

The impact of insomnia disorder on the night and the day in males and females

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Introduction

- Insomnia disorder, affecting approximately 10% of adults globally, is approximately 50% more prevalent in women than men.¹
- Studies, however, investigating potential sex-related differences in the clinical manifestation of insomnia and its impact on daytime functioning, remain limited.
- The large dataset of patients with insomnia disorder enrolled in the daridorexant phase 3 clinical program² has the potential to help address these gaps through the extensive baseline data collected on objective and subjective measures of nighttime sleep and daytime functioning in both male and female individuals.²

Study objective

To assess the nocturnal and diurnal clinical characteristics of males and females with insomnia disorder.

Methods

- Post hoc analyses by sex (male; female) were performed on data from screened patients from two global, randomized, double-blind, placebo-controlled phase 3 trials (NCT03545191, NCT03575104).²

Screened patients:

- Adults aged ≥18 years
- Insomnia disorder according to DSM-5 criteria³
- Insomnia severity index (ISI) score ≥15
- Self-reported history of ≥30 min to fall asleep, wake time during sleep ≥30 min, and subjective total sleep time [sTST] ≤ 6.5 h on ≥ 3 days/week and for ≥ 3 months.
- This analysis included all subjects screened with data records on selected parameters.
- Subjects with significant sleep comorbidities (obstructive sleep apnea, periodic limb movements, restless legs syndrome, circadian rhythm disorder, rapid-eye-movement sleep behavior disorder or narcolepsy) were excluded.

Assessments during the screening period (7-18 days)

One-night polysomnography (PSG) in the sleep laboratory.

- PSG measurements included: wake after sleep onset (WASO), latency to persistent sleep (LPS), total sleep time (TST), rapid eye movement (REM) quantity, number of awakenings and number/duration of wake bouts.

eDiary, completed daily by the patient, which included:

- Morning and evening visual analog scales (VAS) to assess quality and depth of sleep, morning sleepiness, ability to function and daytime alertness.

VAS scores range: 0-100; higher scores indicate better outcomes.

- Insomnia Daytime Symptoms and Impacts questionnaire (IDSIQ) completed every evening to assess daytime functioning. IDSIQ total score range: 0-140; lower score indicates better daytime functioning.

