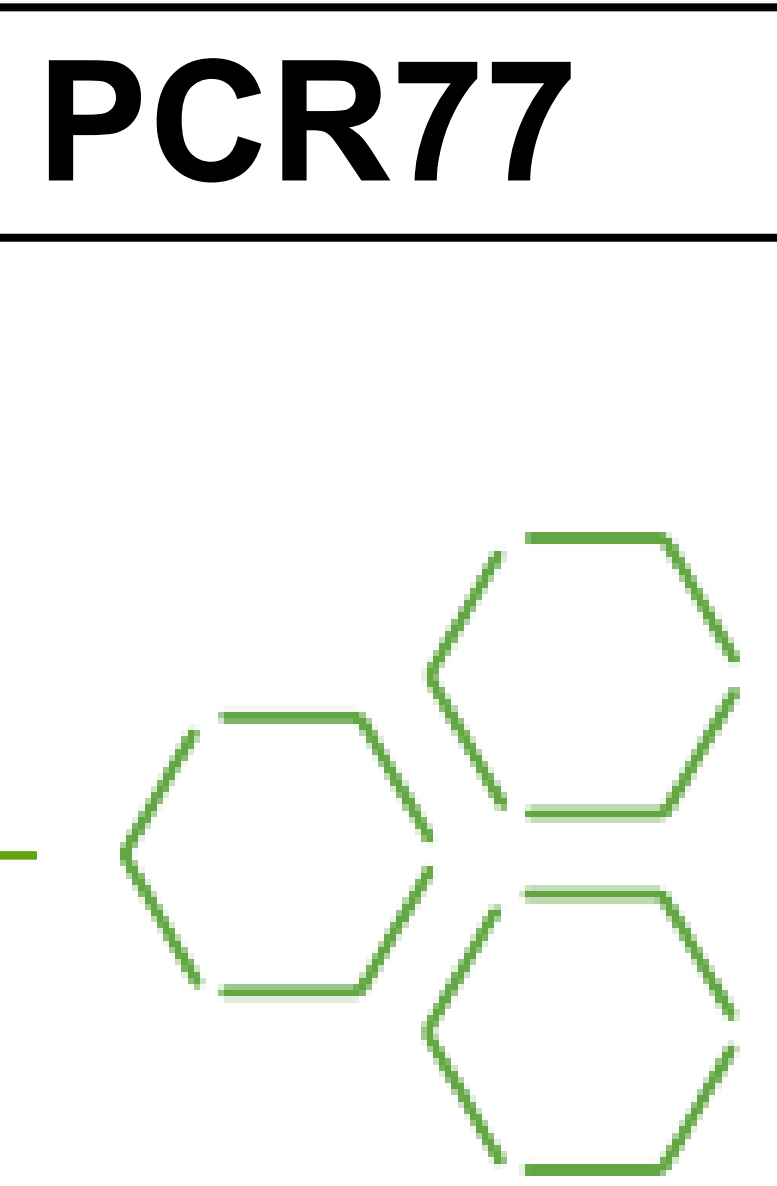# Development of a conceptual model of the patient experience with idiopathic hypersomnia: Patient interviews from a clinical trial (NCT05156047)

Johnston K[1], Insana S[2], Merikle E[1], Manuel M[2], Wilmsen K[2], Presnall C[1], Carlson C[1], Nomikos G[2]

[1]Fortrea Patient-Centered Assessment, USA; [2]Harmony Biosciences, Plymouth Meeting, PA

Background

- Idiopathic hypersomnia (IH) is a rare neurological disorder characterized by excessive daytime sleepiness (EDS), sleep inertia, cognitive difficulties, and compromised alertness (Arnulf et al 2019)
- To date, few qualitative studies have been conducted to describe IH symptoms and impacts; the extent to which IH symptoms such as EDS affect daily functioning has not been fully explored from the patient perspective
- This study provides patient experience data about IH symptoms, and which symptoms (e.g., tiredness, dozing off) matter most to individuals with IH

Objectives

- Explore the salient symptoms and their functional consequences in individuals with IH
- Develop a conceptual model depicting the experience living with IH to inform the selection of endpoints for clinical trials that investigate treatments for IH

Methods

- Qualitative interviews with a subset of participants (n=61) who were consecutively recruited at the completion of study NCT05156047
- 1:1 semi-structured interviews (≈ 60 mins) conducted at the end of the last study visit via video conference
- Interviewer elicited participants' descriptions of their experience living with IH prior to enrolling in the study via open-end questions with probes for further details as appropriate
- Interviews were recorded and professionally transcribed. Technical difficulties precluded one interview from being transcribed
- Transcripts (n=60) were analyzed following principles in line with applied thematic (content) analysis (Guest et al 2012) to identify salient symptoms and functional consequences of IH using NVivo qualitative data analysis software
- Symptoms and impacts were grouped by themes during analysis

