A Conceptual Disease Model of the Symptoms and Impacts of Idiopathic Hypersomnia From the Patient Perspective

Mean (SD)

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Figure 1. Symptoms of Idiopathic Hypersomnia

A. Frequency, Severity, and Bothersomeness of Salient Symptoms

Introduction

- Idiopathic hypersomnia is a central disorder of hypersomnolence characterized by multiple interrelated symptoms, including excessive daytime sleepiness (EDS), sleep inertia, prolonged nighttime sleep, long and unrefreshing naps, and subjective cognitive impairment¹⁻³
- Previous cross-sectional analyses have quantitatively reported the symptom burden of idiopathic hypersomnia and the impact of this burden on quality of life and daily functioning using patient-reported outcomes^{4,5}
- There is limited qualitative research on patients' experiences living with idiopathic hypersomnia
- Symptoms of idiopathic hypersomnia are complex and heterogeneous and often overlap with symptoms of other conditions, so it is important to collect data directly from individuals with idiopathic hypersomnia to holistically understand patients' experiences

Objective

 This qualitative study explored patients' perspectives on the most relevant and important symptoms and impacts of idiopathic hypersomnia, resulting in a comprehensive conceptual disease model

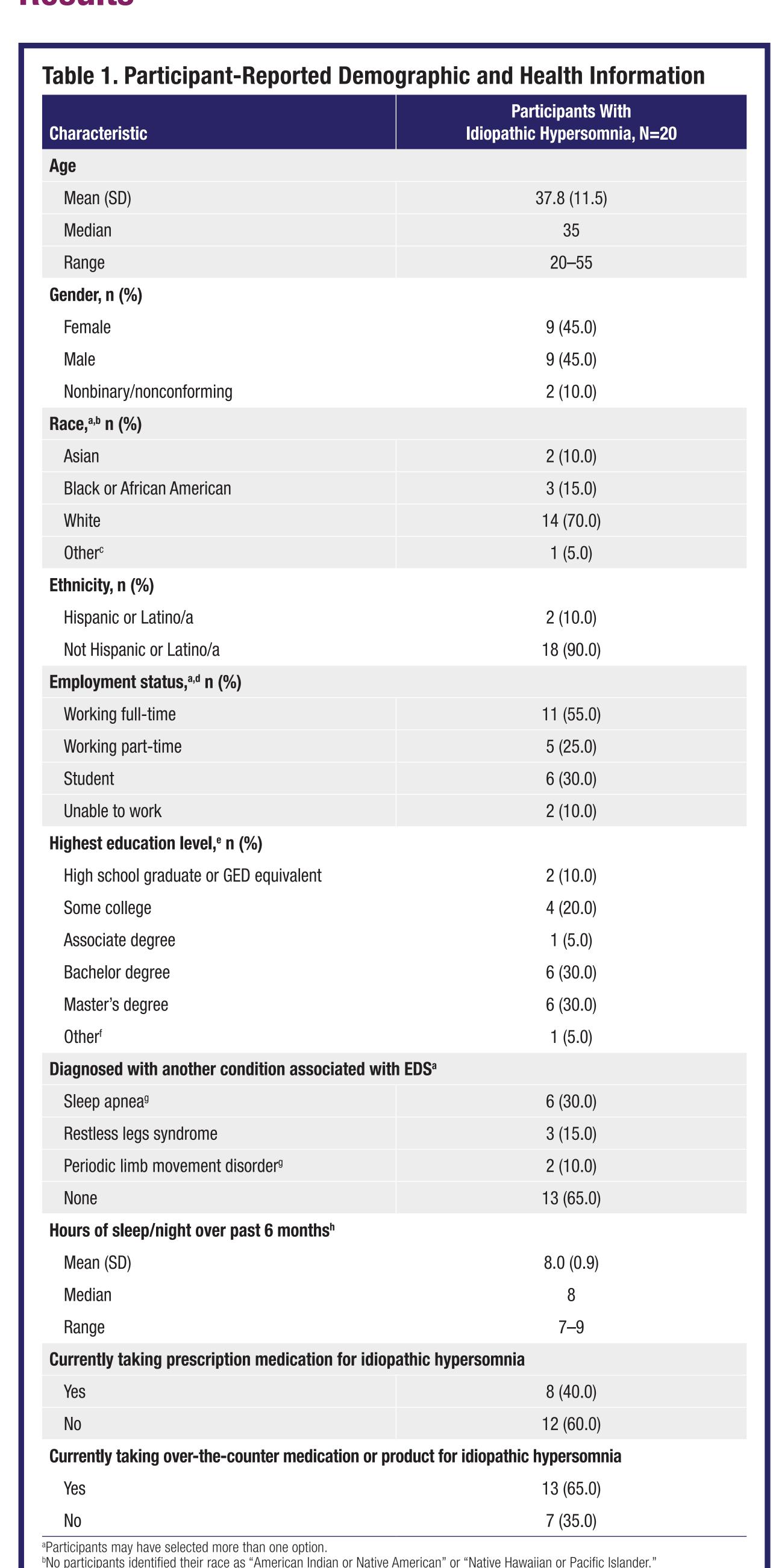
- A targeted literature review was conducted to identify published articles describing patients' experiences with idiopathic hypersomnia and to develop a preliminary conceptual disease model of the symptoms and impacts of this condition
- The search was limited to English-language publications appearing within the past 10 years and involving adults 18–64 years of age
- Symptoms were defined as internal experiences of idiopathic hypersomnia best reported through patient expression (eg, brain fog), and impacts were defined as effects of symptoms on participants' day-to-day lives and functioning (eg, difficulties with work, relationships, and activities of daily living)
- This preliminary conceptual disease model was used to inform the development of the concept elicitation (CE) discussion guide, which included both open-ended questions and probes on concepts of interest; CE interview exercises (lasting up to 60 minutes) were completed with 20 adult participants with idiopathic hypersomnia
