CNS Drugs (2025) 39 (Suppl 1):S23–S36
https://doi.org/10.1007/s40263-024-01142-8

ORIGINAL RESEARCH ARTICLE

A Survey of People Living with Narcolepsy in the USA: Path to Diagnosis, Quality of Life, and Treatment Landscape from the Patient's Perspective

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Accepted: 26 November 2024 / Published online: 20 March 2025

Abstract

Background Narcolepsy is a chronic, burdensome neurologic disorder that significantly impacts the daily life of people with narcolepsy (PWN). Real-world perspectives from PWN can help address their unique experiences and treatment needs. PWN were surveyed to examine the path to a narcolepsy diagnosis, the breadth of symptom burden experienced by PWN, and current trends in treatment.

Methods A 15-min online survey was sent by email to 3959 US members of MyNarcolepsyTeam (February 2022). The survey was divided into three sections (screening [patient characteristics], diagnosis/symptoms, and patient quality of life) for a total of 27 questions.

Results In total, 110 members completed the survey. Of these, most were female (84%) and nearly half (48%) were diagnosed with narcolepsy type 1 (with cataplexy). Approximately one-third (31%) of members reported receiving a definitive diagnosis ≥ 10 years after first speaking with a clinician; most were previously diagnosed with depression (73%). Excessive daytime sleepiness (EDS, 93%) and fatigue (84%) were the most frequently reported symptoms that prompted respondents to seek a diagnosis or feel that something was wrong. Additionally, EDS was reported as the most troubling symptom (92%). Respondents' most desired treatment outcome was to stop sleeping during the day (77%). Most (76%) indicated an extremely or very severe impact on daily life. One in eight respondents were not taking any medication for their narcolepsy. Of those taking medication, 58% received polypharmacy to address narcolepsy symptoms.

Conclusions These survey findings further characterize the diagnostic delay, symptom burden, and treatment needs of PWN. Understanding the breadth of impact of narcolepsy from the patients' perspective could improve shared decision-making between PWN and their treating clinicians.

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1 Introduction

Narcolepsy is a rare, chronic neurologic disorder characterized by a classic symptom pentad in which the most sensitive and disabling symptom is excessive daytime sleepiness (EDS) [1, 2]. The other cardinal symptoms that can be present include cataplexy, disrupted nighttime sleep (DNS), sleep paralysis, and sleep-related hallucinations [1]. Narcolepsy consists of two subtypes: narcolepsy type 1 (NT1; previously known as narcolepsy with cataplexy) and type 2 (NT2; previously known as narcolepsy without cataplexy). Cataplexy, which is only experienced by people with NT1, is the sudden loss of voluntary muscle tone and can occur following a strong emotional trigger. These intrusive daytime and nighttime symptoms [1] impose a significant burden on

Key Points

This survey examined patient-reported experiences of their path to a narcolepsy diagnosis, their symptom burden, and trends in treatment, which may help support clinicians' ability to recognize the condition, characterize individual treatment burden, and personalize treatment in narcolepsy.

The majority of people with narcolepsy wait many years for a diagnosis, with almost one-third having a > 10-year delay, while struggling with the burden of narcolepsy-specific and associated symptoms across 24 h of the day.

People with narcolepsy frequently sought out information from resources such as websites and advocacy groups, indicating their desire for readily available narcolepsy-related content and education materials.

the daily life of people with narcolepsy (PWN) [3] and cause severe disability and socioeconomic burden [4]. In addition, non-pentad symptoms experienced by both people with NT1 and people with NT2 include challenges with brain fog, automatic behaviors, rapid eye movement (REM) sleep behavior disorder (RBD), weight gain, feeding abnormalities, and more, that further compound the negative impact of narcolepsy [5]. This is illustrated by the difficulties PWN experience that intrude on daily activities and negatively impact work, academic development, social interactions, and personal relationships [6]. Further adding to the complexity of diagnosis and treatment for narcolepsy is the variable symptomatology among PWN and the resulting variability in treatment effectiveness, safety, tolerability, and lifestyle modifications to adapt to treatment [6].

Symptoms of narcolepsy typically develop in adolescence or early adulthood; however, diagnosis of narcolepsy is often delayed. The average time of symptom onset to diagnosis ranges from 8 to 22 years [7]. A proposed contribution to this delay includes the presence of comorbid conditions that can obscure timely recognition of narcolepsy [8, 9]. There is an urgent need to improve the time to diagnosis for PWN to reduce the severe disease burden, optimize narcolepsy-related treatment outcomes, and potentially reduce the culmination of physical and psychologic comorbidities. To characterize the lived experiences of PWN, real-world perspectives directly from PWN provide critical insights into the symptom burden of narcolepsy and treatment of narcolepsy. The lived experiences of PWN may be more candidly captured within a closed patient community.

In the present study, PWN were surveyed as part of real-world evidence generation to better characterize the path to a narcolepsy diagnosis, symptom description and frequency, and the impact on daily life. In addition, desired treatment outcomes from the patient perspective and how those outcomes align with commonly experienced symptoms, educational resources on treatment, and medication use were investigated.

2 Methods

2.1 Study Design

A 15-min online survey was sent by email in February 2022 to 3959 US members of MyNarcolepsyTeam, a social network of > 10,000 members that provides emotional support and clinical insights on treatment management for individuals with narcolepsy. Respondents needed to be ≥ 21 years of age, reside in the USA, and have self-reported narcolepsy; respondents were required to indicate whether they had NT1, had NT2, or were unsure of their narcolepsy type. Respondents were not incentivized to participate, and all responses were anonymous. The goal of this study was to obtain ≥ 100 responses, which was based on an estimate of response rates given the number of MyNarcolepsyTeam members at the time of the survey and the minimum threshold for subanalyses. Descriptive statistics were used to analyze all captured data from the survey. All responses were collected and analyzed using Qualtrics (Provo, UT). This study qualified for institutional review board (IRB) exemption.

The survey was divided into three sections: screening (respondent characteristics), diagnosis/symptoms, and respondent quality of life (QoL); there were 27 questions in total. In the screening portion of the survey, respondents were initially asked a series of questions to collect demographic information and were not permitted to continue the survey if they indicated that they were < 21 years of age, lived outside of the USA, were a caregiver for someone with narcolepsy, or were not a person with narcolepsy. The survey included multiple choice, select all that apply, and rating scale questions, with the exception of the final question, which was open ended and asked respondents to provide feedback to manufacturers of narcolepsy treatments. Some questions allowed respondents to select "other" and describe their answer in a text box.

