Sleep Medicine 139 (2026) 108690



Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep





Clinical and socioeconomic burden among people with narcolepsy or idiopathic hypersomnia: A retrospective cohort analysis of the Danish National Patient Registry

Poul Jørgen Jennum [a,*], Michael Ibsen [b], Sam Mettam [c], Sarah C. Markt [d], Douglas S. Fuller [d], Jessica K. Alexander [d], Rikke Ibsen [b], Jakob Kjellberg [e], Caroleen Drachenberg [d]

[a] Danish Center for Sleep Medicine, Department of Clinical Neurophysiology, Faculty of Health Sciences, University of Copenhagen and Department of Health Technology, Technical University of Denmark, Rigshospitalet, Denmark
[b] i2minds, Noerrebrogade 18B,1, 8000, Aarhus C, Denmark
[c] Jazz Pharmaceuticals, Business Park, Spires House, 5700 John Smith Drive, Oxford Business Park, South, Oxford, OX4 2RW, UK
[d] Jazz Pharmaceuticals, 3170 Porter Drive, Palo Alto, CA, 94304, USA
[e] Danish National Institute for Local and Regional Government Research, Købmagergade 22, 1150, Copenhagen, Denmark

ARTICLE INFO

JEL classification:
Narcolepsy
Idiopathic hypersomnia
Hypersomnolence
Statistics
Sleep and medical disorders

Keywords:
Narcolepsy
Idiopathic hypersomnia
Central disorders of hypersomnolence
Comorbidity
Unemployment
Income
Healthcare costs

ABSTRACT

Objective/background: To assess the clinical and socioeconomic burden of narcolepsy and idiopathic hypersomnia (IH) in Denmark.
Patients/methods: This retrospective cohort study using Danish National Patient Registry data included individuals diagnosed with narcolepsy or IH (1/1/2005–12/31/2017). Individuals with narcolepsy were matched 1:4 with controls without narcolepsy; matching was repeated for individuals with IH. Comorbidities, employment, income, and healthcare costs were assessed in the 3 years before and after diagnosis using logistic regression and generalized linear models.
Results: 1183 individuals with narcolepsy (4728 controls) and 1801 individuals with IH (7204 controls) were assessed. Before diagnosis, individuals with narcolepsy had higher odds (odds ratio [OR]; 95 % confidence interval [CI]) of having nervous system (7.92 [6.46, 9.71]) or circulatory system diseases (2.45 [1.95, 3.07]) than controls, in addition to higher unemployment (2.30 [1.79, 2.96]). Individuals with narcolepsy had lower mean income before (€22,076 vs €26,538) and after (€21,786 vs €27,090) diagnosis and higher mean healthcare costs before (€4547 vs €1909) and after (€7411 vs €2178) diagnosis. Before diagnosis, individuals with IH had higher odds (OR [95 % CI]) of having nervous system (9.37 [7.93, 11.08]) or circulatory system diseases (1.80 [1.49, 2.16]) than controls, in addition to higher unemployment (1.73 [1.42, 2.10]). Individuals with IH had lower mean income before (€31,947 vs €34,503) and after (€30,262 vs €35,139) diagnosis and higher mean healthcare costs before (€4050 vs €1840) and after (€5124 vs €2106) diagnosis.
Conclusions: Danish individuals with narcolepsy or IH had a greater clinical and socioeconomic burden than controls.

1. Introduction

Narcolepsy is a central disorder of hypersomnolence primarily characterized by excessive daytime sleepiness (EDS); people with narcolepsy often experience cataplexy (present in narcolepsy type 1 [NT1] but not narcolepsy type 2 [NT2]), disrupted nighttime sleep, sleep-related hallucinations, and sleep paralysis [1]. Idiopathic hypersomnia, another central disorder of hypersomnolence, is also primarily characterized by EDS but is distinct from narcolepsy; cataplexy is absent, and the symptoms of idiopathic hypersomnia are not adequately explained by another disorder. Other symptoms of idiopathic hypersomnia include severe sleep inertia, long and unrefreshing naps, prolonged nighttime sleep, autonomic complaints, and cognitive impairment [1].

