536 Demographic and Clinical Characteristics in Narcolepsy and Idiopathic Hypersomnia at Treatment Initiation

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Introduction

- Narcolepsy and idiopathic hypersomnia are central disorders of hypersomnolence primarily characterized by excessive daytime sleepiness[1]
- The American Academy of Sleep Medicine guidelines for the treatment of central disorders of hypersomnolence, published in 2021, recommend multiple therapies on- and off-label to treat narcolepsy or idiopathic hypersomnia, including sodium oxybate (SXB) and alerting agents (ie, traditional stimulants and wake-promoting agents)[2]
- In addition to these therapies, low-sodium oxybate (LXB) is approved in the United States to treat cataplexy or excessive daytime sleepiness in patients aged ≥7 years with narcolepsy; LXB became the only FDA-approved therapy for idiopathic hypersomnia in adults in 2021[3-7]
- Individuals with narcolepsy or idiopathic hypersomnia have a substantial comorbidity burden, including cardiovascular and cardiometabolic conditions;[8-10] given the potential cardiovascular side effects of the therapies used to treat either condition,[2,11-17] information on clinical characteristics at treatment initiation is necessary

Objective

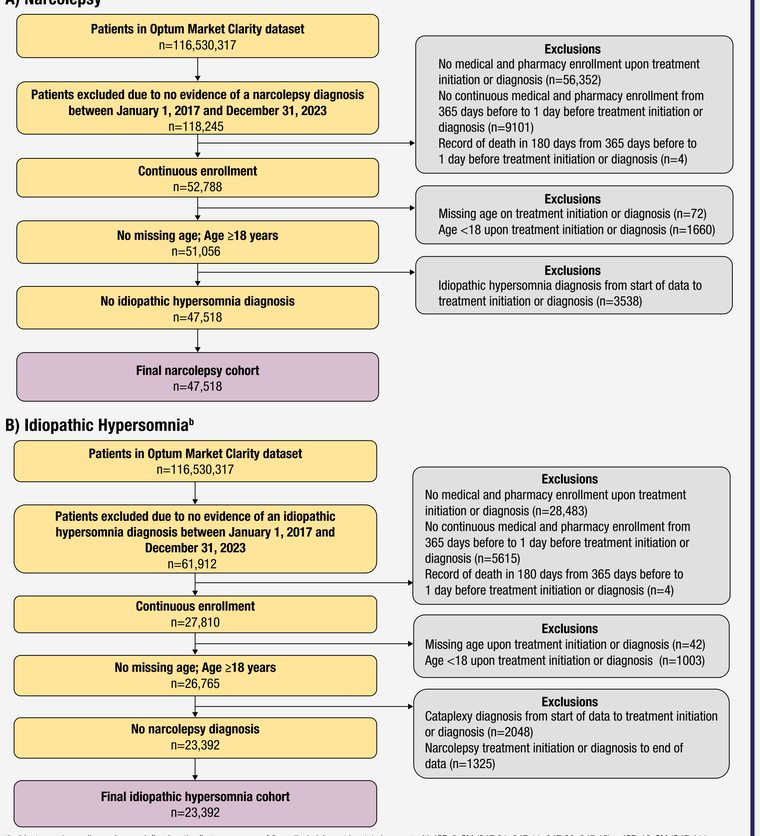
- To assess the demographic and clinical characteristics of people with narcolepsy and people with idiopathic hypersomnia, overall and at treatment initiation

Methods

- This retrospective study utilized the Optum® Market Clarity™ database, a linked electronic health records (EHR) and claims database, to identify people diagnosed with narcolepsy or idiopathic hypersomnia from January 1, 2017 to December 31, 2023
- Narcolepsy diagnosis was defined as the first occurrence of 2 medical claims at least 1 day apart with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) and *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) codes
- Idiopathic hypersomnia diagnosis was defined as any medical claim with ICD-9-CM or ICD-10-CM diagnosis codes
- Demographic and clinical characteristics were assessed for narcolepsy and idiopathic hypersomnia, and among these cohorts at initiation of alerting agents (traditional stimulants and wake-promoting agents) or LXB
  - Additional treatment groups assessed among individuals diagnosed with narcolepsy were:
    - Initiators of SXB
    - Early switchers from SXB to LXB, defined as those who initiated LXB with prior SXB treatment, with a gap between the end of SXB treatment and the start of LXB treatment of ≤30 days
    - Late switchers from SXB to LXB, defined as those who initiated LXB with prior SXB treatment, with a gap between the end of SXB treatment and the start of LXB treatment of >30 days
- Demographic characteristics were assessed at index; comorbidities, defined by diagnosis claims (hypertension: diagnosis or antihypertensive medication use), were assessed in the 365-day period before index
- Data were analyzed descriptively