3 Results

3.1 Respondent Characteristics

From 17 February to 15 March 2022, a total of 142 MyNarcolepsyTeam members began the survey. Thirteen

were disqualified during screening owing to failure to provide consent for participation ($n = 8$), non-US residency ($n = 1$), or lack of a narcolepsy diagnosis ($n = 4$). An additional seven individuals were disqualified as they did not complete the screening portion of the survey. Of the 122 individuals who completed the screening questions and qualified for the survey, 110 completed the full survey. Most respondents were female (84%), and approximately half (48%) were diagnosed with narcolepsy type 1 (NT1) or narcolepsy with cataplexy (Table 1). Of respondents who reported a diagnosis of narcolepsy type 2 (NT2, 32%) or who were unsure of their diagnosis (20%), 11% were potentially misdiagnosed, as they had self-reported symptoms consistent with cataplexy. Overall, 40% of respondents reported cataplexy prior to a diagnosis; of these respondents, 82% had NT1, 5% had NT2, and 14% were unsure of their narcolepsy type. Of respondents who did not report cataplexy symptoms prior to diagnosis, 25% had NT1, 51% had NT2, and 24% were unsure of their narcolepsy type. Overall, most (77%) respondents were ≥ 40 years of age; respondents with NT2 were younger on average (46% were < 40 years old). More than half (57%) of the respondents started to experience symptoms before the age of 20 years (Table 1).

Table 1 Respondent characteristics

Characteristic, %	NT1 ($n = 53$)	NT2 ($n = 35$*)	Overall ($N = 110$)
Female	83	86	84
Narcolepsy type	48	32	80†
Age range, years			
≤ 39	17	46	23
40–49	34	11	24
50–59	21	23	23
≥ 60	29	20	30
Age at first symptom appearance, years			
< 10	23	9	15
10–15	26	26	23
16–19	17	20	19
20–24	6	14	7
25–34	8	11	8
35–64	16	15	18
≥ 65	0	6	3
Not sure	6	0	5

NT1 narcolepsy type 1, *NT2* narcolepsy type 2

*Small sample size

†Proportion of respondents having a definitive NT1 or NT2 diagnosis

3.2 Path to Narcolepsy Diagnosis and Impact on QoL

Daytime and nocturnal symptoms were almost universally present (Fig. 1A, B). EDS (93%) and fatigue (84%) were the most common daytime symptoms that led respondents to either seek a diagnosis or feel that something was wrong. The majority of individuals with NT1 or NT2 (72% of respondents) experienced some form of nocturnal sleep disturbance, such as DNS and fragmented sleep. Additionally, approximately 67% of individuals recalled challenges with cognition and memory prior to diagnosis (Fig. 1C). More than two-thirds (68%) of respondents with NT1 sought a diagnosis owing to symptoms of cataplexy. Respondents with self-reported NT2 (6%) and respondents who were unsure of their narcolepsy type (27%) also reported that symptoms of cataplexy led them to seek a diagnosis, suggesting that these respondents may actually have NT1. A higher proportion of participants with NT1 experienced sleep or night paralysis (43%) and automatic behaviors (38%) prior to diagnosis compared with participants with NT2 (26% and 20%, respectively). Poor-quality sleep (63%) and vivid dreams (54%) were experienced by a higher proportion of participants with NT2 prior to diagnosis compared with participants with NT1 (49% and 34%, respectively). From the time of initial discussions with clinicians about narcolepsy symptoms, the majority (69%) of respondents experienced a ≥ 2-year period before diagnosis. More than one-third (38%) of respondents experienced a 2- to 9-year delay, and 31% experienced a ≥ 10-year delay. Many (64%) respondents were initially incorrectly diagnosed, potentially through subjective diagnostic criteria, with a condition other than narcolepsy (misdiagnosis), or experienced a "missed" diagnosis, meaning that a comorbidity was correctly diagnosed, likely through objective diagnostic criteria, but the opportunity to also correctly diagnose narcolepsy was missed (Fig. 1D). Common misdiagnoses or "missed" diagnoses among respondents of all narcolepsy types included depression (NT1, 64%; NT2, 77%; unsure, 91%), followed by sleep apnea (NT1, 30%; NT2, 31%; unsure, 64%), insomnia (NT1, 24%; NT2, 8%; unsure, 27%), and attention-deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD, combined; NT1, 18%; NT2, 8%; unsure, 27%). Approximately 62% of people with NT1 and 74% of people with NT2 were initially diagnosed with something else first. Of these PWN, 20% were diagnosed with narcolepsy within 1 year of symptom onset, while another 20% waited ≥ 21 years (Fig. 1E). In contrast, of PWN who were correctly diagnosed with narcolepsy first, 53% were diagnosed within 1 year of symptom onset and only 3% waited ≥ 21 years. Of the 63 respondents who reported cataplexy at any point, nearly half (49%) reported having a cataplexy episode at least once per week (Fig. 2A). When asked which potential triggers caused cataplexy episodes, most (70%) respondents with cataplexy

