Real-World Experience and Impact of Fatigue in Narcolepsy and Idiopathic Hypersomnia: Survey Results From the ASPIRE Study

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Introduction

- Narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH) are chronic sleep disorders primarily characterized by excessive daytime sleepiness (EDS)[1,2]
- People living with narcolepsy and IH may also experience fatigue as a common and debilitating symptom[3,4]
  - Fatigue is characterized by exhaustion and low energy, which can affect outcomes such as education, employment, social relationships, and overall health-related quality of life (HRQoL)[5,6]
  - Patients may experience symptoms of fatigue even while taking medications for narcolepsy or IH[5,7]
  - It is unclear how fatigue is associated with common measures of HRQoL assessed among those with narcolepsy, including the Functional Outcomes of Sleep Questionnaire - Short Form (FOSQ-10) and EuroQol-5D-5L index (EQ-5D-5L)

Objective

- The ASPIRE study characterized symptoms of NT1, NT2, and IH including fatigue
  - This study also explored the association between fatigue and functional and HRQoL outcomes

Methods

Study design

- The ASPIRE study was an online survey of participants with NT1, NT2, and IH conducted in alignment with the US Food and Drug Administration Patient-Focused Drug Development Guidance on the collection and use of patient experience data (**Table 1**)[8,9]
- Participants were recruited through Rare Patient Voice (RPV, a qualified third-party research panel), the Hypersomnia Foundation, and the Sleep Consortium. Participants who completed and submitted the survey received a nominal honorarium

Table 1: Study population

NT1 (n = 116)	NT2 (n = 127)	IH (n = 123)
Participants were ≥ 18 years of age, resided in the US, and reported a clinician's diagnosis of NT1, NT2, or IH		

IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; US, United States.

Statistical analysis

- No imputation methods were used for missing data. Data from participants who did not complete the survey were not included in analyses
- Descriptive analyses included means and standard deviations (SDs) for continuous variables, and frequencies and percentages for categorical variables
- Differences in patient outcomes were examined using one-sample *t* tests, two-sample *t* tests, and analysis of variance. Statistical significance was defined as $P < 0.05$ (two-sided) without adjustment for multiplicity

Study measures and outcomes

Symptom severity

- Fatigue severity over the past week was assessed using the Patient Reported Outcomes Measurement Information System® Item Bank v1.0 - Fatigue - Short Form 6a (PROMIS-Fatigue)

Burden on functional and HRQoL outcomes

- Daily functioning was assessed using the FOSQ-10
- Work and activity impairment were evaluated using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI:SHP)
- Self-reported health status was assessed using the EQ-5D-5L, including the visual analogue scale (EQ VAS)

Results

Participant demographics and disposition

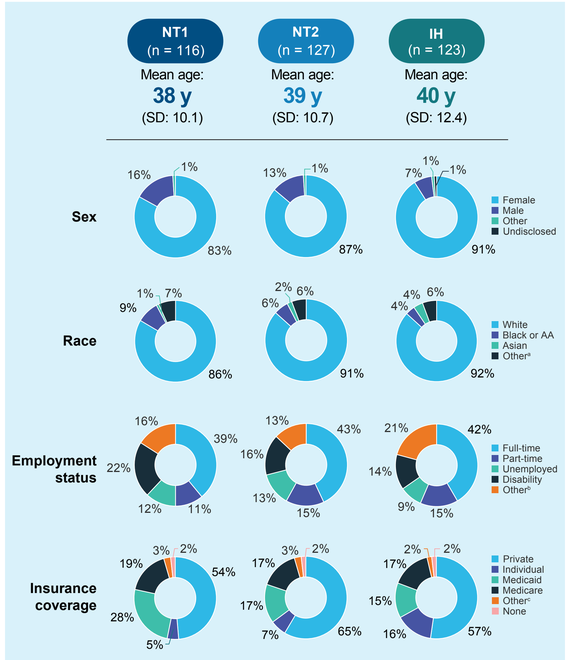
- A total of 366 participants (NT1, n = 116; NT2, n = 127; IH, n = 123) were included. Baseline characteristics are shown in **Figure 1**
- Many participants were taking nonstimulant wake-promoting agents (modafinil, armodafinil, solriamfetol, and pitolisant; 30.1%–48.3%), or stimulants (methylphenidates or amphetamines; 43.1%–48.8%)
  - Almost half (48.3%) of participants with NT1 were taking antidepressants for cataplexy

