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Characteristics and Disease Burden of Patients With Idiopathic Hypersomnia With and Without Long Sleep Time: The Real World Idiopathic Hypersomnia Outcomes Study (ARISE)

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Introduction

- Idiopathic hypersomnia is a debilitating neurologic sleep disorder characterized by chronic excessive daytime sleepiness (EDS).[1-3] In addition to EDS, symptoms may include severe sleep inertia (prolonged difficulty waking with frequent reentries into sleep, confusion, and irritability), as well as cognitive impairment, long and unrefreshing naps, and prolonged nighttime sleep[1,3]
- Limited information is available on the burden of symptoms in patients with idiopathic hypersomnia, and particularly how the experience may differ among those with long sleep time (LST; characterized as ≥11 hours in a 24-hour period in the *International Classification of Sleep Disorders*, 3rd Edition [ICSD-3])[1]
  - The ICSD-2 previously recognized a separate subtype of patients with idiopathic hypersomnia who sleep >10 hours at night, but this distinction was later removed in the ICSD-3, where criteria included patients both with and without LST[1,4]
- No treatment was US Food and Drug Administration (FDA) approved for idiopathic hypersomnia at the time of the study; lower-sodium oxybate received FDA approval for adults with idiopathic hypersomnia in August 2021[5]
- The Real World Idiopathic Hypersomnia Outcomes Study (ARISE) evaluated the impact of idiopathic hypersomnia on patients' lives and patient perspectives regarding their current treatment

Objective

- To assess symptoms, functioning, quality of life, and treatment satisfaction in ARISE participants with idiopathic hypersomnia with or without LST

Methods

- Eligible ARISE participants included adults 21–65 years of age with idiopathic hypersomnia with or without LST (≥11 hours of sleep in a 24-hour period [self-reported])
- ARISE was a US-based virtual cross-sectional survey comprising multiple patient-reported outcome measures assessing:
  - Symptom severity (Epworth Sleepiness Scale [ESS]; Idiopathic Hypersomnia Severity Scale [IHSS])
  - Daily functioning (Functional Outcomes of Sleep Questionnaire, short version [FOSQ-10])
  - Quality of life (Neuro-QoL [Quality of Life in Neurological Disorders])
  - Cognition (British Columbia Cognitive Complaints Inventory [BC-CCI])
  - Depression (Patient Health Questionnaire-9 [PHQ-9])
  - Work/Activity impairment (Work Productivity and Activity Impairment Questionnaire: Specific Health Problem, v2.0 [WPAI:SHP])
  - Treatment satisfaction (Treatment Satisfaction Questionnaire for Medication, version II [TSQM-vII])
- Continuous variables were summarized with descriptive statistics (n, mean, standard deviation [SD], median, quartiles, minimum, and maximum). Frequency counts and percentage of participants within each category were provided for categorical data

Results

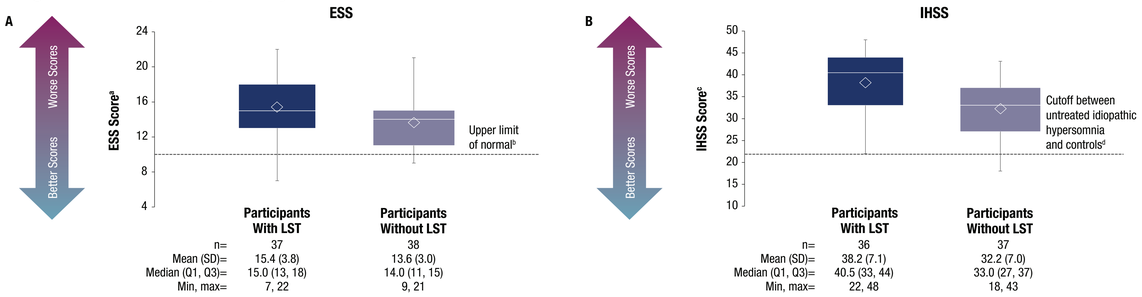
- Seventy-five participants enrolled with a mean (SD) age of 34.1 (10.7) years; most were female and most were taking medications for idiopathic hypersomnia
- More participants with LST reported taking off-label medications than those without LST

Table 1. Demographics and Participant Characteristics

Characteristic	Participants With LST (n=37)	Participants Without LST (n=38)	All Participants (N=75)
Age, years, mean (SD)	33.7 (10.7)	34.4 (10.9)	34.1 (10.7)
Female, n (%)	27 (73.0)	34 (89.5)	61 (81.3)
Time since idiopathic hypersomnia diagnosis, years, n (%)			
<2	5 (13.5)	7 (18.4)	12 (16.0)
2–4	20 (54.1)	14 (36.8)	34 (45.3)
5–9	8 (21.6)	10 (26.3)	18 (24.0)
≥10	4 (10.8)	7 (18.4)	11 (14.7)
Patient-reported sleep duration, mean (SD)			
Approximate hours of sleep in a typical 24-hour period	14.3 (2.7)	8.9 (1.1)	11.6 (3.4)
Approximate hours of sleep in a typical night	9.8 (1.7)	8.0 (0.8)	8.9 (1.6)
Approximate hours of sleep in a typical day	4.5 (2.9)	0.9 (1.0)	2.7 (2.8)
Taking off-label medications for idiopathic hypersomnia, n (%)	36 (97.3)	31 (81.6)	87 (89.3)

LST, long sleep time; SD, standard deviation.