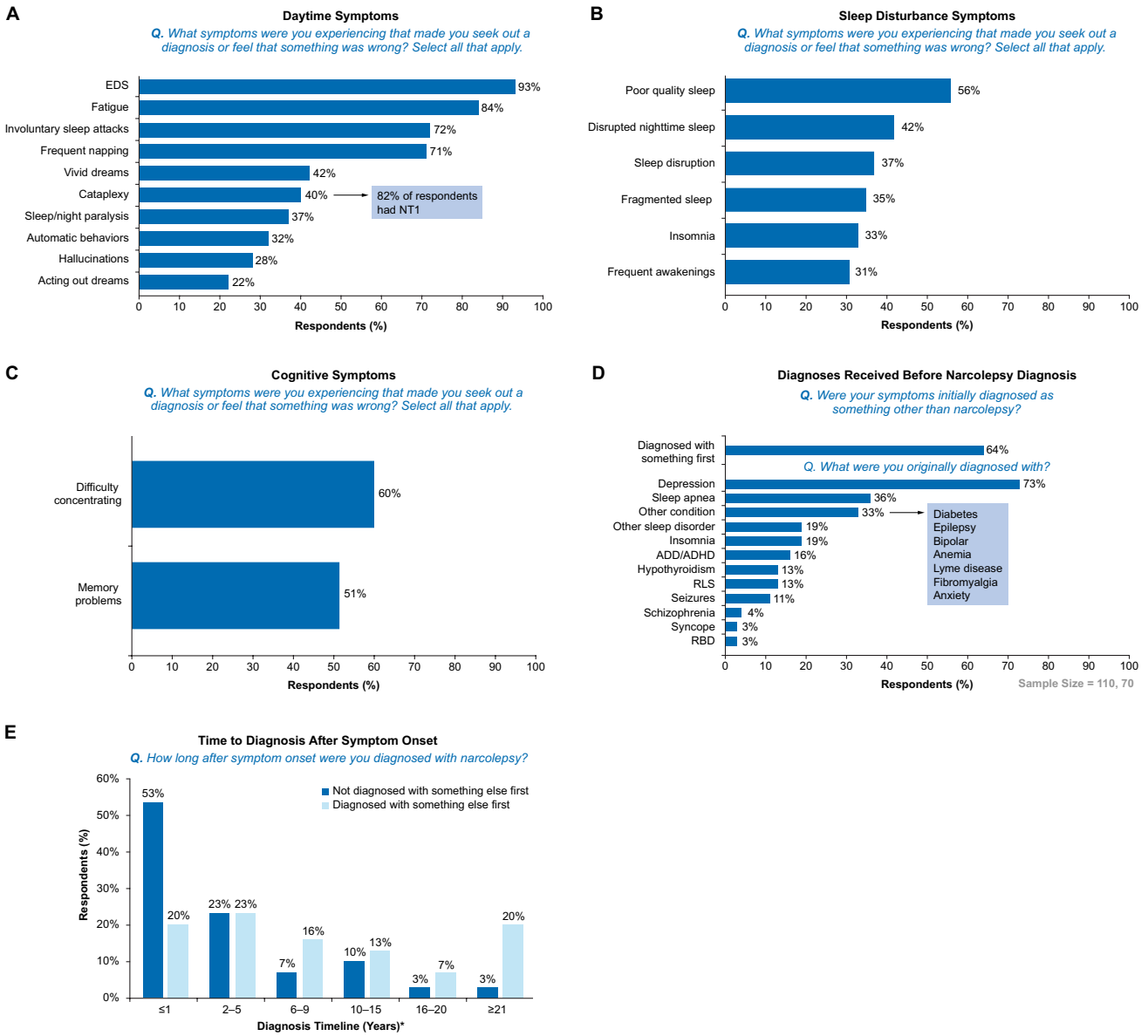

Fig. 1 Pathway to a narcolepsy diagnosis. Bars represent the proportion of respondents reporting symptoms that made them seek out a diagnosis or feel that something was wrong, including daytime disturbances (**A**), sleep disturbances (**B**), and cognitive challenges (**C**), and the proportion of respondents reporting an initial diagnosis other than narcolepsy (**D**) and time to diagnosis after symptom onset (**E**). *Of 70 respondents who were diagnosed with something else first, 1% were never diagnosed by a doctor. *ADD* attention-deficit disorder, *ADHD* attention-deficit/hyperactivity disorder, *DNS* disrupted nighttime sleep, *EDS* excessive daytime sleepiness, *RBD* rapid eye movement sleep behavior disorder, *RLS* restless legs syndrome

reported being overly tired as a trigger, and approximately half (44–48%) reported emotional triggers of fear, laughter, anger, and being startled (Fig. 2B).

When evaluating responses on the basis of the presence or absence of cataplexy prior to diagnosis, a similar trend in symptoms that led respondents to seek a diagnosis was observed for respondents with cataplexy (EDS, 91%; fatigue, 86%) and without cataplexy (EDS, 94%; fatigue, 82%). Consistent with findings from all respondents, depression and sleep apnea were among the most common initial diagnoses for respondents with cataplexy prior to diagnosis (depression, 62%; sleep apnea, 45%) and those without cataplexy (depression, 80%; sleep apnea, 29%). Of respondents who experienced cataplexy prior to diagnosis, 38% were diagnosed > 6 years after initially discussing symptoms with a clinician, and almost half (45%) reported a cataplexy episode at least once a week. Being overly tired (68%), laughter (55%), and being surprised or startled (52%) were the most common cataplexy triggers among those who experienced cataplexy prior to diagnosis. Of