Results

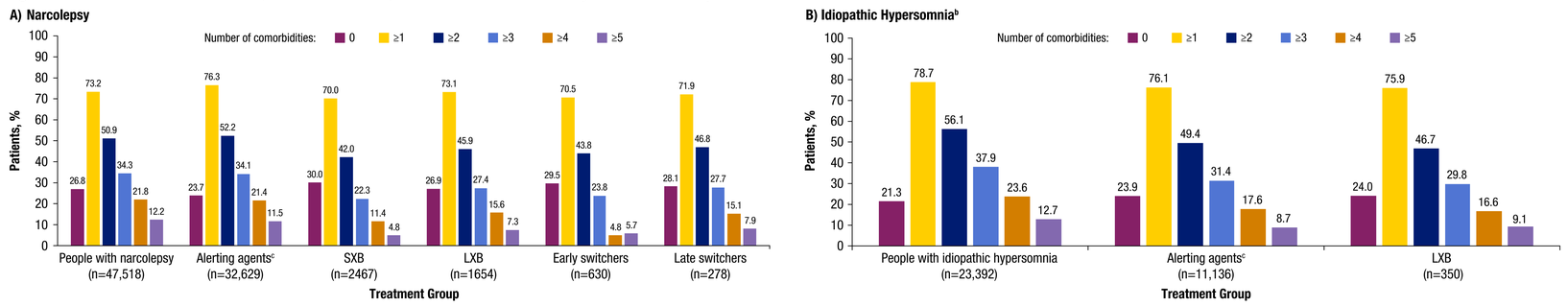
Figure 1. Population Attrition



[a]Incident narcolepsy diagnosis was defined as the first occurrence of 2 medical claims at least 1 day apart with ICD-9-CM (347.01, 347.11, 347.00, 347.10) or ICD-10-CM (G47.411, G47.421, G47.419, G47.429) diagnosis codes in any position. Patients entered the cohort on the date of the second of the 2 medical claims. [b]Idiopathic hypersomnia diagnosis was defined as any medical claim with ICD-9-CM (327.11, 327.12) or ICD-10-CM (G47.11, G47.12) diagnosis codes in any position.
ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; ICD-10-CM, *International Classification of Diseases, Tenth Revision, Clinical Modification*.

- Overall, 47,518 people with narcolepsy and 23,392 with idiopathic hypersomnia were identified

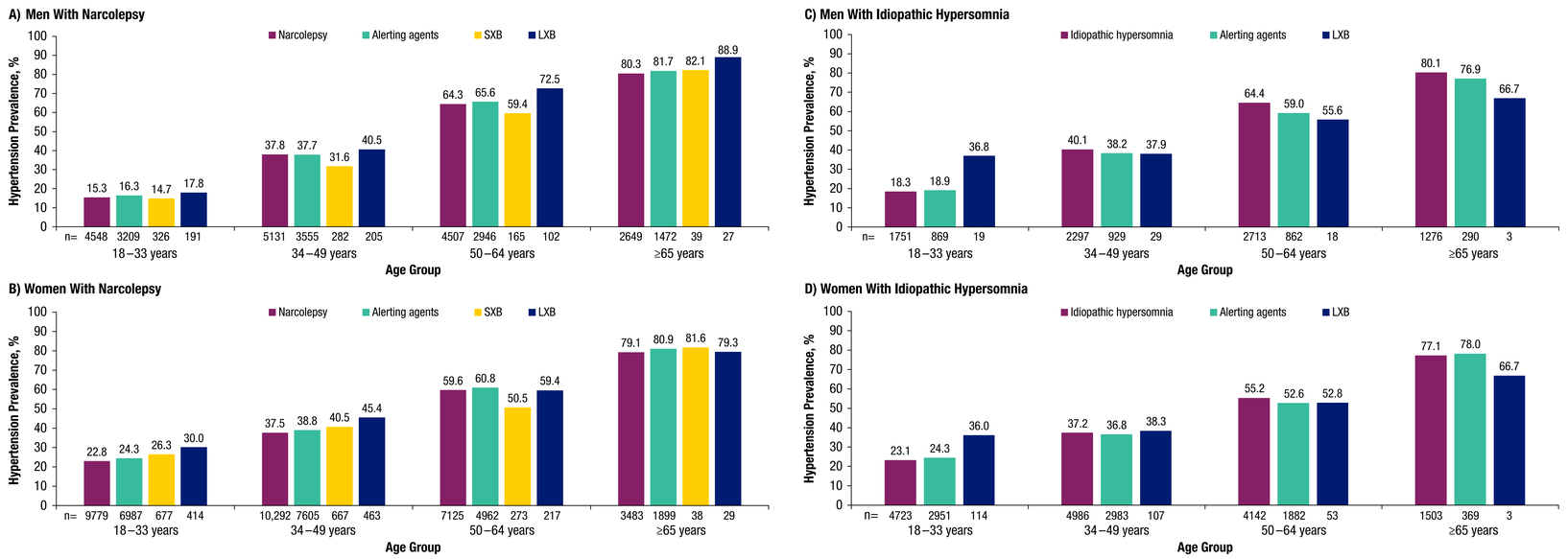
Figure 2. Number of Cardiovascular, Cardiometabolic, or Renal Comorbidities[a] by Treatment Group