Fatigue

- The mean (SD) PROMIS-Fatigue T-score for all participants was 65.74 (7.52), which falls into the "moderate fatigue" category (**Figure 2A**)
  - Mean (SD) scores were similar across groups, with each group being categorized as "moderate fatigue" (NT1: 66.08 [7.78]; NT2: 65.03 [7.47]; IH: 66.16 [7.34])
- Ninety-one percent of all participants reported mild-to-severe fatigue (NT1: 90%; NT2: 89%; IH: 95%) (**Figure 2B**)
  - Participants with narcolepsy and IH had similar levels of fatigue

Results continued

Figure 1: Study participant baseline characteristics by diagnosis group



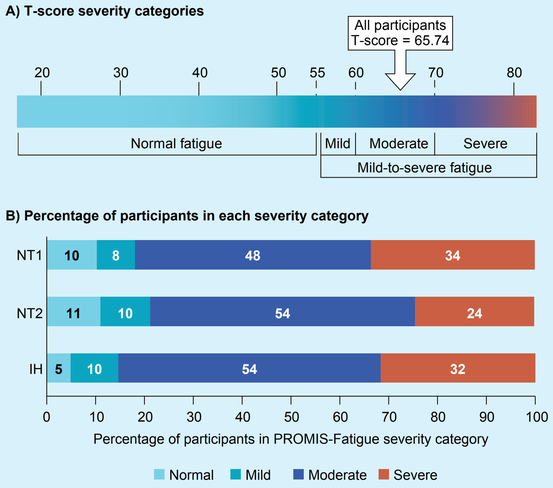
[a]"Other" category includes response options of "American Indian or Alaska Native," "Native Hawaiian or Other Pacific Islander," "Other," and "Prefer not to answer." Percentages may exceed 100% because some participants reported multiple races.

[b]"Other" category includes response options of "Student," "Stay-at-home parent/homemaker," "Retired," "Voluntary job," and "Prefer not to answer."

[c]"Other" category includes response options of "Veterans administration/TRICARE" and "I don't know." Percentages may exceed 100% because participants could report enrollment in multiple types of insurance.

AA, African American; IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; SD, standard deviation; y, years.

Figure 2: Fatigue as assessed by PROMIS-Fatigue in participants diagnosed with NT1, NT2, and IH



IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PROMIS-Fatigue, Patient Reported Outcomes Measurement Information System® Item Bank v1.0 - Fatigue - Short Form 6a.

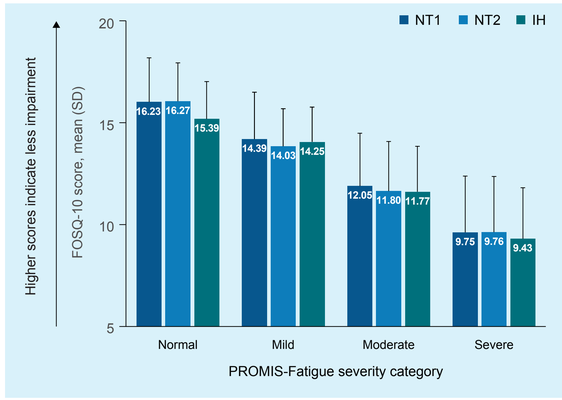
Fatigue and daily functioning

- The mean (SD) FOSQ-10 score for the overall study cohort was 11.79 (3.07)
- Participant scores for the FOSQ-10 were similar across groups, with a mean (SD) of 11.89 (3.28) for NT1, 12.03 (3.09) for NT2, and 11.45 (2.84) for IH
  - Scores demonstrated meaningful impairment on the FOSQ-10, with all groups scoring significantly below the normative value of 17.8 (all $P < 0.001$)[10]
- Participants with mild-to-severe fatigue had lower mean FOSQ-10 scores versus those with normal fatigue (11.38 vs 16.09, $P < 0.001$). Results were consistent across groups (NT1: 11.39 vs 16.23 [$P < 0.001$]; NT2: 11.50 vs 16.27 [$P < 0.001$]; IH: 11.24 vs 15.39 [$P < 0.001$])
- Across all groups, FOSQ-10 scores decreased as fatigue severity increased (**Figure 3**)