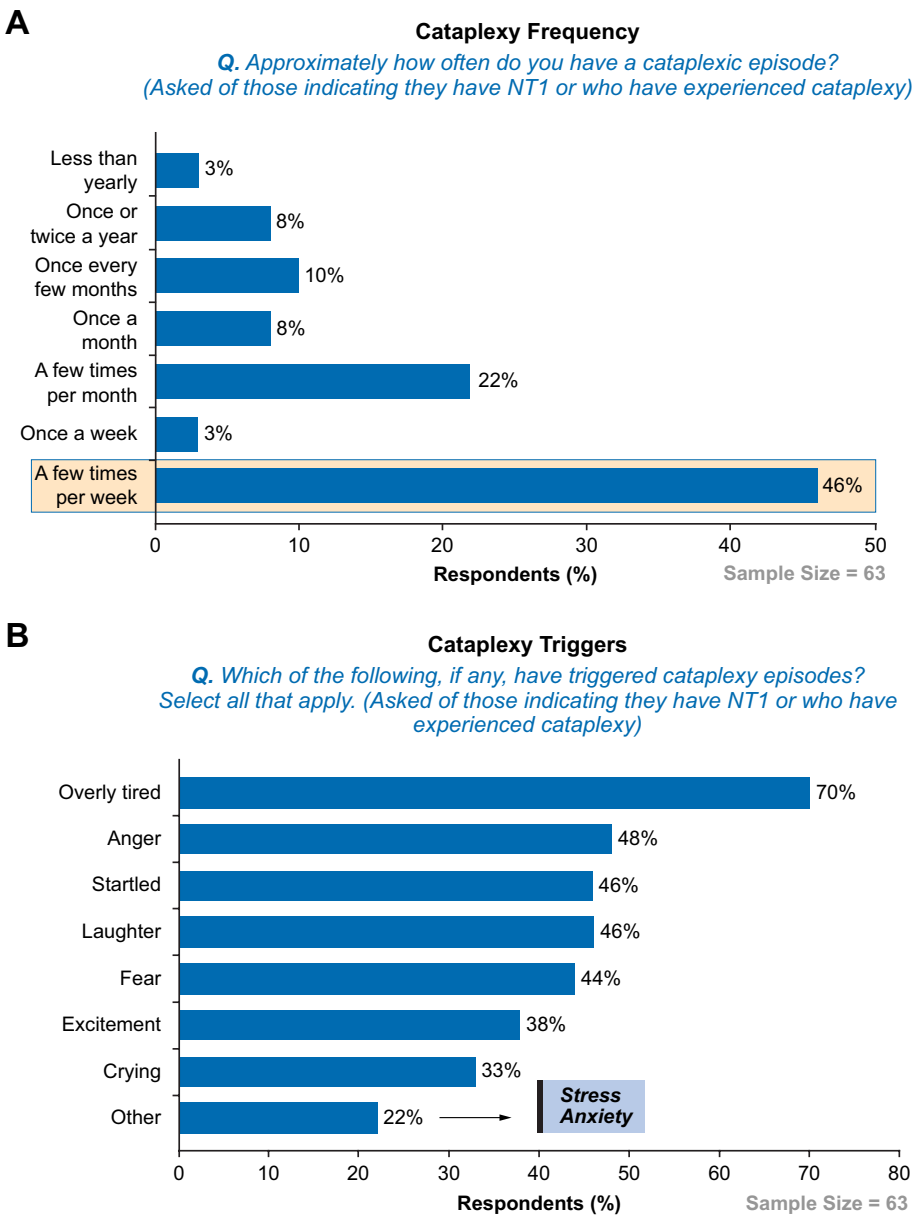

Fig. 2 Cataplexy frequency and triggers. Bars represent the proportion of respondents who reported a specific cataplexy episode frequency (**A**) and who experienced specific cataplexy triggers (**B**). Respondents were allowed to select all answers that applied to the survey question in panel B. Both survey questions were asked of respondents with NT1 or who experienced cataplexy. *NT1* narcolepsy type 1

respondents reporting no cataplexy prior to diagnosis, 46% experienced a diagnostic delay of > 6 years. Among the 19 respondents who did not initially have cataplexy prior to diagnosis but now find it to be among the more troubling symptoms they experience, 58% experienced cataplexy at least once a week; the most common triggers were being overly tired (74%), anger (53%), and fear (42%).

When asked to describe how narcolepsy impacted daily life, 76% of all respondents indicated that the impact was extremely or very severe; the impact was particularly negative among respondents with NT1, 80% of whom experienced an extremely or very severe impact. Moreover, the far-reaching impact of narcolepsy on QoL was evident, as most respondents reported interference with work (88%), social life (86%), everyday chores (85%), and exercise (85%). In addition, many reported that narcolepsy limited career options (76%) and made it difficult to concentrate (92%). Consequently, the emotional toll of narcolepsy was stark, as most respondents reported manifesting feelings of isolation (83%), depression (81%), and anxiety (80%) (Fig. 3).

3.3 Symptom Burden of Narcolepsy and Desirable Treatment Outcomes

The most troubling symptoms reported by respondents included EDS (92%), fatigue (79%), difficulty concentrating (64%), and memory problems (55%) (Fig. 4A). Overall,

63% of respondents reported their most troubling symptoms to be some form of sleep disturbance (including poor quality of sleep, DNS, sleep disruption, fragmented sleep, insomnia, or frequent awakenings). Among respondents who indicated that they were not sure of their narcolepsy type diagnosis, 27% reported cataplexy as their most troubling symptom. Cataplexy remained a frequent troubling symptom among respondents with a diagnosis of NT1 (74%). Respondents who reported cataplexy prior to their narcolepsy diagnosis indicated EDS (89%), cataplexy (75%), and fatigue (73%) as their most troubling current symptoms. For respondents who did not experience cataplexy prior to diagnosis, EDS (94%), fatigue (84%), and difficulty concentrating (64%) were among their most troubling current symptoms.

When asked to consider their desired treatment goals, responses aligned with the most troubling symptoms: respondents wanted to stop sleeping during the day (77%), increase their energy (62%), improve their memory (36%), be more productive in their daily life (29%), and improve sleep continuity (22%; Fig. 4B). Stopping cataplexy was a desirable treatment priority in only 28% of respondents with NT1. Notably, 33% of respondents currently taking oxybates reported that their top goal was a treatment to help them sleep through the night. Overall, a common underlying theme was a desire for a medication that would treat the underlying cause rather than improve a specific symptom. When asked about what they would like to tell the manufacturers of narcolepsy treatment about their needs or hopes for treatment, respondents wanted a cure found (28%), improved QoL (25%), reduced medication side effects (15%), and cost/insurance-related barriers addressed (12%) (Table 2).

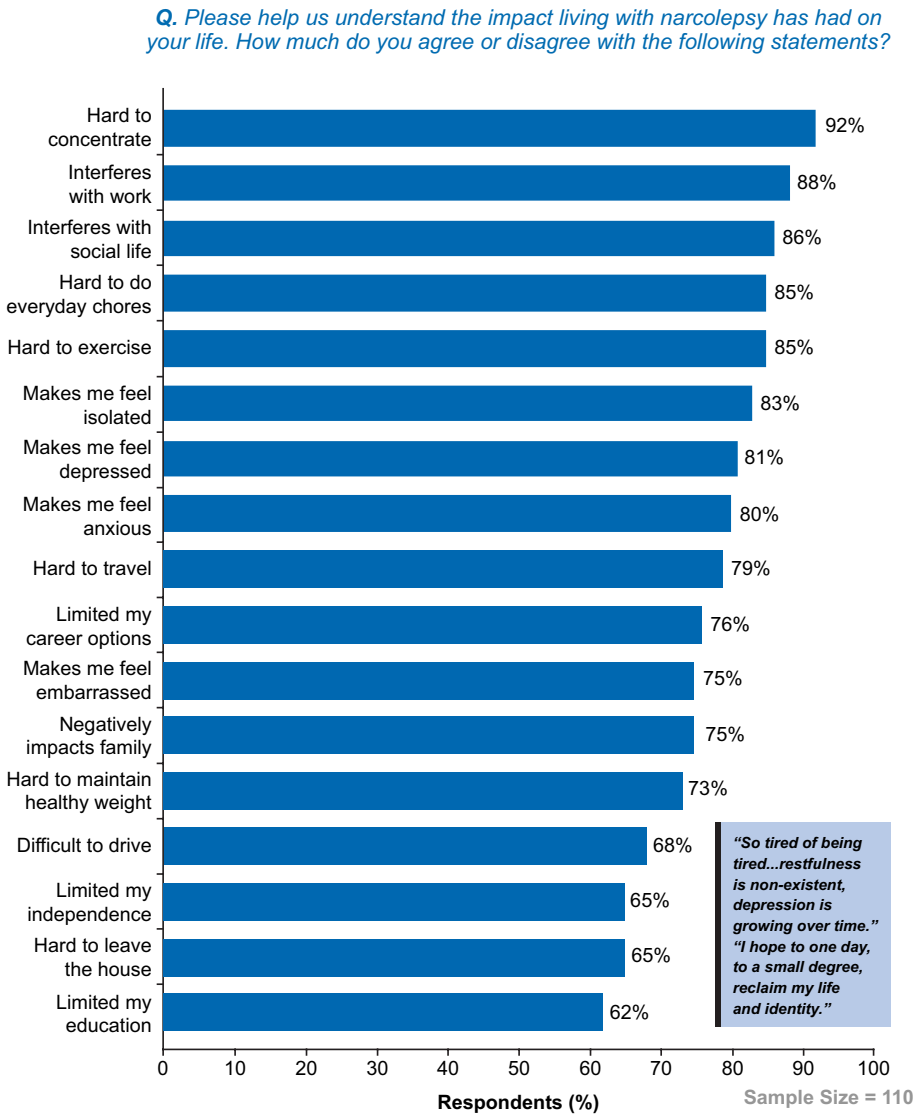

Fig. 3 Impact of narcolepsy on quality of life. Bars represent the proportion of respondents who strongly or somewhat agreed that they experienced specific negative impacts on daily life