- Key inclusion criteria for participants included 18–64 years of age at time of screening, a confirmed idiopathic hypersomnia diagnosis, and current experience with EDS; key exclusion criteria for participants were a diagnosis of a medical condition (other than idiopathic hypersomnia) associated with EDS, untreated or inadequately treated sleep-disordered breathing or periodic limb movement disorder resulting in daytime sleepiness, average total sleep time <7 hours/night over the preceding 6 months, and an occupation that required nighttime or variable shift work
- During their interviews, participants were asked about the symptoms and impacts associated with their idiopathic hypersomnia; they were then asked to provide severity ratings (0-10) for all past/current symptoms and bothersomeness ratings (0-10) for each current symptom and impact, and to report their 3 worst and 3 most bothersome symptoms and impacts
- Interviews were conducted in four waves (n=5 for each wave) to enable assessment of saturation (point at which no new concepts were reported)
- Interview transcripts were coded using qualitative analysis software (MAXQDA) with a focus on identifying reported symptoms and impacts; coding was guided by a prespecified coding framework and codebook, which were informed by the preliminary conceptual disease model, discussion guide, and research objectives, and was overseen by study scientists
- Concept frequencies and bothersomeness ratings were used to evaluate salience (reported by ≥50% of participants; average bothersomeness rating ≥5) and finalize the conceptual disease model

References: 1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders – Third Edition, Text Revision*. Darien, IL: American Academy of Sleep Medicine; 2023. 2. Arnulf I, et al. Sleep Med Rev. 2023;69:101766. 3. Vernet C, et al. J Sleep Res. 2010;19(4):525-534. 4. Schneider LD, et al. Nat Sci Sleep. 2023;15:89-101. 5. Stevens J, et al. Nat Sci Sleep.

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Disclosures: C Casstevens, M Whalen, and **M Wraight** are full-time employees of Jazz Pharmaceuticals who, in the course of have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals. plc. A Sterkel and HN Viswanathan are former full-time employees of Jazz Pharmaceuticals who, in the course of this employment, received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc. CA Graham, JA Price, F Ginchereau Sowell, and M Farrell are full-time employees of IQVIA, which was contracted by Jazz Pharmaceuticals to conduct this study. **J Black** is a part-time employee of Jazz Pharmaceuticals and shareholder of Jazz Pharmaceuticals, plc.