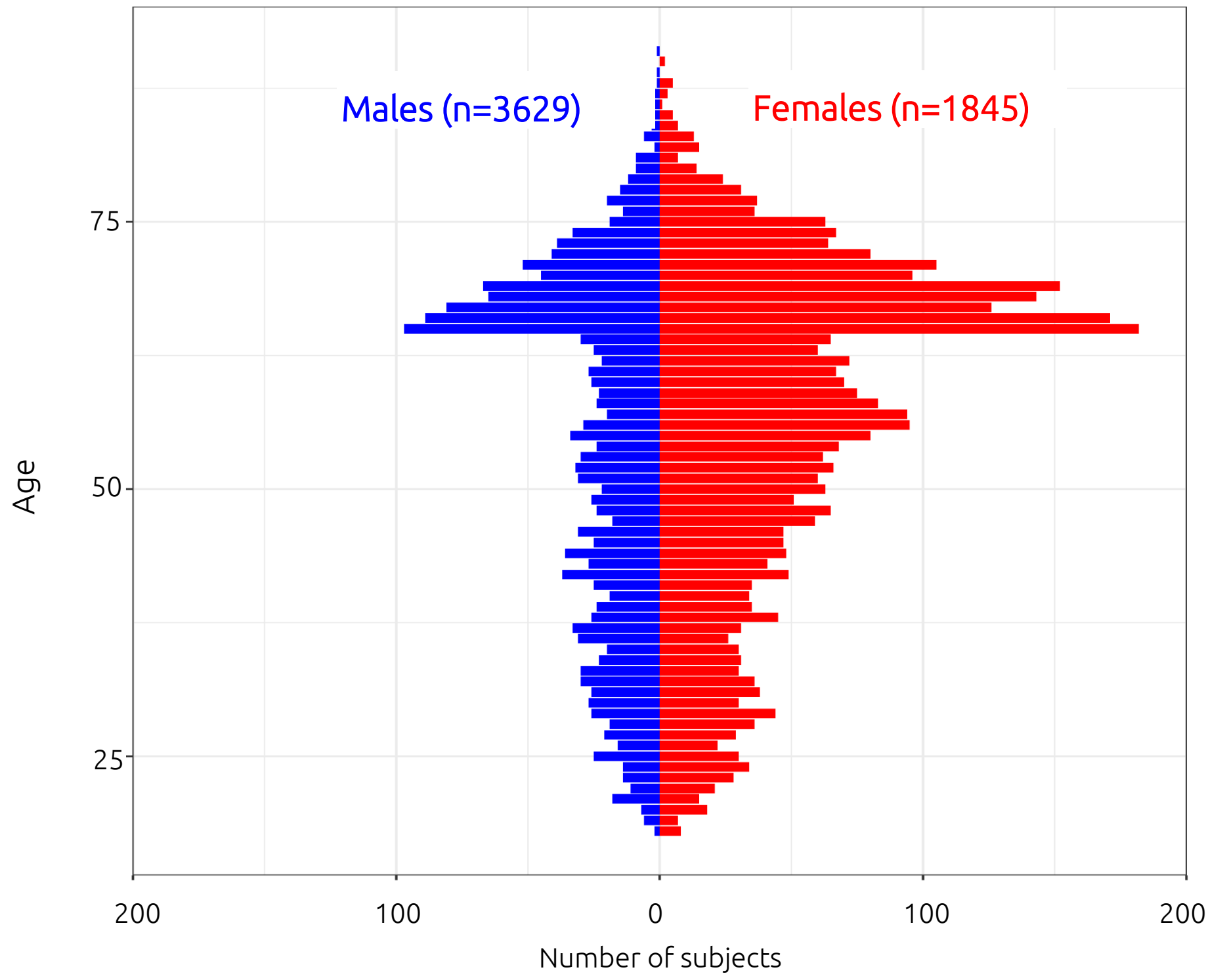
- ISI scale to assess the severity of insomnia. ISI total score range: 0-28; higher scores indicate more severe insomnia.
- Morning questionnaire to assess self-reported TST (sTST), self-reported WASO (sWASO) and self-reported latency to sleep onset (sLSO).

Results

Patients

- 5474 screened subjects were included in the analysis, of which 3629 (66%) were females and 1845 (34%) were males.
- Mean age (range) was 56.1 (18, 90) years and 54.0 (18, 91) years in females and males respectively. The age distribution was similar for both sexes (Figure 1).

Figure 1. Age distribution by sex



Sleep parameters in males and females with insomnia disorder (Table 1)

- At screening, mean ISI score was 19.8 in males and 20.4 in females, indicating moderate/severe insomnia in both subgroups.
- Among objective PSG measures, males vs females had numerically shorter TST (312 vs 324 min) due primarily to a greater WASO (110 vs 99 min), particularly during the last two quarters of the night.
- There were no notable sex-related differences in other PSG-reported sleep parameters.
- No sex-related differences were observed among subjective sleep measures, including sTST and sWASO.
- Subjective vs objective sleep measures indicated a higher sleep misperception in males than females:
 - in males, mean sTST was numerically longer than TST (325 vs 312 min) and sWASO was numerically shorter than WASO (82 vs 110 min).
 - in females, objective and subjective values were relatively similar (e.g. sTST vs TST: 326 vs 324 min).

Daytime functioning in males and females with insomnia disorder (Tables 2)

- No sex-related differences were observed among subjective measures of daytime functioning.
- In both subgroups, IDSIQ total scores indicated moderate/severe daytime impairment. Impairment was observed in all three domains: alert/cognition, mood and sleepiness.
- Mean VAS scores for daytime ability to function and daytime alertness scores also indicated moderate/severe daytime impairment in both males and females. Males and females also both reported moderate/severe morning sleepiness, as reflected by low mean VAS values.

