmet need still exists in this patient population and that patients, and possibly their physicians, have a low expectation of success in symptom control.

The impact of symptoms on patient quality of life is demonstrated by the SF-36, where all domains were scored significantly lower than the US norms ($p < 0.001$; $p < 0.05$ for role emotional); this effect increased with the severity of the symptoms, as measured by the UNS.¹⁰

Other more qualitative measures captured the negative day-to-day effects of the symptoms, with 84% of patients reporting a negative impact. The negative effects included the avoidance of social or sporting events and the strain that symptoms place on relationships and family/home life. These qualitative measures correlate with the

Table 2: Differences in Symptom Impact Ratings Between the Patient's Physician and Partner/Friend

Symptom	n	Percentage of Physicians Rating Impact on QoL Lower than Patients	Percentage of Physicians Rating Impact on QoL Higher than Patients	Percentage of Partner/Friend Rating Impact on QoL Lower than Patients	Percentage of Partner/Friend Rating Impact on QoL Higher than Patients
Cataplexy	66	30.3	12.2	27.3	4.5
Hallucinations	45	40.0	8.9	33.3	15.6
Sleep paralysis	43	55.8	4.7	27.9	11.6
Microsleep	53	28.3	15.1	37.7	7.5
Excessive daytime sleepiness	62	32.3	11.3	19.4	11.3
Trouble getting to sleep at bedtime	18	50.0	11.1	38.0	0.0
Trouble staying asleep at night	62	46.8	9.7	27.4	9.7
Mood disorder	49	59.2	10.2	38.8	18.4

QoL = quality of life.

SF-36 where, in particular, social functioning and role emotional scored significantly lower than the US norms. This study demonstrates the range of symptoms and impacts that patients experience on a regular basis, despite taking prescribed medications. These effects on daily life need to be emphasised when taking a symptom history to establish just what causes the patient the most distress each day in order that treatment can be tailored to the individual's needs.

Uniquely, in this study we also identified the impact of a patient's symptoms on his or her partner or friend. The major impact is typically on social functioning and relationships, both of which are elements of normal life. Negative effects on mood and feelings of EDS were also reported, although not to the same extent as by the patient. This effect on the patient's partner/friend highlights the burden of living with a sufferer of narcolepsy, which has not previously been recognised.

We were also able to directly compare the frequency and impact of symptoms on the patient's quality of life as reported by the patient, his/her partner/friend and his/her physician. Overall, the frequency and impact of symptoms on the patient's quality of life tended to be underestimated by the physicians and, to a lesser extent, by the patient's partner/friend. The underestimation by physicians was particularly prominent for mood disorders and night-time sleep-related issues, and by the partner/friend for mood disorders and night-time sleep-related issues. This underestimation by physicians of the frequency and impact may be due to a lack of recognition of the broad range of symptoms experienced in narcolepsy and could lead to complacency with regard to adjusting treatment to obtain better symptom control and quality of life.

Of the partners/friends included in the study, 48% acted as carers and 34% of these individuals spent more than two hours per day in this role. The symptoms experienced by the narcoleptic patients had a

significant impact on the quality of life of their partners. This study highlights the plight of living with narcolepsy with cataplexy for patients, as well as the impact and strain placed on their families and friends. It is important to discuss these issues in more detail during consultations with patients. Obtaining a full impression of the patient's symptoms by including the partner in the interview provides a more holistic view of the frequency and impact of symptoms, and symptom management may be improved.

Conclusions

Even with current treatments, symptoms of narcolepsy with cataplexy have a severe impact on the quality of life of patients and has a negative impacts on their partner or friend. This impact is broader than previously recognised, and this study has identified additional and important previously unrecognised symptoms of narcolepsy with cataplexy.

Further studies taking into account symptoms at baseline, before treatment and after treatment are required to identify which symptoms that are present at the onset of the disorder are due to inadequate management. Current treatments should be employed more widely and the doses of these drugs optimised so that symptoms are better controlled. This requires careful consideration of a wide range of symptoms both in the daytime and at night to better focus the treatment and treat the narcolepsy in its entirety. This may improve not only the patient's quality of life but also that of his/her partner or friend.

Further investigation of the previously under-recognised symptoms of narcolepsy with cataplexy is required to fully understand the impact of the condition. This may prompt changes in the diagnostic criteria to improve both the accuracy of the initial diagnosis and the long-term treatment. ■

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