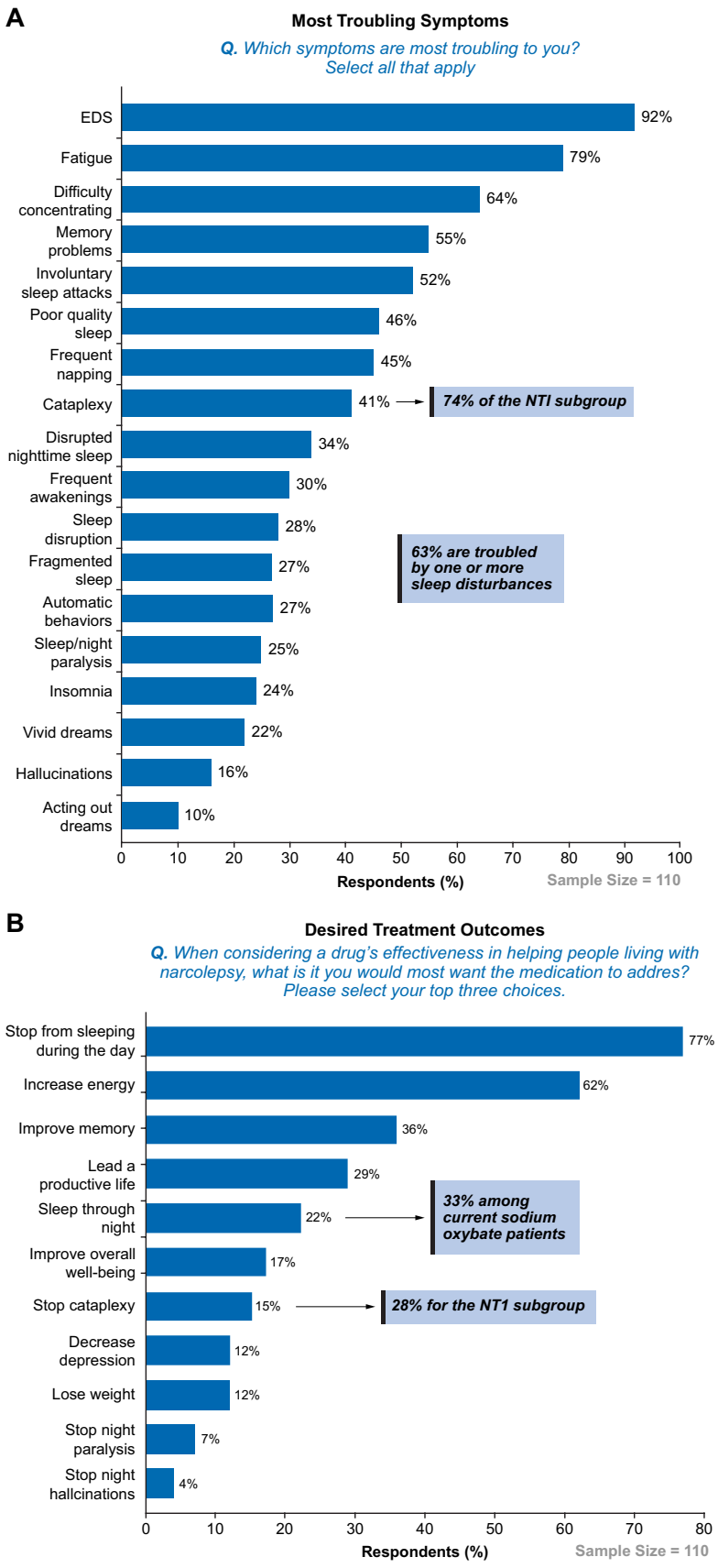

Fig. 4 Most troubling symptoms and desired treatment outcomes. Bars represent the proportion of respondents who reported that a specific symptom was the most troubling (**A**) and who selected a response as one of their top three desired treatment goals (**B**). *Sleep disturbances include poor quality sleep, DNS, sleep disruption, fragmented sleep, insomnia, or frequent awakenings. *DNS* disrupted nighttime sleep, *EDS* excessive daytime sleepiness, *NT1* narcolepsy type 1

3.4 Treatment Landscape and Educational Resources Used

One in eight PWN were not currently taking any type of medication to address narcolepsy symptoms at the time of survey completion (Table 3). Of those taking medication, 58% were receiving polypharmacy to address narcolepsy symptoms. The most commonly reported current treatments were dextroamphetamine or dextroamphetamine–amphetamine (35%), modafinil (20%), melatonin (16%), armodafinil (15%), venlafaxine (14%), oxybate (14%), and methylphenidate (12%). Frequently combined medications included antidepressants with an amphetamine-based alerting agent and oxidates with an amphetamine-based alerting agent or non-amphetamine-based alerting agent (Table 4). The most common current treatments among respondents who reported cataplexy prior to diagnosis and respondents who did not report cataplexy prior to diagnosis were dextroamphetamine or dextroamphetamine–amphetamine (32% and 37%, respectively) and modafinil (20% and 21%, respectively). The sources most commonly accessed by respondents to learn about available treatments were narcolepsy-specific websites (53%), MyNarcolepsyTeam (45%), clinicians (42%), scientific articles (42%), and advocacy groups (37%) (Fig. 5).