* Corresponding author. Nordre Ringvej 57, 2600 Glostrup, Denmark.
E-mail addresses: poul.joergen.jennum@regionh.dk (P.J. Jennum), michael@i2minds.dk (M. Ibsen), sam.mettam@jazzpharma.com (S. Mettam), sarah.markt@jazzpharma.com (S.C. Markt), doug.fuller@jazzpharma.com (D.S. Fuller), jessica.alexander@jazzpharma.com (J.K. Alexander), rikke@i2minds.dk (R. Ibsen), jakj@vive.dk (J. Kjellberg), caroleen.drachenberg@jazzpharma.com (C. Drachenberg).

https://doi.org/10.1016/j.sleep.2025.108690
Received 8 July 2025; Received in revised form 30 October 2025; Accepted 30 November 2025
Available online 2 December 2025
1389-9457/© 2025 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Abbreviations used in manuscript

BEF	Population Statistics Register (Befolkning)
CI	Confidence Interval
DNPR	Danish National Patient Registry
EDS	Excessive Daytime Sleepiness
IH	Idiopathic Hypersomnia
ICD-10	*International Classification of Diseases, Tenth Revision*
NT1	Narcolepsy Type 1
NT2	Narcolepsy Type 2
OR	Odds Ratio
SD	Standard Deviation
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
WHO	World Health Organization

Several US- and European-based studies have described the humanistic, clinical, and socioeconomic burden associated with narcolepsy. Previous studies have demonstrated that individuals with narcolepsy experience a wide range of medical comorbidities [2–7] and have lower health-related quality of life [8], higher healthcare utilization, and higher medical costs compared with matched controls [9–11]. Prior studies using Danish National Patient Registry (DNPR) data found that, compared with matched controls, individuals with narcolepsy had higher morbidity across a wide range of domains, including metabolic, psychiatric, neurological, and other diseases [6,12], as well as increased socioeconomic consequences, including lower income and increased healthcare utilization and costs [11,13].

While research assessing the burden experienced by individuals with idiopathic hypersomnia is limited, the clinical and socioeconomic burden observed is comparable to that experienced by individuals with narcolepsy; compared with controls, individuals with narcolepsy or idiopathic hypersomnia experience substantial symptom burden [14], lower health-related quality of life [15], significantly higher prevalence of a wide range of comorbid conditions [16–18], and greater healthcare resource utilization and medical costs [19]. Other studies using the DNPR have investigated the health and socioeconomic consequences of hypersomnia; however, these studies were not specific to an idiopathic hypersomnia diagnosis [20,21].

The objectives of this study were to assess the clinical and socioeconomic burden, including comorbidity prevalence, employment, income, and healthcare costs from the healthcare system perspective, among individuals with narcolepsy or idiopathic hypersomnia, comparing each group with matched controls having neither narcolepsy nor idiopathic hypersomnia in Denmark. This analysis builds on prior literature by aiming to evaluate the clinical and socioeconomic burden experienced by individuals with narcolepsy and idiopathic hypersomnia, to determine whether this burden persists in Denmark, and to compare the higher burden observed in US-based studies with the burden experienced by individuals in Denmark.

2. Methods

2.1. Study design and data source

This study's methods and results follow Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [22]. The current study was approved by Statistics Denmark (project number 706775) in compliance with Danish data protection laws and ethical standards. The DNPR provides longitudinal monitoring of inpatient, outpatient, and emergency department health service utilization in Denmark and thereby constitutes a valuable research database covering diseases, treatments, and diagnostic examinations [23]. This national retrospective cohort study used de-identified DNPR data linked to other Danish registries containing longitudinal sociodemographic information—including the Civil Registration System, the National Health Insurance Service, the Danish National Prescription Register, the Population Statistics Register (BEF), and other Statistics Denmark registers containing data on the total Danish population [23]. The Civil Registration System uses a unique personal identification number that is assigned to all citizens in Denmark, which allows for individual linkage across all registers used in this study. Since 1978, the DNPR has included data on all individuals covered under Denmark's universal healthcare system; it contains information on all hospitalized patients from 1977 onward, and all outpatient, emergency department, and psychiatric visits from 1994 onward, though the DNPR's merge with the Psychiatric Central Research Register was not completed until 1995. DNPR data are updated continuously, and its content has changed over time [23]. From 2002 onward, the DNPR also has contained information on inpatient and outpatient tariffs from the diagnosis-related groups of diagnoses and procedures used to calculate healthcare costs.

2.2. Study population

To be included in this analysis, individuals were required to have a record of contact with a hospital with a diagnosis of narcolepsy (*International Classification of Diseases, Tenth Revision* [ICD-10], G47.4) or idiopathic hypersomnia (ICD-10, G47.1) between January 1, 2005, and December 31, 2017. The narcolepsy and idiopathic hypersomnia cohorts were analyzed separately. Because of uncertainty regarding correct