Fatigue and self-reported health status

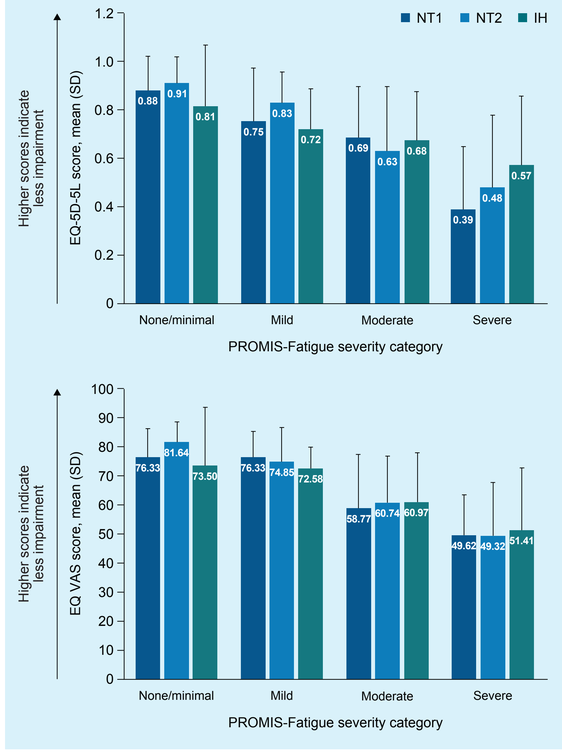
- Participants showed impairment on the EQ-5D-5L and EQ VAS scores, with mean (SD) scores of 0.64 (0.27) and 60.13 (18.52), respectively
- Participant scores for the EQ-5D-5L (NT1: 0.61; NT2: 0.65; IH: 0.65) and EQ VAS (NT1: 58.87; NT2: 61.7; IH: 59.6) were similar across all three groups
  - Scores indicated meaningful impairment on both the EQ-5D-5L index and EQ VAS, with all groups scoring significantly below normative values of 0.85 and 80.4, respectively (all $P < 0.001$)[11]
- Participants with mild-to-severe fatigue had lower mean EQ-5D-5L and EQ VAS scores versus those with normal fatigue (EQ-5D-5L: 0.61 vs 0.88 [$P < 0.001$]; EQ VAS: 58.4 vs 78.13 [$P < 0.001$]).
- Across all groups, EQ-5D-5L and EQ VAS scores were inversely associated with fatigue, with lower scores observed at higher PROMIS-Fatigue severity categories (between group significance for both scales in all diagnosis groups was $P < 0.001$, except for EQ-5D-5L in the IH group, which was $P = 0.027$) (**Figure 4**)
- On average, the most severe EQ-5D-5L dimensions in all diagnosis groups were "Activity," "Pain or Discomfort," and "Anxiety or Depression"

Figure 3: FOSQ-10 scores by PROMIS-Fatigue severity category and diagnosis group



FOSQ-10, Functional Outcomes of Sleep Questionnaire - Short Form; IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PROMIS-Fatigue, Patient Reported Outcomes Measurement Information System® Item Bank v1.0 - Fatigue - Short Form 6a; SD, standard deviation.

Figure 4: EQ-5D-5L and EQ VAS scores by PROMIS-Fatigue severity category and diagnosis group

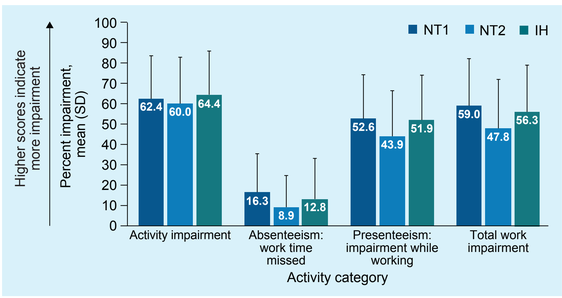


EQ-5D-5L, EuroQol-5D-5L index; EQ VAS, EuroQol Visual Analogue Scale; IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PROMIS-Fatigue, Patient Reported Outcomes Measurement Information System® Item Bank v1.0 - Fatigue - Short Form 6a; SD, standard deviation.