4 Discussion

On their journey to a narcolepsy diagnosis, PWN routinely experienced a misdiagnosis or a "missed" diagnosis. One-third of respondents received disparate initial diagnoses that included anxiety, bipolar disease, epilepsy, fibromyalgia, anemia, and Lyme disease. As many of these conditions (e.g., sleep apnea and epilepsy) require objective diagnostic testing, these survey findings underscore the potential for complex comorbidities in PWN that lead to "missed" diagnoses of narcolepsy [10, 11]. Initial diagnoses based on subjective criteria and symptom presentation, such as insomnia, may contribute to an array of possible misdiagnoses by clinicians [10]. Clinicians often do not have expertise in narcolepsy, owing to limited disease awareness and lack of sleep training in general medical education [12, 13]. Given these experiences, it is not surprising that participants sought out information from a variety of resources, such as websites and advocacy groups. For example, nearly 50% of participants used scientific articles as a resource. This introduces an opportunity for patients and clinicians to share awareness of available resources and reinforces the need to make resources accessible, ideally as peer-reviewed plain language summaries, to empower people living with narcolepsy to guide their own care.

Table 2 Respondents' desired treatment objectives

Q: Finally, what would you like to tell the manufacturers of treatment for narcolepsy about your needs or hopes for treatment?	
Objective	Direct responses
Find a cure	Hurry in fixing the root cause, not just treating the symptoms
	I'm always told they only can treat the symptoms and hope that helps. There's nothing that can treat narcolepsy itself
	Hoping one day for a medication that can treat the problem and not just the symptoms
	It would be amazing to have a treatment that addresses the cause
Improve QoL	I hope to one day just enjoy my children and be able to play and keep up with them
	I want my life back. I want to live a normal life and to be able to work and drive
	I want a better quality of life
	I have had one day in the past year that I remember being able to sit through class without falling asleep. I remember how thrilled I was about it
Fewer side effects	My dream is for a treatment that will work where I can wake up and not feel like I was put under anesthesia
	Less heavy-duty side effects
	Depression, anxiety, and suicidal ideation cases are high among patients with narcolepsy. Stop making drugs that make it worse
	On occasion I feel like the meds make me feel a bit agitated. That is so opposite of my personality
Lower costs/hurdles	Make it affordable and more easily available
	Bring down cost of name brands Adderall and Strattera, which work! Generics are inconsistent at best
	Make brand name Provigil affordable because the generic does NOT work the same
	Lower medical costs
	I'm on Medicaid. Let them take my insurance

QoL quality of life

Table 3 Commonly prescribed narcolepsy treatments (≥ 2% of all respondents)

Treatment, %	NT1 ($n = 53$)	NT2 ($n = 35$*)	Respondents ($N = 110$)
Dextroamphetamine/ dextroamphetamine–amphetamine	40	43	35
Modafinil	17	26	20
Melatonin	21	17	16
Armodafinil	17	14	15
Venlafaxine	15	9	14
Oxybate	17	12	14
Methylphenidate	11	15	12
Solriamfetol	6	14	10
Fluoxetine	13	3	8
Sertraline	2	9	4
Pitolisant	6	0	3
Lisdexamfetamine	0	3	2
Zolpidem	4	0	2
None currently or never been on treatment	10	9	13

NT1 narcolepsy type 1, *NT2* narcolepsy type 2

*Small sample size

Table 4 Commonly combined narcolepsy treatments

Treatment, %	Amphetamine-based alerting agent* ($n = 47$)	Non-amphetamine-based alerting agent ($n = 48$)	Oxybate ($n = 15$)	Sleep aid ($n = 20$)	Antidepressant ($n = 26$)
Amphetamine-based alerting agent*	–	35	60	55	62
Dextroamphetamine/ dextroamphetamine–amphetamine	–	25	47	45	42
Methylphenidate	–	10	13	15	19
Dexamphetamine sulfate	–	6	0	2	8
Methylphenidate ER	–	4	7	10	8
Lisdexamphetamine dimesylate	–	0	7	–	4
Non-amphetamine-based alerting agent	36	–	60	40	38
Modafinil	15	–	27	30	31
Armodafinil	15	–	13	10	8
Solriamfetol	9	–	20	5	4
Pitolisant	2	–	7	–	0
Oxybate	19	19	–	10	8
Sodium oxybate	13	13	–	5	8
Mixed-salt oxybates	6	6	–	5	0
Sleep aid	23	17	13	–	38
Melatonin	19	15	13	–	35
Zolpidem	2	2	0	–	4
Antidepressant	34	21	13	50	–
Venlafaxine	19	15	13	35	–
Fluoxetine	11	6	0	20	–
Sertraline	9	2	0	5	–

ADHD attention-deficit/hyperactivity disorder, *ER* extended release

*Amphetamine-based stimulants were used for narcolepsy and/or ADHD treatment

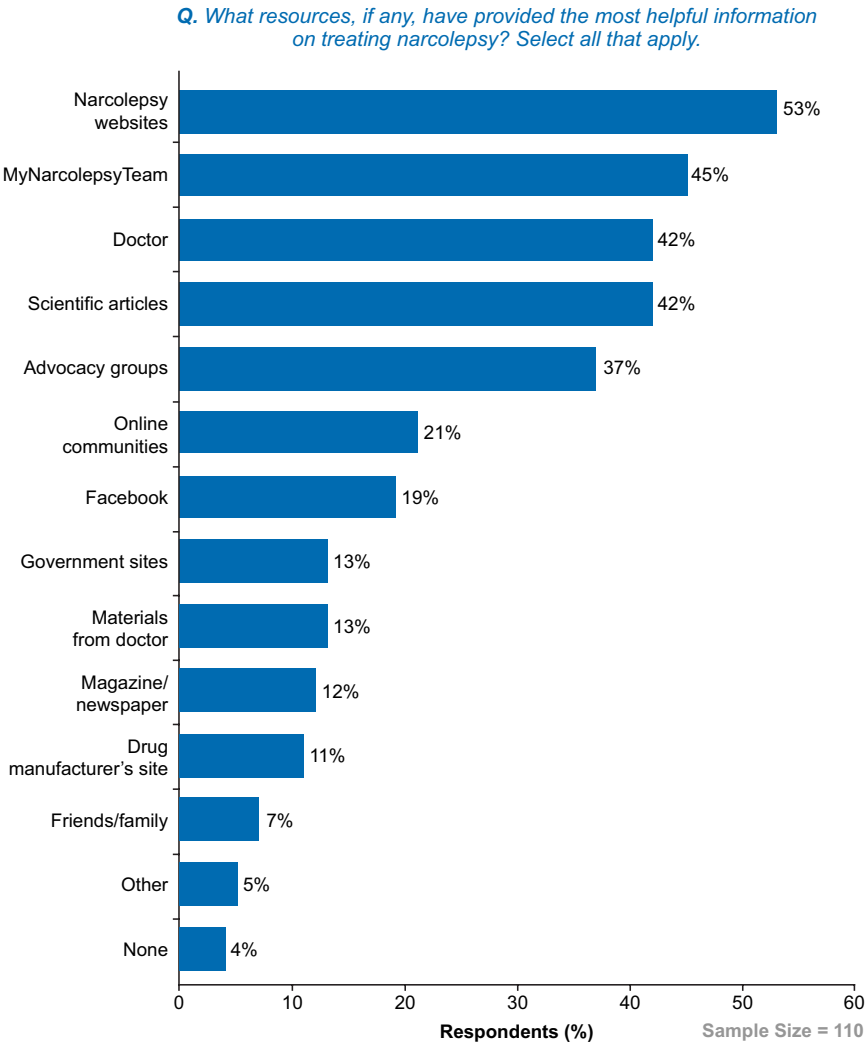

Fig. 5 Educational resources utilized. Bars represent the proportion of respondents who reported that specific resources were the most helpful sources of information for treating narcolepsy