Results



The participant who selected "Other" reported their race as "Hispanic or Latino/a."

central sleep apnea) or periodic limb movement disorder resulting in daytime sleepiness.

the majority were White (n=14, 70.0%)

hypersomnia (n=13, 65.0%)

independent of time in bed over past 6 months.

^dNo participants identified their employment status as "Seeking work opportunities," "Retired," or "Homemaker.

'The participant who selected "Other" reported their highest education level as "Naval nuclear power school."

⁹Eligibility criteria allowed for enrollment of participants with adequately treated sleep-disordered breathing (ie, obstructive sleep apnea,

hFligibility criteria required that enrolled participants with idiopathic hypersomnia had average total self-reported sleep time ≥7 hours/night

numbers of male (n=9, 45.0%) and female (n=9, 45.0%) participants, and

Participants' mean (SD) age was 37.8 (11.5) years; there were equal

While a majority of participants were not currently taking a prescription

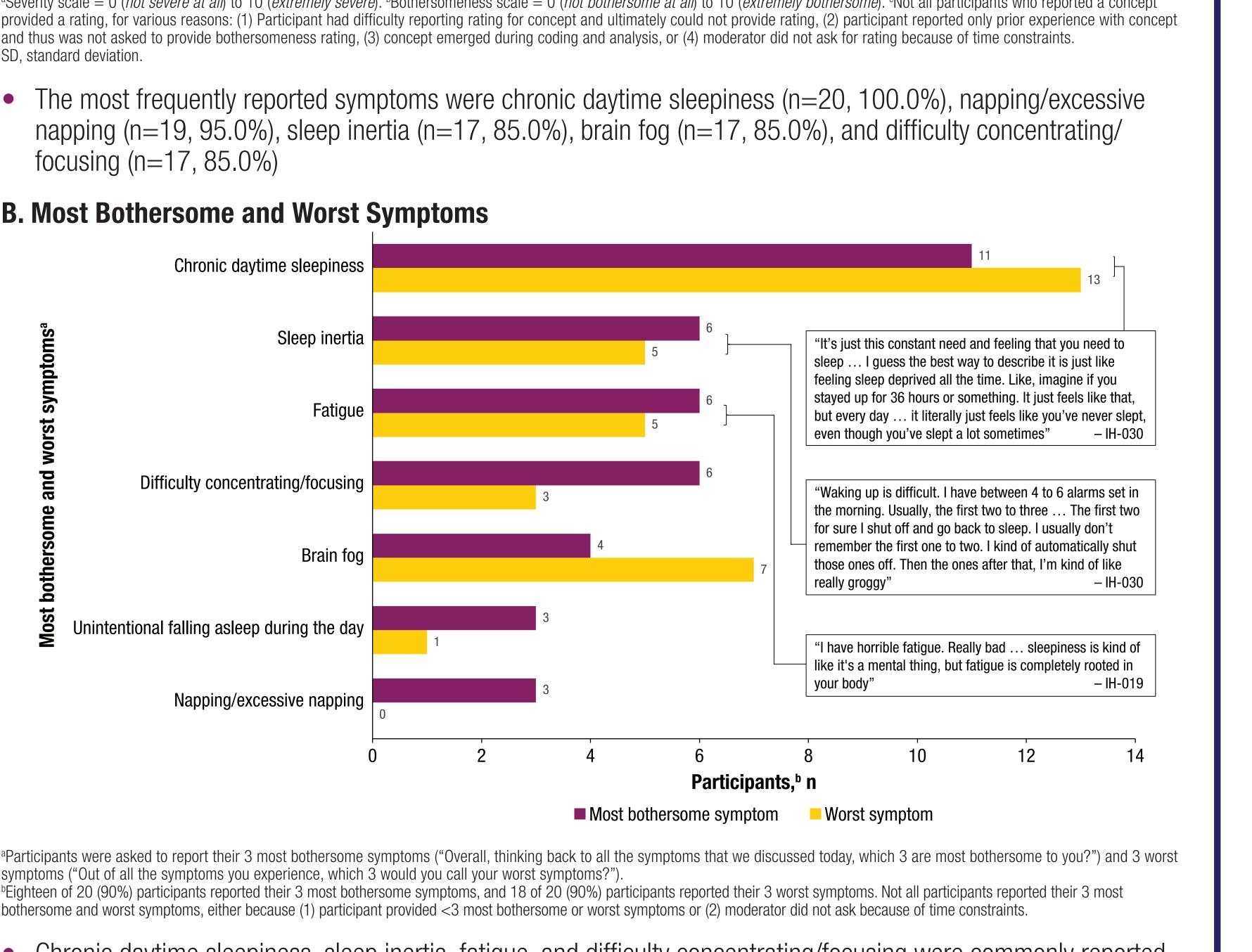
medication for idiopathic hypersomnia (n=12, 60.0%), a majority were