Fatigue and work

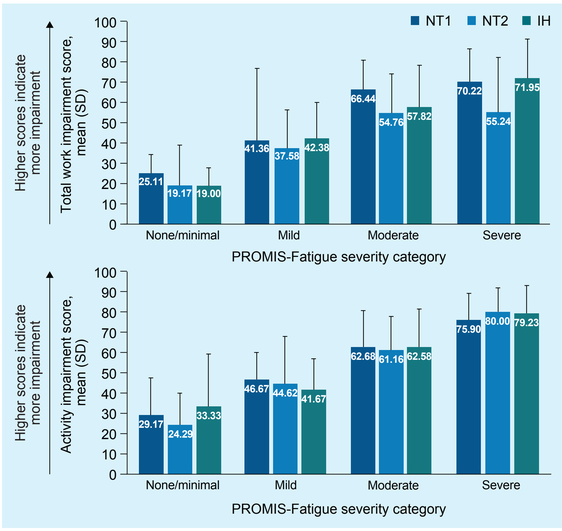
- Participants had high levels of activity impairment, describing 60% or more of their daily activities as being affected by narcolepsy or IH (**Figure 5**)
- Of those employed (NT1: 50%; NT2: 58%; IH: 56%), participants reported over 45% of their work as being impaired (**Figure 5**)
  - Total work impairment was also high across subtypes and was largely driven by presenteeism while at work
- All participants who reported mild-to-severe fatigue had greater impairments in work (59% vs 21%; $P < 0.001$) and activity (66% vs 28%; $P < 0.001$) versus the normal fatigue group
- Total work impairment and activity impairment were higher in participants with more severe fatigue ($P < 0.001$ for all comparisons) (**Figure 6**)

Figure 5: WPAI:SHP scores by diagnosis group



IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; SD, standard deviation; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.

Figure 6: WPAI:SHP total work impairment and activity impairment scores by PROMIS-Fatigue severity category and diagnosis group



IH, idiopathic hypersomnia; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PROMIS-Fatigue, Patient Reported Outcomes Measurement Information System® Item Bank v1.0 - Fatigue - Short Form 6a; SD, standard deviation; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.

Study limitations

- Though physician diagnosis of narcolepsy or IH was self-reported, confidence in diagnosis was supported by recruitment from RPV and advocacy groups
- Online survey administration limited participation to those with internet access and those interested in participating
- This study used a convenience sample, which may not reflect overall patient populations
- Participants from advocacy groups may have distinct experiences and a more active role in understanding and managing their conditions compared with the wider populations living with NT1, NT2, and IH

Conclusions

- Fatigue was common across participants with NT1, NT2, and IH
  - Over 90% of all participants reported mild-to-severe fatigue
- Fatigue was associated with significant burden across outcomes
  - The greatest burden was observed among participants with more severe fatigue
- This study highlighted the need to address the common and burdensome symptom of fatigue for those living with NT1, NT2, and IH
  - It also highlighted the importance of using established and relevant patient-reported outcome measures in research to support standardized interpretation and characterization of disease burden and treatment benefit

References

1. American Academy of Sleep Medicine, ed. International Classification of Sleep Disorders, Third Edition. American Academy of Sleep Medicine; 2014. 2. Blattner M et al. *Sleep Medicine Clinics*. 2023;18(2):183-99. 3. Foldvary-Schaefer N et al. *J Clin Sleep Med*. 2025;22(1):6. 4. Bassetti CLA et al. *Nat Rev Neurol*. 2019;15(9):519-39. 5. Doane M et al. Poster at SLEEP 2025 Meeting; June 8-11, 2025; Seattle, WA. 6. Schokman A et al. *Sleep Med*. 2024;116:62-70. 7. Doane M et al. Poster at SLEEP 2024 Meeting; June 8–11, 2024; Houston, TX. 8. US Food and Drug Administration. Patient-Focused Drug Development Guidance 3: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments. Published online 2025. https://www.fda.gov/media/159500/download. 9. US Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders. Published online December 2009. https://www.fda.gov/media/77832/download. 10. Chasens ER et al. *Sleep*. 2009;32(7):915-9. 11. Jiang R et al. *Qual Life Res*. 2021;30:803-16.

Acknowledgments

The authors thank all the participants in this study for their time and valuable input. This study was funded by Alkermes, Inc. Medical writing support was provided by Caroline Leitschuh, PhD, of Oxford PharmaGenesis Inc., Wilmington, DE, USA, and funded by Alkermes, Inc., Waltham, MA, USA.

Disclosures

MJD and **GM** are employees and shareholders of Alkermes. **JLT** and **KM** are employees of IQVIA Inc. **CW-W** received payment for expert testimony, support for attending meetings and/or travel, and holds leadership or fiduciary roles for Hypersomnia Foundation and Sleep Consortium. **LJ** has received grants or contracts (disbursed to Hypersomnia Foundation and Sleep Consortium) from Jazz, Centessa, Harmony Biosciences, Avadel, Alkermes, Takeda Pharmaceuticals, and Zevra; received consulting fees from Takeda Pharmaceuticals and Harmony Biosciences; and holds a leadership or fiduciary role with Hypersomnia Foundation.

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