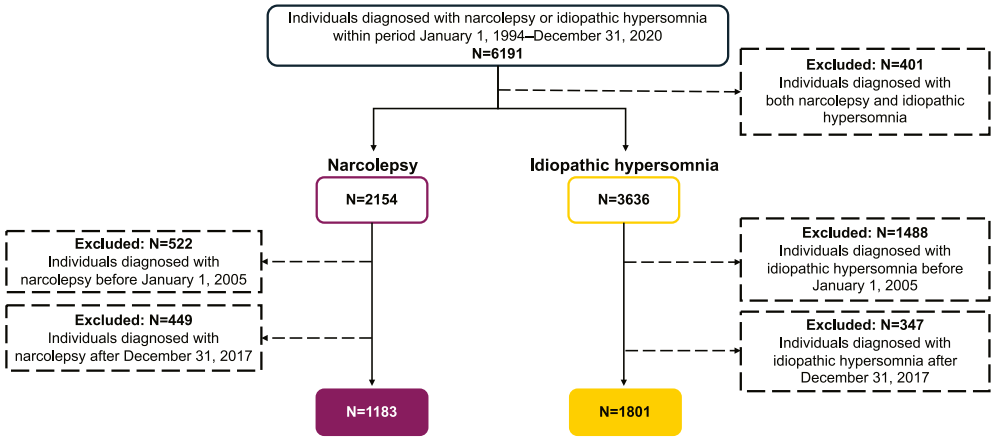


Fig. 1. Participant flow.

Table 1
Cohort characteristics at index date.[a]

	Narcolepsy		Idiopathic Hypersomnia	
	Individuals (N = 1183)	Matched Controls (N = 4728)	Individuals (N = 1801)	Matched Controls (N = 7204)
Sex, n (%)				
Female	642 (54.3)	2564 (54.2)	905 (50.2)	3620 (50.2)
Male	541 (45.7)	2164 (45.8)	896 (49.8)	3584 (49.8)
Age, years, mean (SD)	38 (20)	38 (20)	41 (15)	41 (15)
Age group, n (%)				
<18 years	168 (14.2)	672 (14.2)	74 (4.1)	296 (4.1)
18–29 years	362 (30.6)	1446 (30.6)	424 (23.5)	1696 (23.5)
30–39 years	191 (16.1)	764 (16.2)	388 (21.5)	1552 (21.5)
40–49 years	138 (11.7)	552 (11.7)	390 (21.7)	1560 (21.7)
50–64 years	162 (13.7)	648 (13.7)	401 (22.3)	1604 (22.3)
≥65 years	162 (13.7)	646 (13.7)	124 (6.9)	496 (6.9)
Marital status, n (%)				
Married/cohabiting	466 (39.4)	1860 (39.3)	1069 (59.4)	4276 (59.4)
Living alone	717 (60.6)	2868 (60.7)	732 (40.6)	2928 (40.6)
Education, n (%)[b]				
Primary	397 (33.6)	1577 (33.4)	505 (28.0)	1964 (27.3)
Secondary	135 (11.4)	583 (12.3)	166 (9.2)	714 (9.9)
Vocational	295 (24.9)	1160 (24.5)	621 (34.5)	2377 (33.0)
College, short	43 (3.6)	163 (3.4)	95 (5.3)	314 (4.4)
College, medium	149 (12.6)	560 (11.8)	274 (15.2)	1055 (14.6)
College, long + PhD	66 (5.6)	284 (6.0)	91 (5.1)	528 (7.3)
Unknown	98 (8.3)	401 (8.5)	49 (2.7)	252 (3.5)
Employment status, n (%)[c]				
Employed	450 (38.0)	2157 (45.6)	1076 (59.7)	4618 (64.1)
Education	173 (14.6)	784 (16.6)	199 (11.0)	843 (11.7)
Unemployed	115 (9.7)	256 (5.4)	171 (9.5)	429 (6.0)
Sick pay (publicly funded)	38 (3.2)	55 (1.2)	40 (2.2)	97 (1.3)
Disability pension	79 (6.7)	163 (3.4)	116 (6.4)	398 (5.5)
Early retirement	11 (0.9)	51 (1.1)	24 (1.3)	139 (1.9)
Age pension	149 (12.6)	586 (12.4)	101 (5.6)	380 (5.3)
Child <18 years of age	168 (14.2)	672 (14.2)	74 (4.1)	296 (4.1)

[a] Characteristics were balanced between groups after matching on age, sex, marital status, and municipality (residence) at index year.
[b] Short and medium college education cycles typically have a duration of 1–2 and 2–4 years, respectively, and build upon an upper secondary education. Long-cycle college education lasts 5 years in total and is typically divided into a 3-year bachelor's degree program and a 2-year master's degree program.
[c] Employment status based on Statistics Denmark variable SOCIO13 for labor market affiliation status in index calendar year; variable based on information regarding most important source of income or employment for each person in year. https://www.dst.dk/da/Statistik/dokumentation/Times/personindkomst/socio13.
SD, standard deviation.

diagnoses, individuals diagnosed with both narcolepsy and idiopathic hypersomnia during the period 1994–2020 were excluded from this analysis. Additionally, individuals with either diagnosis before January 1, 2005, were excluded to ensure the cohorts were naive of a diagnosis for narcolepsy or idiopathic hypersomnia. Only individuals between 18 and 64 years of age were included in models assessing income from employment.