More than half of respondents experienced symptoms of narcolepsy within the first two decades of life, underscoring that narcolepsy is often a pediatric disease [14], and education of pediatricians, school faculty, and parents is essential to shorten the time to referral and adequate evaluation and diagnosis by sleep clinicians. In this study, approximately 40% of respondents received a diagnosis between 2 to 9 years from the initial consultation with a clinician regarding their symptoms, and nearly one-third waited ≥ 10 years. These findings align with a recent registry study that estimated an average time of 4.5 years from first consultation to diagnosis using self-reported data in adult PWN [10]. Prior to diagnosis, the majority of PWN, irrespective of narcolepsy type, were suffering from a sleep disturbance, characterized by either poor quality sleep, DNS, sleep disruption, fragmented sleep, insomnia, or frequent awakenings, highlighting the 24-h nature of narcolepsy. These symptoms, particularly when described in a primary care setting, may distract from considering narcolepsy. Most respondents with a definitive NT1 diagnosis experienced consistent episodes of cataplexy that were often triggered by feelings of being overtired, which is consistent with existing literature reporting an association between "tiredness" and more frequent cataplexy [15]. Overtiredness, which may be more common in PWN, may increase an individual's susceptibility to a cataplexy episode based on an emotional trigger. While clinicians educate PWN about emotions and cataplexy, greater awareness around overtiredness predisposing a person to cataplexy episodes may be needed. Further, a consistent sleep routine, with naps as needed, should be encouraged as a behavioral strategy for PWN.

Overall, many respondents indicated that narcolepsy imposed a significant negative impact on their personal and professional lives, especially when contending with the emotional toll associated with narcolepsy. Polypharmacy was common and likely reflective of the invasive, 24-h nature of narcolepsy and desire of PWN to experience relief from a wide range of both daytime and nighttime symptoms. Sleeping through the night was a desired treatment goal among all survey respondents, but particularly among

those who were taking an immediate-release oxybate medication. Given the twice-nightly dosing regimen of immediate-release oxybates [16, 17], these formulations may hinder the ability of patients to achieve their desired treatment goals. Notably, a once-nightly, extended-release formulation of sodium oxybate has been approved by the US Food and Drug Administration (FDA) for the treatment of narcolepsy in adults and children, eliminating the need for a second, middle-of-the-night dose [18]. Importantly, this survey reveals that many PWN in the USA are self-motivated and seek out additional information and resources to augment their understanding of narcolepsy, as well as options available for symptom improvement. Owing to the complexities in the diagnosis of narcolepsy, treatments, and the associated comorbidities, PWN often utilized ongoing resources and education. Supplementary internet sources were most commonly utilized.

Real-world evidence obtained through the lived experience of PWN clearly illustrates that narcolepsy is a challenging disorder related to its multiple and varying symptoms, and optimal management of these symptoms can be difficult. Low treatment adherence is common among PWN [19]. Adherence directly impacts the ability of PWN to achieve optimal outcomes, and with most respondents requiring polypharmacy, there is greater treatment burden, increased risk of adverse events, and risk of drug–drug interactions [20]. While polypharmacy often results from inadequate response to narcolepsy treatment [21], failure to recognize nonadherence may also contribute to use of multiple medications in some PWN. In the present study, most respondents reported experiencing a multitude of troubling pentad and non-pentad symptoms including EDS, fatigue, difficulty concentrating, and memory impairment. Notably, more than half of the respondents considered one or more sleep disturbances as their most troubling symptoms, with poor sleep quality, DNS, and frequent awakenings among the top ten; daytime medications, especially traditional stimulants, may contribute to these underlying sleep disturbances [22].

Approaches to address sleep-related issues varied. Melatonin, an over-the-counter sleep supplement, was the most commonly used sleep-related treatment, reported by approximately 16% of respondents. Almost 20% of respondents receiving an amphetamine-based alerting agent reported melatonin use. Limited information is available about endogenous or exogenous melatonin for PWN. Endogenous melatonin and circadian rhythm may be dysregulated in some PWN [23]. In general, exogenous melatonin has been used to alter ultradian rhythm in PWN and people without narcolepsy; however, exogenous melatonin can increase time spent in REM sleep [24]. While there are reports suggesting that melatonin may be of use in treating RBD in PWN [25, 26], there is no clinical evidence of its efficacy in narcolepsy. Additionally, the content of melatonin in supplements is frequently inconsistent with that indicated on the label [27].

PWN were frequently treated with stimulants such as dextroamphetamine or dextroamphetamine–amphetamine, whereas interventions strongly recommended by the American Academy of Sleep Medicine (e.g., modafinil, pitolisant, sodium oxybate, and solriamfetol) [28] were underutilized (3–20% of respondents). Together, these findings suggest that opportunities exist for improvement in the care of PWN and highlight the persistent use of stimulants, which have historically been used to treat EDS [29], despite their addiction potential and potential to increase blood pressure and heart rate. Education of and advocacy to managed care organizations about the need for access to additional medications that are aligned with the American Academy of Sleep Medicine guidelines continue to be needed.