currently taking an over-the-counter medication or product for idiopathic

eNo participants identified their highest education level as "Less than high school" or "Doctorate degree."

EDS, excessive daytime sleepiness; GED, General Educational Development; SD, standard deviation.

Chronic daytime sleepiness 20 (100.0) 8.5 (1.2), n=17 8.4 (1.9), n=20 19 (95.0) Napping/excessive napping 8.2 (1.7), n=17 7.4 (2.6), n=17 **Difficulty concentrating/focusing** 7.9 (1.5), n=15 7.7 (2.2), n=13 8.5 (1.4), n=13 7.9 (2.0), n=15 7.4 (1.8), n=15 7.5 (2.7), n=14 13 (65.0) Difficulty communicating thoughts 6.5 (2.0), n=10 6.9 (1.8), n=10 Unintentional falling asleep during the day and thus was not asked to provide bothersomeness rating, (3) concept emerged during coding and analysis, or (4) moderator did not ask for rating because of time constraints The most frequently reported symptoms were chronic daytime sleepiness (n=20, 100.0%), napping/excessive napping (n=19, 95.0%), sleep inertia (n=17, 85.0%), brain fog (n=17, 85.0%), and difficulty concentrating/ focusing (n=17, 85.0%) **B. Most Bothersome and Worst Symptoms** Chronic daytime sleepiness sleep ... I guess the best way to describe it is just like feeling sleep deprived all the time. Like, imagine if you staved up for 36 hours or something. It just feels like that but every day ... it literally just feels like you've never slept, even though you've slept a lot sometimes" — IH-030 Difficulty concentrating/focusing "Waking up is difficult. I have between 4 to 6 alarms set in the morning. Usually, the first two to three ... The first two for sure I shut off and go back to sleep. I usually don't those ones off. Then the ones after that, I'm kind of like Unintentional falling asleep during the day "I have horrible fatigue. Really bad ... sleepiness is kind of like it's a mental thing, but fatigue is completely rooted in Napping/excessive napping symptoms ("Out of all the symptoms you experience, which 3 would you call your worst symptoms?") ^bEighteen of 20 (90%) participants reported their 3 most bothersome symptoms, and 18 of 20 (90%) participants reported their 3 worst symptoms. Not all participants reported their 3 most bothersome and worst symptoms, either because (1) participant provided <3 most bothersome or worst symptoms or (2) moderator did not ask because of time constraints.