Individuals with narcolepsy or idiopathic hypersomnia were exact matched 1:4 with controls who had neither narcolepsy nor idiopathic hypersomnia (hereafter referred to as *matched controls*) based on key demographic factors: age, sex, marital status, and geographic location/municipality at time of diagnosis. Each matched control was randomly selected from the total Danish population using the BEF. The linked DNPR was then used to exclude those with narcolepsy or idiopathic hypersomnia from the control pool. There was no overlap between the control cohorts (ie, inclusion in one disqualified inclusion in the other).

For individuals with narcolepsy or idiopathic hypersomnia, the diagnosis date (index date) was defined as the date of first hospital contact with a primary or secondary diagnosis of narcolepsy or idiopathic hypersomnia during the period 2005 to 2017 (inclusion period). The matched control's index dates were matched to the diagnosis date of their counterparts with narcolepsy or idiopathic hypersomnia.

2.3. Outcomes

The outcomes assessed in this analysis in the 3 years before and 3 years after diagnosis included comorbidities represented by World Health Organization (WHO) categories [24]; employment status; income from employment; and direct total healthcare costs. Detailed comorbidity conditions assessed in the 3-year pre-index period included hypertension (diagnosis or medication for hypertension), cardiovascular disease (diagnosis other than hypertension), type 2 diabetes (diagnosis or medication for type 2 diabetes), high cholesterol (diagnosis or medication for high cholesterol), obesity (diagnosis), mental disorder (diagnosis or medication for a mental disorder), and sleep disorder (diagnosis other than narcolepsy or idiopathic hypersomnia).

Employment status was derived from the Statistics Denmark variable SOCIO13, which is based on information about the most important income source for the person in the year; data were available only for individuals between 18 and 64 years of age. Income from employment was calculated from Danish Income Register data. Healthcare costs were calculated from data from the DNPR (inpatient admissions, outpatient services, psychiatric services), the Danish National Prescription Registry (medication costs), and the Danish Health Insurance Registry (costs of health services within the Danish public health insurance system). Rate tariffs, or national averages of hospital operating costs within each diagnosis-related group, were used to calculate hospital costs in euros (€) using the fixed exchange rate of 7.45 Danish kroner to €1. Income and costs were weighted by person-year and reported in 2020 prices using the Statistics Denmark consumer price index. No additional adjustments were applied to address secular trends over the 12-year diagnosis window, as matching controls to individuals with either condition upon index was considered sufficient for temporal comparability.