The presence of cataplexy is a defining feature of NT1 that results from an underlying dysregulation of sleep–wake states and intrusion of REM sleep-related atonia during wakefulness, which manifests with muscle atonia [30]. Ensuring clinicians use understandable and wide-ranging descriptions to explain cataplexy is critical; suggested language for clinical use can be found in the companion article by Lavender et al. [31]. In the present study, 6% of respondents with NT2 reported that they had experienced cataplexy compared with 68% of respondents with NT1. This potentially highlights a discrepancy between the specificity of cataplexy in the pathophysiology of NT1 and the perception of a cataplexy episode by the patient themselves. As reported previously, this may be due to the large phenotypic diversity of cataplexy among PWN and the corresponding difficulty to adequately recognize and diagnose cataplexy in clinical practice [15, 32]. Further, cataplexy may be confused with other disorders such as epileptic seizures, falls from neuromuscular disorders [33], and syncope [34], suggesting that there remains an unmet need to provide PWN definitive criteria to determine the presence of a cataplexy episode. Given that 27% of respondents who were not sure of their narcolepsy type reported cataplexy as their most troubling symptom, respondents with NT1 may be underdiagnosed. In this study, respondents with NT1 were commonly prescribed venlafaxine (15%) and fluoxetine (13%). Antidepressants are commonly used off-label to manage cataplexy symptoms in PWN; however, limited evidence is available to support a favorable risk–benefit profile, and the American Academy of Sleep Medicine does not include antidepressants in its guidelines, on the basis of limited data [5, 28, 35]. While the American Academy of Sleep Medicine guidelines do not recognize antidepressants, the European Narcolepsy Guidelines recognize both sodium oxybate as monotherapy

and antidepressants as strong recommendations for cataplexy treatment [36].

PWN experienced a broad impact on their QoL, reporting interference across several domains including work, social life, daily activities, emotional well-being, cognition, and exercise. In this study, the majority of respondents reported an extremely or very severe impact. In agreement with these findings, a recent review has indicated that the disease burden of narcolepsy is significantly and negatively correlated with key factors associated with health-related QoL (HRQoL) including physical functioning, general health, and social functioning [37]. Of note was the emotional toll experienced by respondents, with feelings of isolation, depression, and anxiety; many desired the development of treatments that address the underlying etiology of narcolepsy given its debilitating symptom burden. Recommending that PWN consider additional emotional support from peer advocacy groups is needed to help reduce feelings of isolation.

There are several strengths and limitations of this study. The approach gathered voluntary responses from individuals currently living with narcolepsy in an online social network dedicated to people living with narcolepsy, where PWN may be more candid than in a healthcare encounter, providing valuable insight into real-world perceptions of disease burden and treatment. The survey used mostly multiple-choice questions, which likely encouraged potential respondents to participate but may have restricted patient responses. Additionally, this study utilized a nonvalidated questionnaire, which may limit the reliability and consistency of the results; patient-reported data may be susceptible to misinformation or bias. These data represent a sample of US-based individuals aged ≥ 21 years with relative lack of detailed socioeconomic and demographic information; further, the respondents were overwhelmingly female ($> 80\%$). Thus, generalizability to PWN who have differing characteristics or who reside in other countries may be limited. An additional limitation is the self-reporting of narcolepsy type by respondents, as many reported symptoms discordant with their diagnosis or were not sure of their diagnosis at all. Notably, some members of MyNarcolepsyTeam have reported being underdiagnosed only to learn through organic conversations that they are actually experiencing cataplexy, further suggesting that some survey respondents may have been incorrectly diagnosed with NT2. In the present study, several respondents who had cataplexy prior to diagnosis did not indicate cataplexy as a troubling current symptom, and a small number of respondents who did not have cataplexy prior to diagnosis reported that it was now a concern; these findings provide further evidence that narcolepsy symptoms and patient perception of these symptoms may change over time [38]. Owing to the low response rate in this study, these findings may not reflect the broader population of PWN in the USA.

5 Conclusions

Understanding the impact of narcolepsy on QoL and the diverse experiences and needs from the patient perspective will further support clinicians in treating and recognizing narcolepsy. It may also help providers encourage PWN to open up about their symptoms. Content readily available on the internet, whether narcolepsy-specific content or social networks, can help PWN proactively discuss treatment options with their clinician. Findings from this study demonstrate that PWN often wait years for a diagnosis while struggling with daytime and nighttime symptoms. Early diagnosis and intervention in narcolepsy have a strong likelihood to lead to better outcomes, particularly as symptoms generally present at a pivotal time as one transitions from adolescence to adulthood.

Acknowledgements Medical writing support was provided by Makaila Wallin, PharmD, of The Curry Rockefeller Group, a Citrus Health Group, Inc., company (Chicago, IL), and was funded by Avadel Pharmaceuticals (Chesterfield, MO).

Declarations

Funding This article has been published as part of a journal supplement wholly funded by Avadel Pharmaceuticals (Chesterfield, MO, USA). This study was funded by Avadel Pharmaceuticals. Avadel Pharmaceuticals was involved in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. Open access publication and publication costs were funded by Avadel Pharmaceuticals.

Conflicts of Interest L.E.O. is a consultant to Harmony Biosciences and has served on advisory boards for Avadel Pharmaceuticals and Jazz Pharmaceuticals. A.M.M. has served as a consultant, speaker, and/or on advisory boards for Avadel Pharmaceuticals, Eisai, Harmony Biosciences, Jazz Pharmaceuticals, Alkermes, and Takeda Pharmaceutical Co; has received grant funding from National Institutes of Health, UCB Pharmaceuticals, Jazz Pharmaceuticals, ResMed Foundation, Coverys Foundation, Harmony Biosciences, and Geisinger Health Plan; is the CEO of DAMM Good Sleep, LLC; and serves as an advisor for Neura Health and Floraworks. L.K. is a consultant for and/or has served on advisory boards for Avadel Pharmaceuticals and Takeda and has received research funding from Takeda and Axsome Therapeutics. M.L. is a speaker or has received consulting fees for participation on advisory boards for Avadel Pharmaceuticals, Harmony Biosciences, and Jazz Pharmaceuticals. M.H. is a consultant to Avadel; has received compensation or honoraria from Alkermes, Axsome Therapeutics, Centessa Pharmaceuticals, and Harmony Biosciences; and is a member of the Sleep Consortium Advisory Board. D.C. and B.S. are employees of MyHealthTeam, which received funding to conduct the research. J.G. is an employee of Avadel Pharmaceuticals.

Ethics Approval This study qualified for institutional review board exemption through Advarra per the US Department of Health and Human Services regulations found at 45 CFR 46.104(d)(2).

Consent to Participate Written informed consent was obtained from each respondent prior to beginning the survey.

Consent for Publication Not applicable.

Data Availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code Availability Not applicable.

Author Contributions L.E.O.: writing—review and editing, formal analysis. A.M.M.: writing—review and editing, formal analysis. L.K.: writing—review and editing, formal analysis. M.L.: writing—review and editing, formal analysis. M.H.: writing—review and editing, formal analysis. D.C.: data curation, writing—review and editing, formal analysis. B.S: data curation, writing—review and editing, formal analysis. J.G.: writing—review and editing, formal analysis. All authors have read and approved the final submitted manuscript and have agreed to be accountable for the work.

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