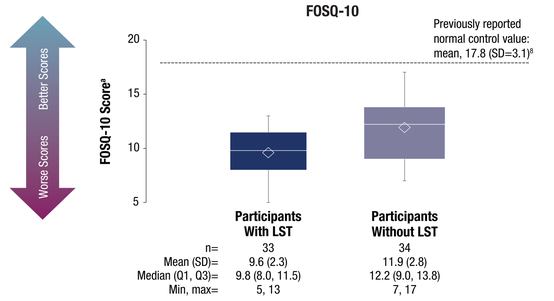
Figure 1. Participants Reported High Levels of Sleepiness and Other Idiopathic Hypersomnia Symptoms on the (A) ESS and (B) IHSS, and Even Higher Levels Were Reported by Participants With LST



The bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values.
ESS, Epworth Sleepiness Scale; IHSS, Idiopathic Hypersomnia Severity Scale; LST, long sleep time; Q1, first quartile; Q3, third quartile; SD, standard deviation.
[a]Range of possible ESS scores is 0–24; higher scores indicate greater sleepiness.
[b]ESS scores of >10 suggest pathologic sleepiness.[6]
[c]Range of possible IHSS scores is 0–50; higher scores indicate greater symptom severity.
[d]IHSS scores of ≥22 are a cutoff separating untreated patients with idiopathic hypersomnia from controls.[7]

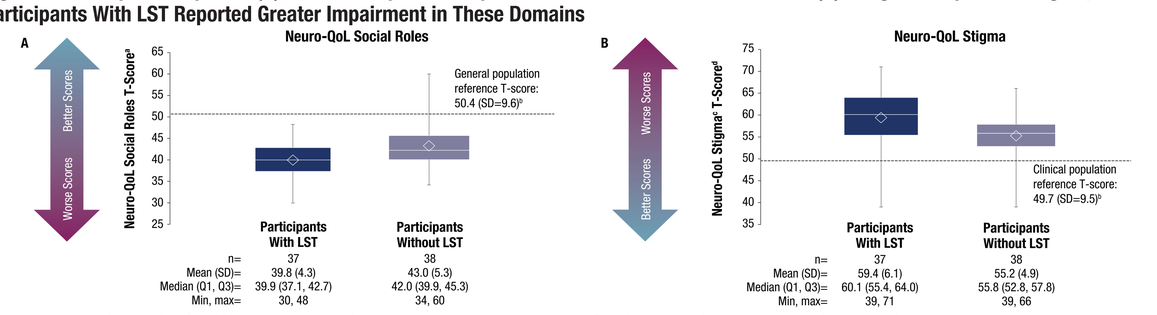
- ESS scores >10 were reported by 89.2% of participants with LST and 86.8% of participants without LST
- IHSS scores ≥22 were reported by 100% of participants with LST and 91.9% of participants without LST

Figure 2. Participants Reported Impairments in Daily Functioning, Which Were Greater in Those With LST



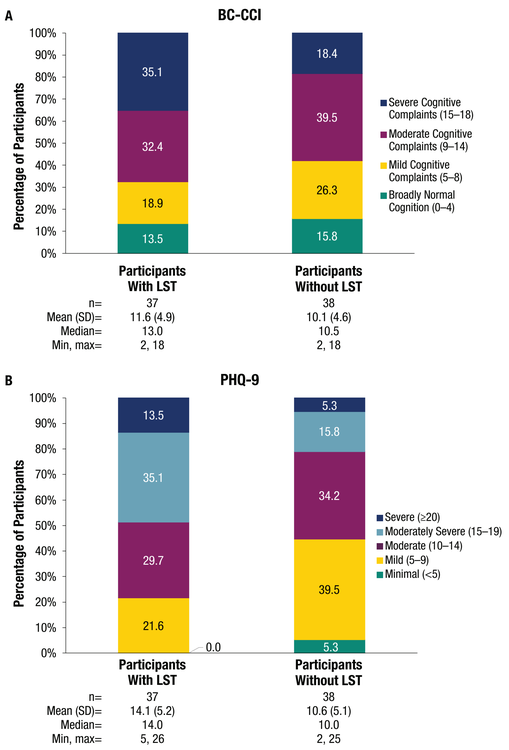
The bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values.
FOSQ-10, Functional Outcomes of Sleep Questionnaire, short version; LST, long sleep time; Q1, first quartile; Q3, third quartile; SD, standard deviation.
[a]Range of possible FOSQ-10 scores is 5–20; lower scores indicate worse impairment.