WHO comorbidity category, employment, income, and cost

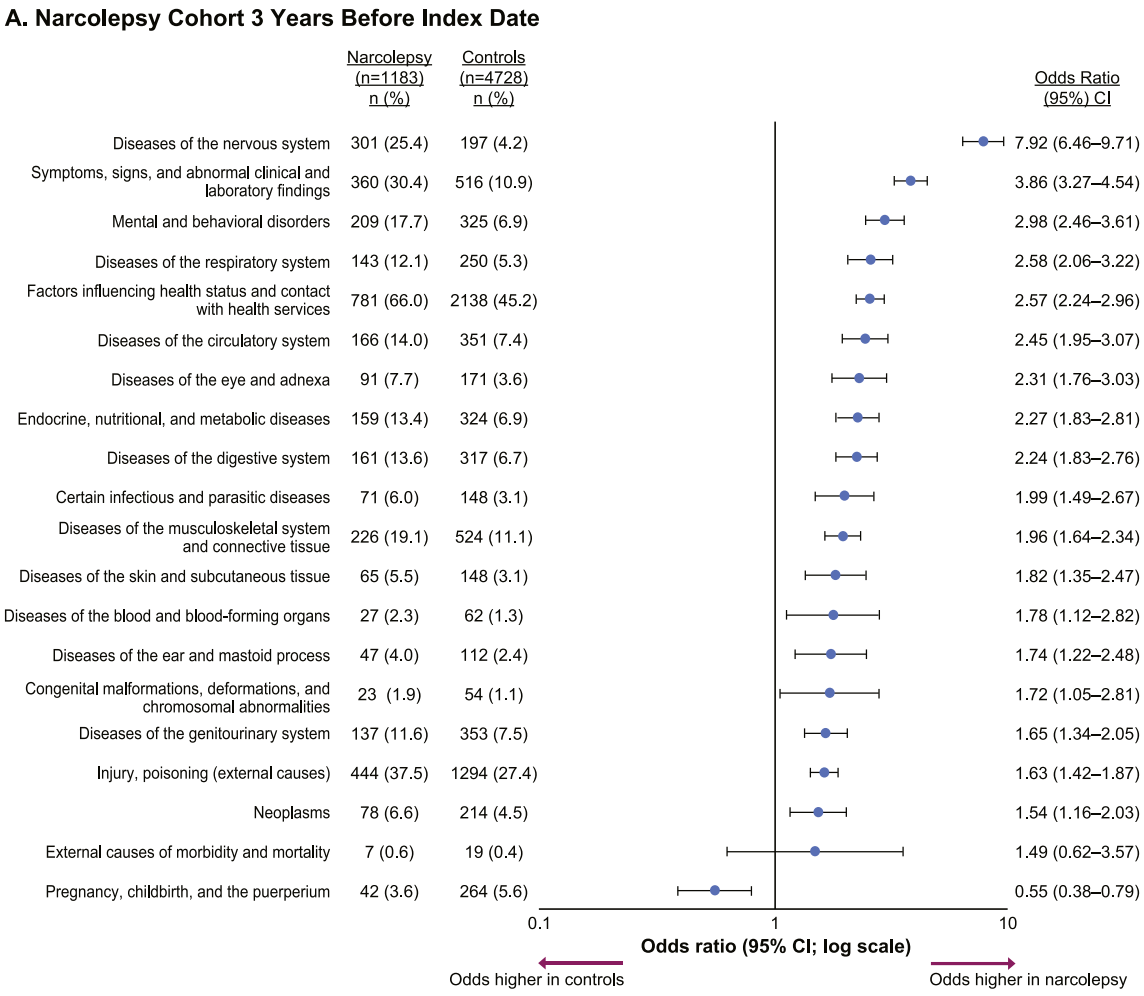


Fig. 2. Odds ratios and 95 % confidence intervals of WHO clinical comorbidities before and after diagnosis.[a]
[a]Comorbidities by World Health Organization classification groups based on *International Classification of Diseases, Tenth Revision* codes. While there are 21 World Health Organization classification groups, the category "Certain conditions originating in the perinatal period" was not assessed in this analysis.
CI, confidence interval; WHO, World Health Organization.

outcomes were assessed by year over 6 years (3 years before and after a diagnosis of narcolepsy or idiopathic hypersomnia) or until death or emigration from Denmark. The 3-year period before and after diagnosis was based on cost and income data availability from January 1, 2002, to December 31, 2019, and was used to ensure a sufficiently large population for robust analysis.

2.4. Statistical analysis

For individuals with narcolepsy or idiopathic hypersomnia and their matched controls, odds ratios (ORs) for having comorbidities were estimated separately for the 3 years before and the 3 years after diagnosis. The ORs and corresponding 95 % confidence intervals (CIs) of having a comorbidity in individuals with narcolepsy or idiopathic hypersomnia, compared with matched controls, were estimated using conditional logistic regression models. A 2-step generalized linear model regression with a gamma distribution and log link function was used to assess significant differences in income and health costs for individuals with narcolepsy or idiopathic hypersomnia and matched controls. This 2-part specification was implemented to address skewness and zero mass [25].This model accounted for individuals who died during the year by incorporating weight for person-years. Multinomial logistic regression models were used to assess employment, adjusting for education level. *P* values were not adjusted for multiplicity.

3. Results

3.1. Study population

In total, 1183 individuals with narcolepsy (with 4728 matched controls) and 1801 individuals with idiopathic hypersomnia (with 7204 matched controls) were identified for analysis (Fig. 1). The narcolepsy cohort was 54.3 % female, had a mean age of 38 years, and 38.0 % were employed; the idiopathic hypersomnia cohort was 50.2 % female, had a mean age of 41 years, and 59.7 % were employed (Table 1).

3.2. Comorbidities

The WHO clinical comorbidity categories with the highest ORs between individuals with narcolepsy and matched controls before diagnosis were diseases of the nervous system (excluding narcolepsy and idiopathic hypersomnia, OR [95 % CI]: 7.92 [6.46, 9.71]); symptoms, signs, and abnormal clinical and laboratory findings (3.86 [3.27, 4.54]); mental and behavioral disorders (2.98 [2.46, 3.61]); diseases of the respiratory system (2.58 [2.06, 3.22]); and factors influencing health status and contact with health services (2.57 [2.24, 2.96]). The OR (95 % CI) for diseases of the circulatory system was 2.45 (1.95, 3.07) (Fig. 2A).