Table 1. Participant Characteristics

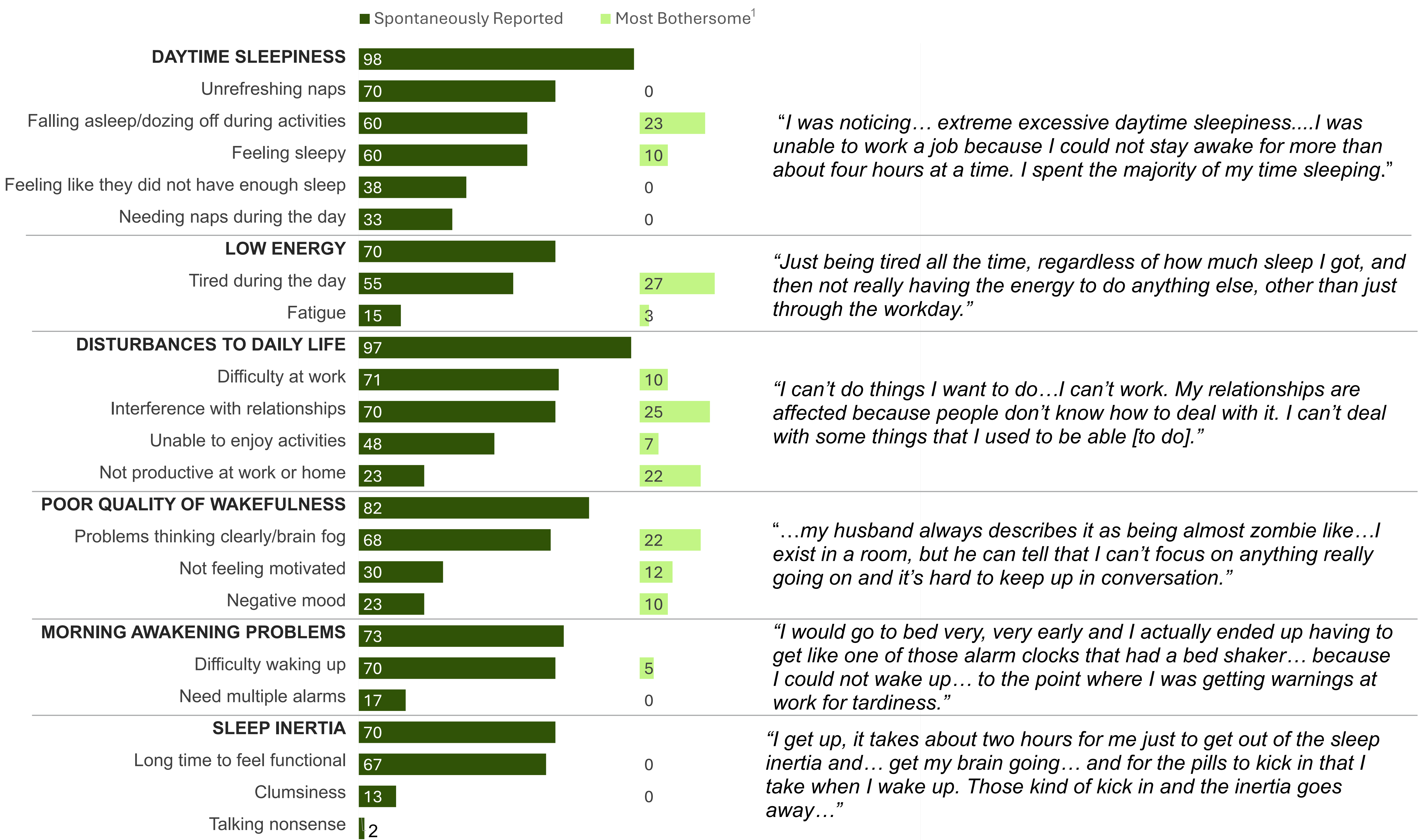| Characteristic	Interviewed (n=60)	Not-interviewed (n=79)
Age (years), mean (SD)	38.5 (10.9)	41.1 (12.6)
Sex, n (%) female	48 (80.0)	62 (78.5)
Race, n (%) White/Caucasian	54 (90.0)	69 (87.3)
Baseline ESS Score[1],mean (SD)	16.3 (3.2)	16.7 (7.9)
Baseline IHSS Score[2], mean (SD)	34.1 (5.8)	33.1 (7.9)
Baseline PGI-S (EDS)[3], mean (SD)	3.9 (0.70)	3.8 (0.70)
Baseline CGI-S (IH)[3], mean (SD)	3.7 (0.60)	3.6 (0.60)