Table 1. Objective and subjective nighttime sleep characteristics of screened subjects

	Males		Females	
	n	Mean (SD)	n	Mean (SD)
Objective (PSG) sleep parameters				
TST, min	1233	312.0 (82.0)	2696	324.4 (80.4)
LPS, min	1225	64.9 (63.3)	2683	62.3 (61.0)
WASO, min	1225	110.2 (58.7)	2683	99.1 (56.7)
WASO per quarter, min				
Quarter 1	1055	11.1 (12.5)	2345	10.8 (12.6)
Quarter 2	1195	26.8 (24.4)	2609	25.7 (24.3)
Quarter 3	1214	31.6 (27.0)	2673	28.6 (27.3)
Quarter 4	1224	43.2 (32.1)	2679	36.4 (28.6)
REM sleep duration, min	1233	58.1 (27.8)	2696	59.6 (27.5)
REM latency, min	1213	149.9 (81.9)	2642	159.5 (83.6)
Number of awakenings	1231	12.9 (5.7)	2690	12.2 (5.3)
Wake bouts	1226		2672	
Total number		31.7 (14.3)		28.9 (12.5)
Mean duration, min		4.7 (11.0)		4.4 (6.8)
Number >6 min ^a		2.9 (2.0)		2.7 (1.9)
Total duration of wake bouts >6 min ^a , min		83.7 (56.9)		75.1 (55.5)
Subjective sleep parameters				
sTST, min	1297	324.9 (66.5)	2765	325.8 (69.0)
sWASO, min	1297	81.5 (67.6)	2765	81.1 (65.2)
sLSO, min	1297	57.1 (43.5)	2765	64.4 (51.9)
VAS depth of sleep (0-100) ^b	1297	38.8 (17.4)	2765	39.7 (17.0)
VAS quality of sleep (0-100) ^b	1297	37.6 (17.0)	2765	39.2 (16.8)
Total ISI score	1625	19.8 (3.8)	3249	20.4 (3.5)

^a >6-min defines a long wake bout³; ^b higher VAS scores indicate better quality and depth of sleep. ISI, insomnia severity index; LPS, latency to persistent sleep; REM, rapid eye movement; sLSO, self-reported latency to sleep onset; sTST, self-reported total sleep time; sWASO, self-reported wake after sleep onset; TST, total sleep time; VAS, visual analog scale; WASO, wake after sleep onset.

Table 2. Subjective daytime characteristics of screened subjects

	Males		Females	
	N	Mean (SD)	N	Mean (SD)
IDSIQ scores				
Total (0-140)	1267	73.0 (23.1)	2728	71.0 (22.2)
Alert/cognition domain (0-60)	1267	31.5 (9.6)	2728	30.7 (9.2)
Mood domain (0-40)	1267	19.4 (8.2)	2728	18.4 (8.1)
Sleepiness domain (0-40)	1267	22.1 (6.6)	2728	21.9 (6.4)
VAS scores (0-100)				
Ability to function	1267	42.3 (18.8)	2728	43.5 (18.4)
Daytime alertness	1267	40.7 (18.9)	2728	42.0 (18.8)
Morning sleepiness	1297	38.9 (17.4)	2765	39.9 (17.6)

IDSIQ, Insomnia Daytime Symptoms and Impacts Questionnaire; VAS, visual analog scale. Lower IDSIQ scores indicate better patient-perceived daytime functioning; Higher VAS scores indicate better scores.

Disclosures

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Conclusions

- These data indicate that insomnia disorder negatively impacts sleep and daytime functioning in males and females with no apparent sex-related differences in subjective parameters.
- Subjective sleep data from females appear to align more closely with objective data than those from males.
- Among objective measures, compared to females, males have shorter TST and longer WASO, mainly in the latter part of the night.