[a]Defined as coronary revascularization, diabetes, cardiovascular disease, hyperlipidemia, hypertension, major adverse cardiovascular event, obesity, sleep apnea, or renal impairment. [b]Because SXB is not indicated to treat idiopathic hypersomnia, the proportion of people with idiopathic hypersomnia treated with SXB or switching from SXB to LXB is not presented. [c]Alerting agents were defined as wake-promoting agents (ie, armodafinil, modafinil, solriamfetol, pitolisant) or stimulants (ie, amphetamines, methylphenidate).
LXB, low-sodium oxybate; SXB, sodium oxybate.

- Across narcolepsy and idiopathic hypersomnia cohorts, overall, and across treatment groups, ≥70% of people had at least 1 cardiovascular, cardiometabolic, or renal comorbidity
- About a quarter to a third of people with narcolepsy and idiopathic hypersomnia across all treatment groups had at least 3 cardiovascular, cardiometabolic, or renal comorbidities (range: 22.3%–37.9%)

Figure 3. Hypertension Prevalence Stratified by Age and Sex



LXB, low-sodium oxybate; SXB, sodium oxybate.

- The prevalence of hypertension in women between the ages of 18 to 33 years with narcolepsy or idiopathic hypersomnia was approximately 23%; hypertension prevalence was 30% and 36% for women aged 18 to 33 years with narcolepsy and idiopathic hypersomnia, respectively, who initiated LXB
  - Publicly available National Health and Nutrition Examination Survey (NHANES) data indicate that the prevalence of hypertension is 9.7% among women in the overall population between the ages of 18 to 33 years[18]

Table 1. Demographic and Clinical Characteristics

A) Narcolepsy

	People With Narcolepsy	Alerting Agents	SXB	LXB	Early Switchers	Late Switchers
	n=47,518	n= 32,629	n=2467	n=1654	n=630	n=278
Demographic characteristics (assessed at index)						
Age, mean (SD)	44.48 (16.51)	43.44 (15.76)	38.47 (13.05)	39.57 (13.20)	41.15 (13.60)	41.00 (12.13)
Female, n (%)	30,679 (64.6)	21,449 (65.7)	1658 (67.2)	1132 (68.4)	421 (66.8)	196 (70.5)
Comorbidities (assessed during 365-day period before index), n (%)						
Anxiety disorders	18,810 (39.6)	14,094 (43.2)	1040 (42.2)	744 (45.0)	270 (42.9)	121 (43.5)
Coronary revascularization	88 (0.2)	52 (0.2)	2 (0.1)	0	0	0
Diabetes	12,649 (26.6)	8321 (25.5)	433 (17.6)	333 (20.1)	113 (17.9)	61 (21.9)
Headache/migraine	12,445 (26.2)	8838 (27.1)	662 (26.8)	460 (27.8)	146 (23.2)	74 (26.6)
Cardiovascular disease	8202 (17.3)	4956 (15.2)	237 (9.6)	180 (10.9)	63 (10.0)	32 (11.5)
Hyperlipidemia	15,548 (32.7)	10,379 (31.8)	501 (20.3)	380 (23.0)	134 (21.3)	68 (24.5)
Hypertension diagnosis or antihypertensive drug use	20,763 (43.7)	14,195 (43.5)	885 (35.9)	708 (42.8)	278 (44.1)	128 (46.0)
Hyperuricemia	137 (0.3)	75 (0.2)	1 (0.0)	2 (0.1)	1 (0.2)	0
Major adverse cardiovascular event	2590 (5.5)	1378 (4.2)	32 (1.3)	31 (1.9)	9 (1.4)	4 (1.4)
Mood disorders	18,742 (39.4)	13,995 (42.9)	1008 (40.9)	664 (40.1)	241 (38.3)	106 (38.1)
Obesity	15,630 (32.9)	11,267 (34.5)	614 (24.9)	485 (29.3)	164 (26.0)	76 (27.3)
Periodic limb movement	1356 (2.9)	1398 (4.3)	161 (6.5)	82 (5.0)	19 (3.0)	10 (3.6)
Pulmonary fibrosis and interstitial lung disease	477 (1.0)	289 (0.9)	12 (0.5)	6 (0.4)	1 (0.2)	2 (0.7)
Rapid eye movement behavior disorder	401 (0.8)	462 (1.4)	47 (1.9)	20 (1.2)	7 (1.1)	4 (1.4)
Restless leg syndrome	3248 (6.8)	2713 (8.3)	233 (9.4)	154 (9.3)	59 (9.4)	22 (7.9)
Renal impairment	1639 (3.4)	933 (2.9)	28 (1.1)	25 (1.5)	13 (2.1)	5 (1.8)
Sleep apnea	18,014 (37.9)	14,445 (44.3)	1035 (42.0)	699 (42.3)	230 (36.5)	105 (37.8)