Abbreviations: CGI-S = Clinician Global Impression of Severity; EDS = excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; IHSS = Idiopathic Hypersomnia Severity Scale; PGI-S = Patient Global Impression of Severity

[1]Ranges from 0 to 24 with scores ≥ 16 indicating severe EDS
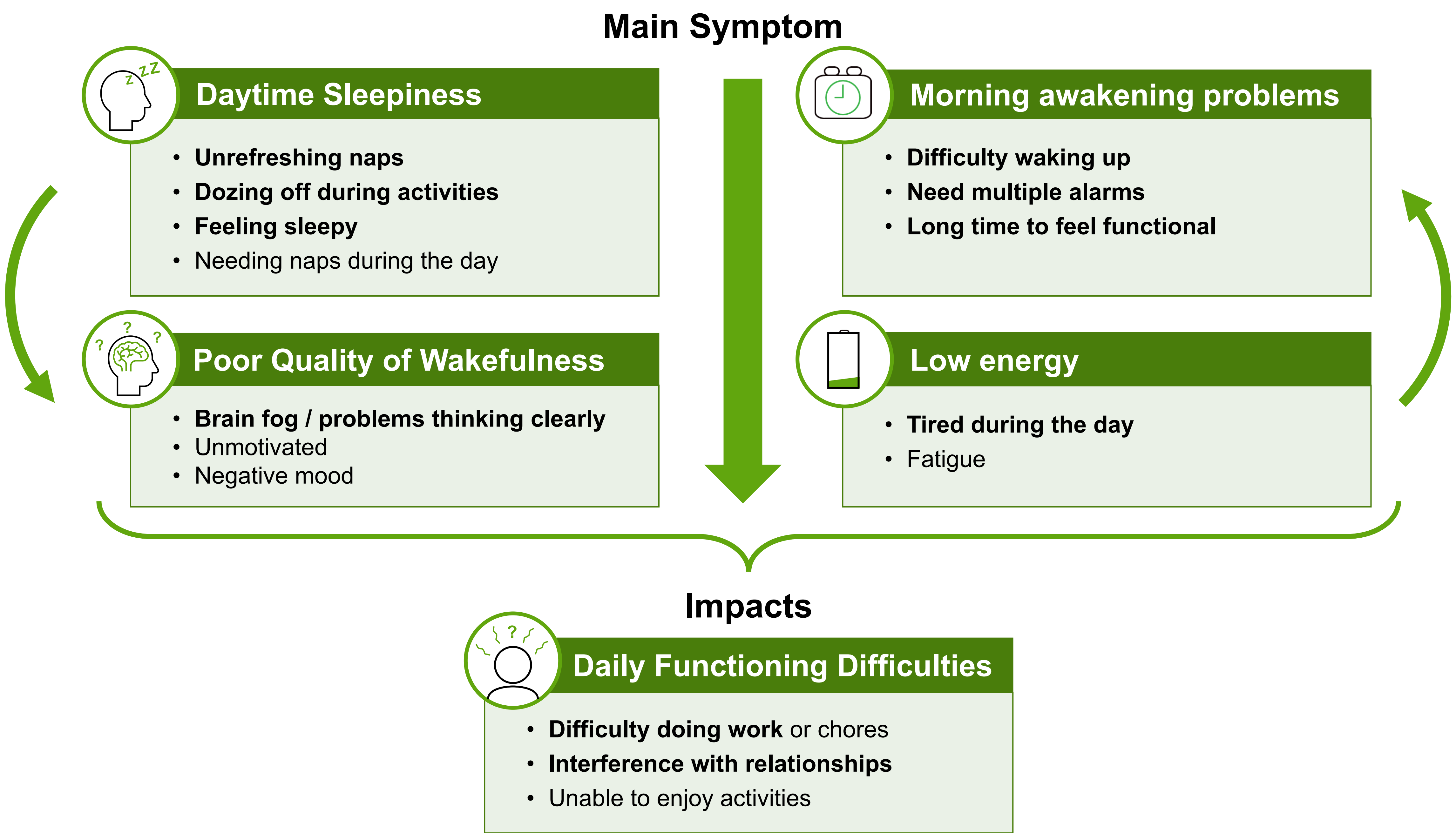[2]Ranges from 0 to 50 with scores ≥ 26 indicating severe symptoms
[3]5-point verbal rating scale ranging from 1 (none) to 5 (very severe)

Figure 1. Elicited and Most Bothersome Symptoms

■ Spontaneously Reported ■ Most Bothersome[1]