Before diagnosis, individuals with narcolepsy had higher odds of all assessed comorbid conditions compared with matched controls,

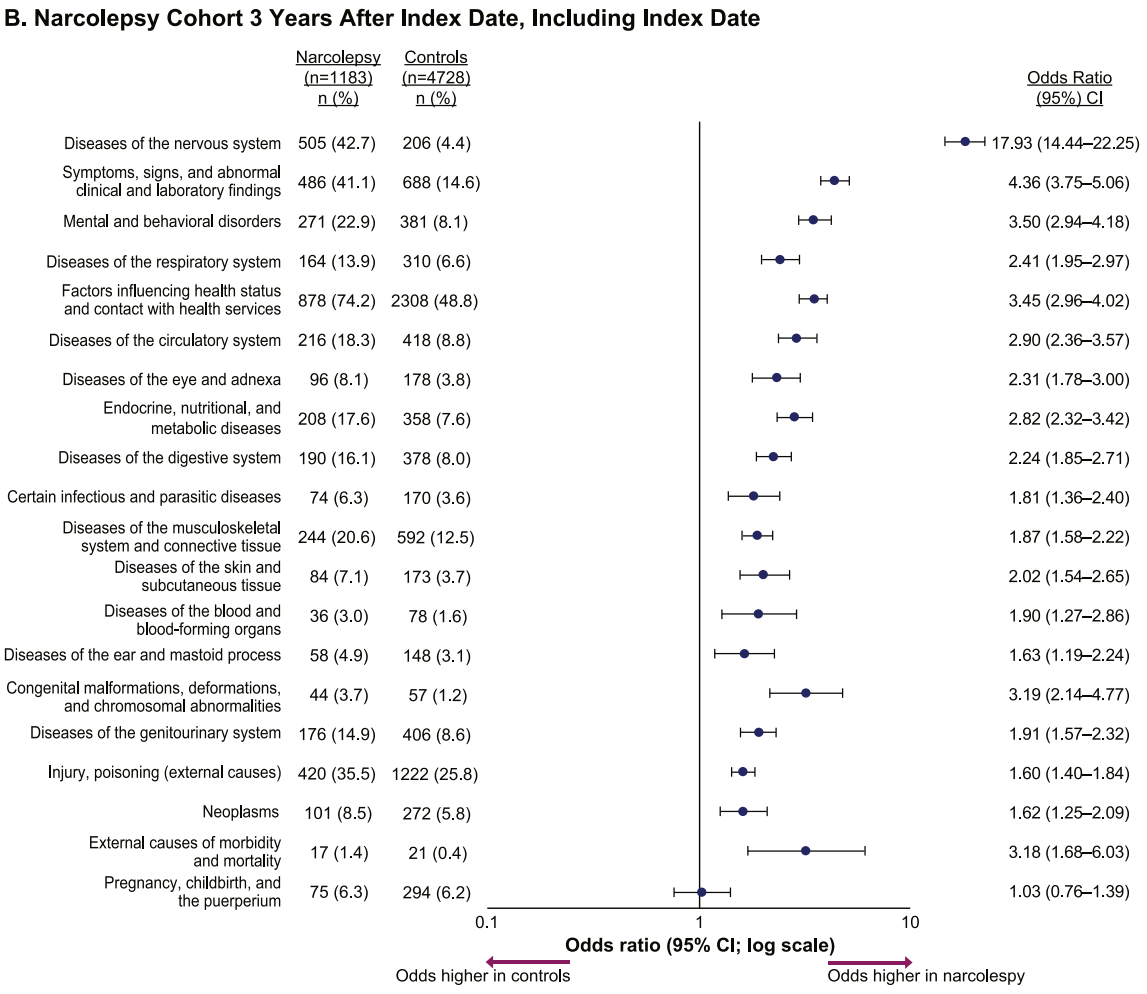


Fig. 2. (*continued*).

including hypertension (OR [95 % CI]: 1.59 [1.29, 1.95]), cardiovascular disease (2.48 [1.95, 3.17]), type 2 diabetes (1.62 [1.18, 2.22]), high cholesterol (1.70 [1.33, 2.18]), obesity (2.38 [1.63, 3.48]), mental disorder (5.83 [4.99, 6.80]), and sleep disorder other than narcolepsy or idiopathic hypersomnia (39.48 [23.98, 65.02]) (Fig. S1A).

After diagnosis, the WHO clinical comorbidity categories with the highest ORs between individuals with narcolepsy and matched controls included diseases of the nervous system (excluding narcolepsy and idiopathic hypersomnia, OR [95 % CI]: 17.93 [14.44, 22.25]); symptoms, signs, and abnormal clinical and laboratory findings (4.36 [3.75, 5.06]); mental and behavioral disorders (3.50 [2.94, 4.18]); factors influencing health status and contact with health services (3.45 [2.96, 4.02]); and congenital malformations, deformations, and chromosomal abnormalities (3.19 [2.14, 4.77]). The OR (95 % CI) for diseases of the circulatory system was 2.90 (2.36, 3.57) (Fig. 2B).