B) Idiopathic Hypersomnia

	People With Idiopathic Hypersomnia	Alerting Agents	LXB
	n=23,392	n=11,136	n=350
Demographic characteristics (assessed at index)			
Age, mean (SD)	45.03 (15.85)	41.23 (14.19)	39.00 (12.12)
Female, n (%)	15,354 (65.6)	8185 (73.5)	280 (80.0)
Comorbidities (assessed during 365-day period before index), n (%)			
Anxiety disorders	9631 (41.2)	5369 (48.2)	191 (54.6)
Coronary revascularization	61 (0.3)	4 (0.0)	0
Diabetes	6529 (27.9)	2531 (22.7)	77 (22.0)
Headache/migraine	6384 (27.3)	3279 (29.4)	132 (37.7)
Cardiovascular disease	3879 (16.6)	1266 (11.4)	49 (14.0)
Hyperlipidemia	8343 (35.7)	3094 (27.8)	89 (25.4)
Hypertension diagnosis or antihypertensive drug use	10,401 (44.5)	4344 (39.0)	144 (41.1)
Hyperuricemia	70 (0.3)	26 (0.2)	0
Mood disorders	8921 (38.1)	5055 (45.4)	167 (47.7)
Obesity	8740 (37.4)	3947 (35.4)	104 (29.7)
Periodic limb movement	1113 (4.8)	718 (6.4)	24 (6.9)
Pulmonary fibrosis and interstitial lung disease	256 (1.1)	82 (0.7)	4 (1.1)
Rapid eye movement behavior disorder	211 (0.9)	119 (1.1)	7 (2.0)
Restless leg syndrome	1457 (6.2)	887 (8.0)	25 (7.1)
Renal impairment	740 (3.2)	196 (1.8)	2 (0.6)
Sleep apnea	10,840 (46.3)	5176 (46.5)	158 (45.1)

LXB; low-sodium oxybate; SD, standard deviation; SXB, sodium oxybate.

- People with narcolepsy had a mean (standard deviation [SD]) age of 44.48 (16.51) years and people with idiopathic hypersomnia had a mean (SD) age of 45.03 (15.85) years; the majority were female (narcolepsy, 65%; idiopathic hypersomnia, 66%)
- Among people with narcolepsy initiating an alerting agent (n=32,629), 44% had hypertension, 35% had obesity, and 44% had sleep apnea
- Among people with narcolepsy initiating SXB (n=2467), 36% had hypertension, 25% had obesity, and 42% had sleep apnea
- Among people with narcolepsy initiating LXB (n=1654), 43% had hypertension, 29% had obesity, and 42% had sleep apnea
- Among people with idiopathic hypersomnia initiating an alerting agent (n=11,136), 39% had hypertension, 35% had obesity, and 47% had sleep apnea
- Among people with idiopathic hypersomnia initiating LXB (n=350), 41% had hypertension, 30% had obesity, and 45% had sleep apnea

Conclusions

- The comorbidity burden experienced by people with narcolepsy or idiopathic hypersomnia is consistent and substantial across demographic and treatment groups at treatment initiation
- The results of this analysis demonstrate that ≥70% of people with narcolepsy or idiopathic hypersomnia have at least 1 cardiovascular, cardiometabolic, and renal comorbidity at alerting agent, SXB, or LXB initiation
- The observed prevalence of hypertension in young women with narcolepsy or idiopathic hypersomnia is higher than that observed in NHANES data for the same demographic group in the overall US population
- Limitations of this analysis include the cross-sectional nature of the design, use of secondary claims data, and potential coding misclassification of comorbidities
- Comorbidities should be considered when selecting treatments to mitigate excess sodium intake and associated cardiovascular and cardiometabolic risk

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