 Chronic daytime sleepiness, sleep inertia, fatigue, and difficulty concentrating/focusing were commonly reported among the 3 most bothersome symptoms

Average bothersomeness rating

Napping/excessive napping

Difficulty communicating thoughts

Unintentional falling asleep during the day

Difficulty planning/organizing

Chronic daytime sleepiness

Chronic daytime sleepiness and brain fog were commonly reported among the 3 worst symptoms

Figure 3. Salient Symptoms and Impacts

Figure 2. Impacts of Idiopathic Hypersomnia

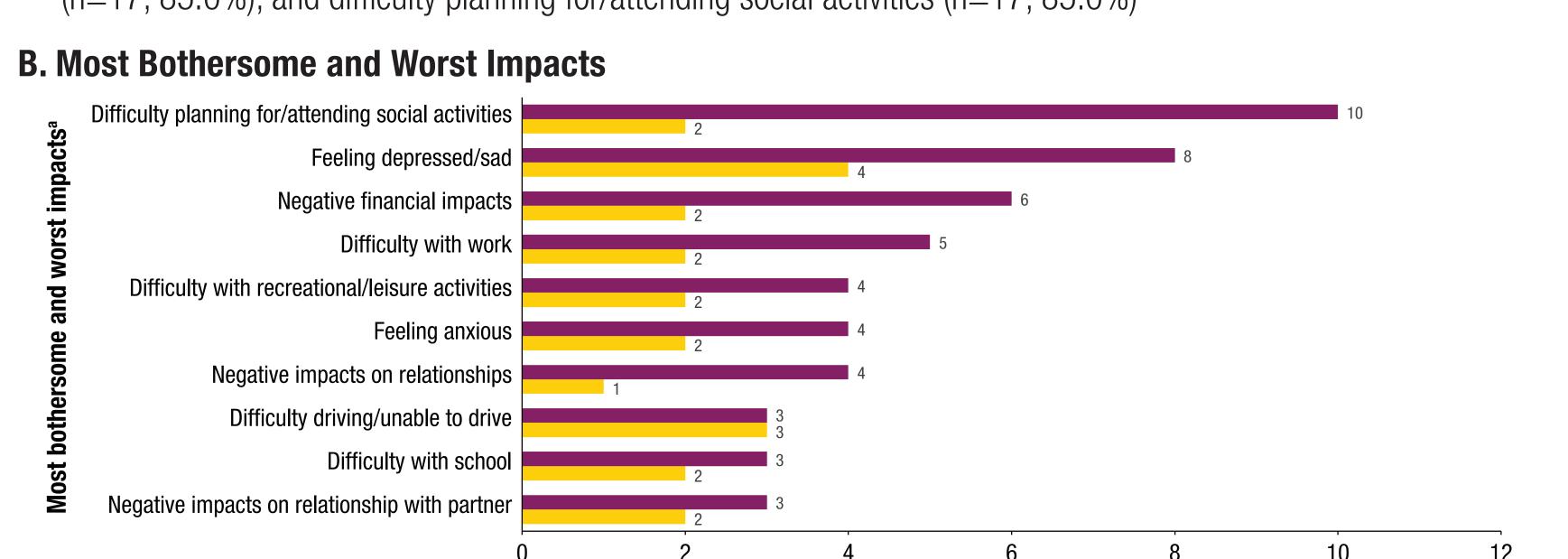
A. Frequency and Bothersomeness of Salient Impacts

emerged during coding and analysis, or (4) moderator did not ask for rating because of time constraints.

iADL, instrumental activity of daily living; SD, standard deviation.

Impact	Participants With Idiopathic Hypersomnia, N=20 n (%)	Spontaneous, n	Probed, n	Bothersomeness Rating, ^{a,b} Mean (SD)
Difficulty with work	20 (100.0)	20	0	7.9 (2.5), n=18
Difficulty driving/unable to drive	18 (90.0)	11	7	7.1 (2.8), n=15
Negative impacts on relationships	17 (85.0)	7	10	7.8 (2.1), n=13
Negative impact on ability to exercise or move	17 (85.0)	10	7	6.9 (2.2), n=13
Difficulty planning for/attending social activities	17 (85.0)	10	7	8.1 (1.6), n=11
Difficulty with recreational/leisure activities	16 (80.0)	6	10	7.7 (2.2), n=11
Feeling depressed/sad	15 (75.0)	12	3	8.1 (1.5), n=13
Difficulties with iADLs (eg, cooking, daily routine/chores)	15 (75.0)	10	5	7.5 (1.4), n=11
Stress	13 (65.0)	4	9	8.8 (1.0), n=9
Difficulty with self-care	12 (60.0)	4	8	8.4 (1.6), n=7
Negative impacts on relationship with partner	12 (60.0)	9	3	7.8 (2.9), n=11
Adaptive behaviors	11 (55.0)	4	7	7.3 (1.7), n=4
Irritability	10 (50.0)	8	2	7.9 (1.5), n=7
Feeling anxious	10 (50.0)	8	2	7.6 (2.2), n=7
Feeling misunderstood/stigmatized	10 (50.0)	10	0	6.5 (3.5), n=2