In individuals with idiopathic hypersomnia compared with matched controls, the WHO clinical comorbidity categories with the highest ORs before diagnosis included diseases of the nervous system (excluding narcolepsy and idiopathic hypersomnia, OR [95 % CI]: 9.37 [7.93, 11.08]); symptoms, signs, and abnormal clinical and laboratory findings (3.70 [3.23, 4.22]); factors influencing health status and contact with health services (3.18 [2.82, 3.58]); mental and behavioral disorders (3.03 [2.57, 3.57]); and diseases of the blood and blood-forming organs (2.70 [1.84, 3.97]). The OR (95 % CI) for diseases of the circulatory system was 1.80 (1.49, 2.16) (Fig. 2C).

Before diagnosis, individuals with idiopathic hypersomnia versus their matched controls had higher odds of comorbid hypertension (OR [95 % CI]: 1.90 [1.64, 2.19]), cardiovascular disease (1.79 [1.47, 2.20]), type 2 diabetes (1.90 [1.49, 2.43]), high cholesterol (1.89 [1.56, 2.29]), obesity (2.01 [1.49, 2.71]), mental disorder (4.33 [3.83, 4.90]), and sleep disorder other than narcolepsy or idiopathic hypersomnia (49.14 [33.64, 71.77]) (Fig. S1B).

After diagnosis, the WHO clinical comorbidity categories with the highest ORs between individuals with idiopathic hypersomnia and matched controls included diseases of the nervous system (excluding narcolepsy and idiopathic hypersomnia, OR [95 % CI]: 15.38 [12.98, 18.22]); symptoms, signs, and abnormal clinical and laboratory findings (4.38 [3.87, 4.96]); factors influencing health status and contact with health services (3.50 [3.08, 3.97]); mental and behavioral disorders (3.47 [2.97, 4.07]); and diseases of the respiratory system (3.15 [2.63, 3.77]). The OR (95 % CI) for diseases of the circulatory system was 1.90 (1.60, 2.26) (Fig. 2D).

3.3. Employment

Both individuals with narcolepsy (Fig. 3A) and individuals with idiopathic hypersomnia (Fig. 3B) had higher odds of unemployment from 3 years before through 3 years after the diagnosis of their respective conditions compared with their respective matched controls (OR range for individuals with narcolepsy: 1.76–2.79; OR range for individuals with idiopathic hypersomnia: 1.46–2.63).

3.4. Income from employment

Compared with their respective matched controls, individuals with narcolepsy had lower mean income in the overall periods before and