DAYTIME SLEEPINESS 98
- Unrefreshing naps 70 | 0
- Falling asleep/dozing off during activities 60 | 23
- Feeling sleepy 60 | 10
- Feeling like they did not have enough sleep 38 | 0
- Needing naps during the day 33 | 0

LOW ENERGY 70
- Tired during the day 55 | 27
- Fatigue 15 | 3

DISTURBANCES TO DAILY LIFE 97
- Difficulty at work 71 | 10
- Interference with relationships 70 | 25
- Unable to enjoy activities 48 | 7
- Not productive at work or home 23 | 22

POOR QUALITY OF WAKEFULNESS 82
- Problems thinking clearly/brain fog 68 | 22
- Not feeling motivated 30 | 12
- Negative mood 23 | 10

MORNING AWAKENING PROBLEMS 73
- Difficulty waking up 70 | 5
- Need multiple alarms 17 | 0

SLEEP INERTIA 70
- Long time to feel functional 67 | 0
- Clumsiness 13 | 0
- Talking nonsense 2

"I was noticing… extreme excessive daytime sleepiness....I was unable to work a job because I could not stay awake for more than about four hours at a time. I spent the majority of my time sleeping."

"Just being tired all the time, regardless of how much sleep I got, and then not really having the energy to do anything else, other than just through the workday."

"I can't do things I want to do…I can't work. My relationships are affected because people don't know how to deal with it. I can't deal with some things that I used to be able [to do]."

"…my husband always describes it as being almost zombie like…I exist in a room, but he can tell that I can't focus on anything really going on and it's hard to keep up in conversation."

"I would go to bed very, very early and I actually ended up having to get like one of those alarm clocks that had a bed shaker… because I could not wake up… to the point where I was getting warnings at work for tardiness."

"I get up, it takes about two hours for me just to get out of the sleep inertia and… get my brain going… and for the pills to kick in that I take when I wake up. Those kind of kick in and the inertia goes away…"

CAPITAL LETTERS indicates main themes
[1]Not mutually exclusive. Some patients indicated that multiple symptoms/impacts were most bothersome.

Figure 2. Conceptual Model of Patient Experience Living with IH

Main Symptom

Daytime Sleepiness
- **Unrefreshing naps**
- **Dozing off during activities**
- **Feeling sleepy**
- Needing naps during the day

Morning awakening problems
- **Difficulty waking up**
- **Need multiple alarms**
- **Long time to feel functional**

Poor Quality of Wakefulness
- **Brain fog / problems thinking clearly**
- Unmotivated
- Negative mood

Low energy
- **Tired during the day**
- Fatigue

Impacts

Daily Functioning Difficulties
- **Difficulty doing work** or chores
- **Interference with relationships**
- Unable to enjoy activities

Bold=reported by > 50% of participants

Results

- The interviewed sample of participants was representative of the overall clinical study population (**Table 1**)
- Almost all participants described difficulty staying awaking or falling asleep during the day (98.3%) that disrupted their daily life (96.7%); including, difficulty at work (71.2%) and interference with relationships/socialization (70.0%) (**Figure 1**)
- Other prevalent symptoms included poor quality of wakefulness (81.6%), morning awakening problems (73.3%), sleep inertia (70.0%) and low energy during the day (66.7%) (**Figure 1**)
- Participants' responses were more varied regarding which of their IH symptoms were most bothersome (**Figure 1**).
  - Disturbances to daily life and having low energy during the day were most frequently reported as most bothersome:
    "Just not having the energy to anything like from household chores to spending time with family, to work, just all of that"
  - Only a few participants reported that sleep inertia and/or problems waking up in the morning were most bothersome primarily because most participants had developed adaptations to lessen the impacts of these symptoms
    "Lots and lots of alarms. Actually, my house gets really annoyed because I set them for every early because I not going to get up. Luckily, I have a very supportive husband that eventually is like…I'm going to roll you out of bed."
- The symptom constellation of daytime sleepiness, poor quality of wakefulness, low energy during the day and difficulty waking up impedes daily activities and maintaining relationships (**Figure 2**)

Conclusions

- Results from these qualitative interviews demonstrate the negative effect the IH symptom constellation of daytime sleepiness, low energy during the day, poor quality of wakefulness and morning awakening problems have on overall functioning in individuals with IH
- The conceptual model delineates the health concepts that are important to individuals with IH. This model can be used to guide the selection of endpoints in clinical trials of new treatments for IH which may demonstrate treatment benefit from the patient perspective

REFERENCES

Arnulf I et al. *Sleep Med Clin.* 2019;14(3):333-350.
Guest G et al. (2012). Applied Thematic Analysis. Sage.

HARMONY BIOSCIENCES