Figure 3. Participants Reported (A) a Low Ability to Participate in Social Roles and Activities and (B) a High Perception of Stigma; Participants With LST Reported Greater Impairment in These Domains



The bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values.
LST, long sleep time; Neuro-QoL, Quality of Life in Neurological Disorders; Q1, first quartile; Q3, third quartile; SD, standard deviation.
[a]Range of possible T-scores for social roles is 24.1–60.2; higher scores indicate better outcomes.
[b]T-score distributions rescale raw scores into standardized scores with approximate mean (SD) of 50 (10).[9]
[c]Perceptions of self and publicly enacted negativity, prejudice, and discrimination as a result disease-related manifestations.
[d]Range of possible T-scores for stigma is 39.2–81.5; higher scores indicate worse outcomes.

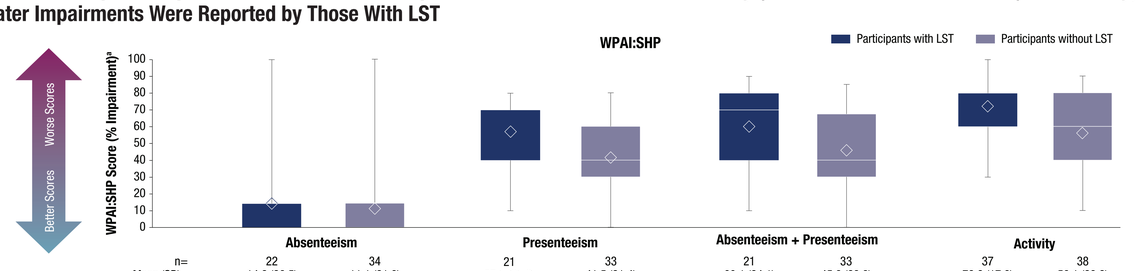
Figure 4. Participants, Especially Those With LST, Often Reported (A) Severe Cognitive Complaints and (B) Moderately Severe to Severe Depressive Symptoms



BC-CCI, British Columbia Cognitive Complaints Inventory; LST, long sleep time; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

- Moderate to severe cognitive impairment was reported by 67.6% of participants with LST and 57.9% of participants without LST
- Moderate to severe depressive symptoms were reported by 78.4% of participants with LST and 55.3% of participants without LST

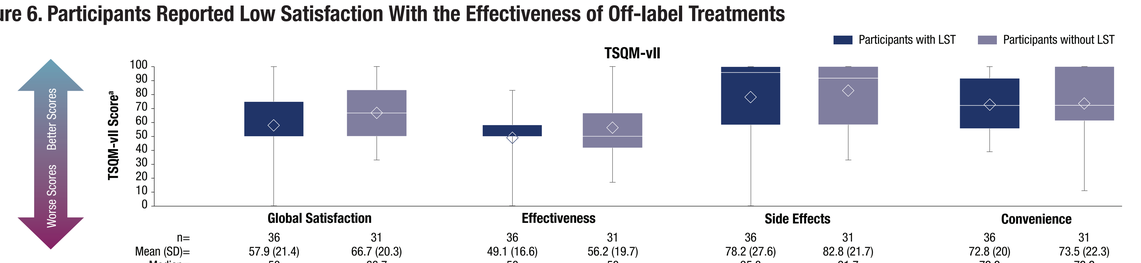
Figure 5. Participants Reported Presenteeism and Impairments in Overall Work Productivity (Absenteeism + Presenteeism) and Activity; Greater Impairments Were Reported by Those With LST



The bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values.
LST, long sleep time; Q1, first quartile; Q3, third quartile; SD, standard deviation; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.
[a]Range of possible scores for the WPAI:SHP is 0–100, with greater numbers indicating greater impairment.[10,11]

- Average absenteeism was >10%, which was lower than presenteeism; this suggests that work impairment in participants with idiopathic hypersomnia manifests as decreased productivity while at work rather than lost work time, although absenteeism greater than 10% is still a concern

Figure 6. Participants Reported Low Satisfaction With the Effectiveness of Off-label Treatments



LST, long sleep time; Q1, first quartile; Q3, third quartile; SD, standard deviation; TSQM-vII, Treatment Satisfaction Questionnaire for Medication, version II.
[a]Range of possible scores is 0–100, with greater numbers indicating higher satisfaction; a poor appraisal of health was previously found to correspond to mean scores of 64.8 (global satisfaction), 63.3 (effectiveness), 75.8 (side effects), and 83.3 (convenience).[12]

- Participants with LST reported lower average ratings on global satisfaction and treatment effectiveness scales than those without LST
- Treatment effectiveness was scored the lowest across all groups of participants

Conclusions

- ARISE participants with idiopathic hypersomnia reported high levels of sleepiness; impaired daily functioning, cognition, and mood; poor quality of life; and impaired work productivity/activity levels, despite the majority of participants taking off-label treatments
- Participants with idiopathic hypersomnia and long sleep time reported greater disease burden on all these assessments compared with those without long sleep time
- These findings from ARISE help to more clearly define the symptom burden of idiopathic hypersomnia, important for evaluating the impact of therapeutic options

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