• The most frequently reported impacts were difficulty with work (n=20, 100.0%), difficulty driving/unable to drive (n=18, 90.0%), negative impacts on relationships (n=17, 85.0%), negative impact on ability to exercise or move (n=17, 85.0%), and difficulty planning for/attending social activities (n=17, 85.0%)



^aParticipants were asked to report their 3 most bothersome impacts ("Overall, thinking back to all the impacts that we discussed today, which 3 are most bothersome to vou?") and 3 worst ^bTwenty of 20 (100%) participants reported their 3 most bothersome impacts, and 13 of 20 (65%) participants reported their 3 worst impacts. Not all participants reported their 3 most iADL, instrumental activity of daily living.

- commonly reported among the 3 most bothersome impacts

Difficulty with work

Figure 4. Final Conceptual Disease Model of Idiopathic Hypersomnia PATIENT POPULATION Adults with idiopathic hypersomnia **SYMPTOMS Daytime Sleepiness** Brain fog Chronic daytime sleepiness Difficulty communicating thoughts Napping/excessive napping Unintentional falling asleep during the day Difficulty concentrating/focusing Memory problems **Impaired Wakefulness** Automatic behaviors **Physical** Sleep inertia ADLs/iADLs School/Work Difficulty with work Difficulty driving/unable to drive Difficulty with iADLs (eg, cooking, daily routine/chores) **Physical Functioning** Difficulty with self-care Negative impact on ability to exercise or move **Recreational/Leisure Social** Difficulty with recreational/leisure activities Difficulty planning for/attending social activities **Behavioral/Emotional** Relationships Feeling anxious Negative impacts on relationships Feeling depressed/sad Negative impacts on relationship with partner

Conclusions

Feeling misunderstood/stigmatized

ADL, activity of daily living; iADL, instrumental activity of daily living

 Qualitative interviews revealed that patients with idiopathic hypersomnia experience salient symptoms beyond EDS, including sleep inertia, cognitive difficulties, and fatigue These salient symptoms were reported to be associated with emotional, social, occupational,

Adaptive Behaviors

- and functional impacts The conceptual disease model represents the most salient symptoms and impacts of idiopathic
- hypersomnia as reported by patients
- Because some concepts were probed during interviews, the conceptual disease model may not completely reflect how participants spontaneously describe their symptoms or the impact of idiopathic hypersomnia on their lives
- The conceptual disease model, directly informed by patient input, supports a greater understanding of idiopathic hypersomnia and can be used to facilitate the selection and development of clinical outcome assessments that capture the idiopathic hypersomnia patient experience
- Findings may inform recognition and management of idiopathic hypersomnia and aid in differentiating idiopathic hypersomnia from other conditions with overlapping symptoms





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impacts ("Out of all the impacts you experience, which 3 would you call your worst impacts?") bothersome and worst impacts, either because (1) participant provided <3 most bothersome or worst impacts or (2) moderator did not ask because of time constraints.

B. Impacts

^aSalient symptoms (A) or impacts (B) were reported by ≥50% of participants with average ≥5.0 bothersomeness rating and are displayed in upper right quadrants. iADL, instrumental activity of daily living.

Participants reported 31 symptoms and 37 impacts; 10 symptoms and 15 impacts were deemed salient

- Difficulty planning for/attending social activities, feeling depressed/sad, and negative financial impacts were
 - Feeling depressed/sad and difficulty driving/unable to drive were commonly reported among the 3 worst impacts