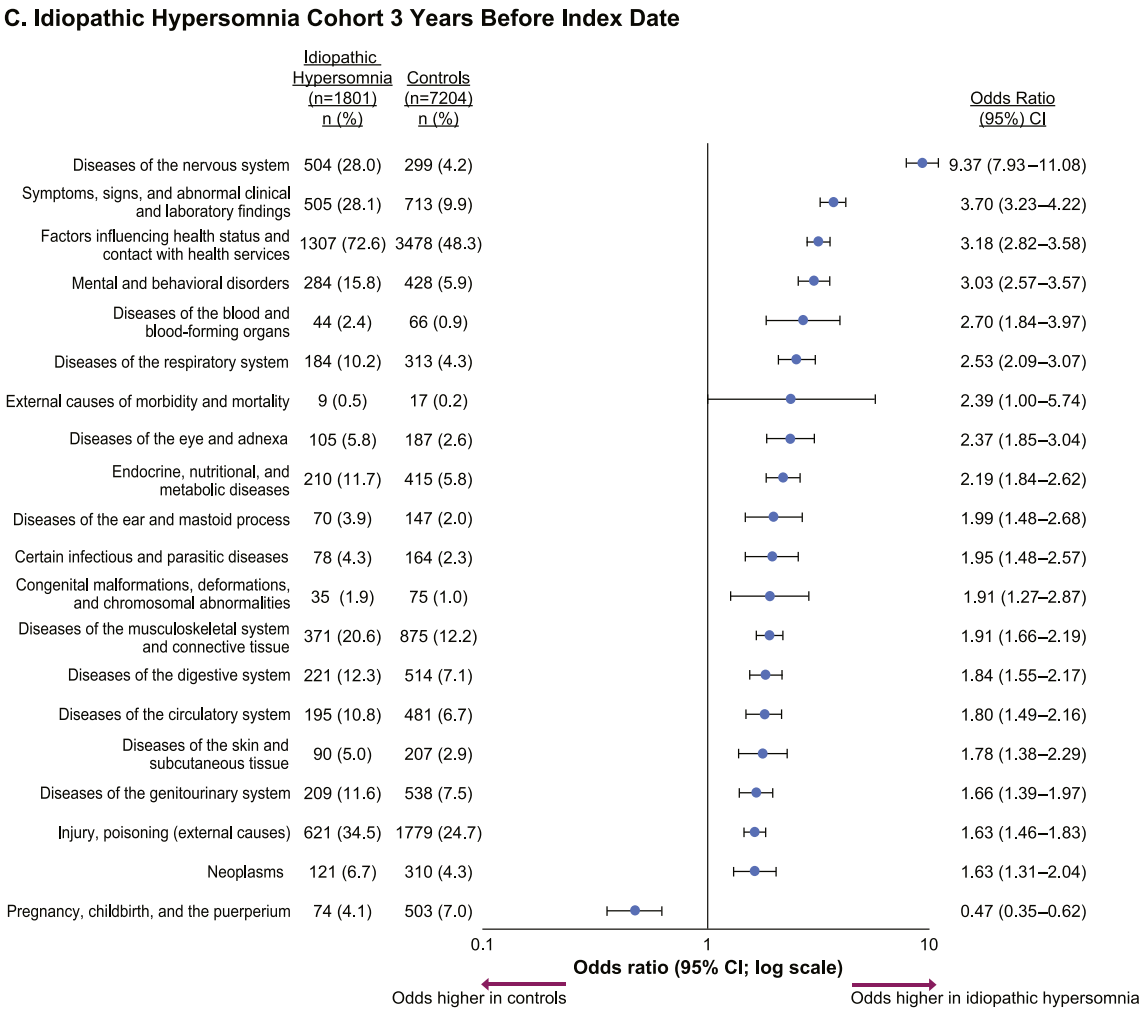


Fig. 2. (*continued*).

after diagnosis (before: €22,076 vs €26,538; $P < 0.001$; after: €21,786 vs €27,090; $P < 0.001$). Individuals with idiopathic hypersomnia also had lower mean income in the overall periods before and after diagnosis compared with matched controls (before: €31,947 vs €34,503; $P < 0.001$; after: €30,262 vs €35,139; $P < 0.001$). Income was lower for individuals with narcolepsy (Fig. 4A) and for individuals with idiopathic hypersomnia (Fig. 4B) compared with their respective matched controls each year during the 3 years before and after diagnosis.

3.5. Direct total healthcare costs

Compared with their matched controls, individuals with narcolepsy had higher mean total healthcare costs per person-year in the overall periods before and after diagnosis (before: €4547 vs €1909; $P < 0.001$; after: €7411 vs €2178; $P < 0.001$). Individuals with idiopathic hypersomnia also had higher mean total healthcare costs per person-year in the overall periods before and after diagnosis compared with matched controls (before: €4050 vs €1840; $P < 0.001$; after: €5124 vs €2106; $P < 0.001$). Mean direct total healthcare costs per person-year were consistently higher for individuals with narcolepsy (Fig. 5A) and individuals with idiopathic hypersomnia (Fig. 5B) compared with their respective matched controls each year during the 3 years before and after diagnosis.

4. Discussion

Previous research has described the substantial clinical comorbidity burden, healthcare resource utilization, and healthcare costs for individuals with narcolepsy or general hypersomnia in Denmark [6,11–13,21,26]. The results of this Danish registry study demonstrate that this clinical and socioeconomic burden persists in individuals with narcolepsy and is present in individuals with idiopathic hypersomnia. Comorbidity prevalence and unemployment were higher in individuals with narcolepsy and idiopathic hypersomnia compared with matched controls. Individuals with narcolepsy or idiopathic hypersomnia had lower mean income and higher mean direct total healthcare costs than matched controls. Although healthcare costs were numerically lower in the 2 years following their peak in the index year, they were still consistently higher than those experienced by the matched controls without either condition.

The clinical comorbidity burden observed in this study aligns with previous research in narcolepsy. Several US-based studies have found that people with narcolepsy have higher odds of comorbidities across several domains, including nervous system, respiratory, cardiovascular, and psychiatric comorbidities [5,7,27]. Two previous studies utilizing the DNPR similarly found that people with narcolepsy had higher odds of several comorbidities, including nervous system disorders, compared with matched controls [6,12]. There are more limited data in idiopathic hypersomnia in the literature; however, the higher prevalence of mental health, cardiovascular, and cardiometabolic comorbidities observed in individuals with idiopathic hypersomnia in the present study were also observed in previous US-based research [16–18].

The present study found that, compared with matched controls, individuals with narcolepsy or idiopathic hypersomnia had lower income

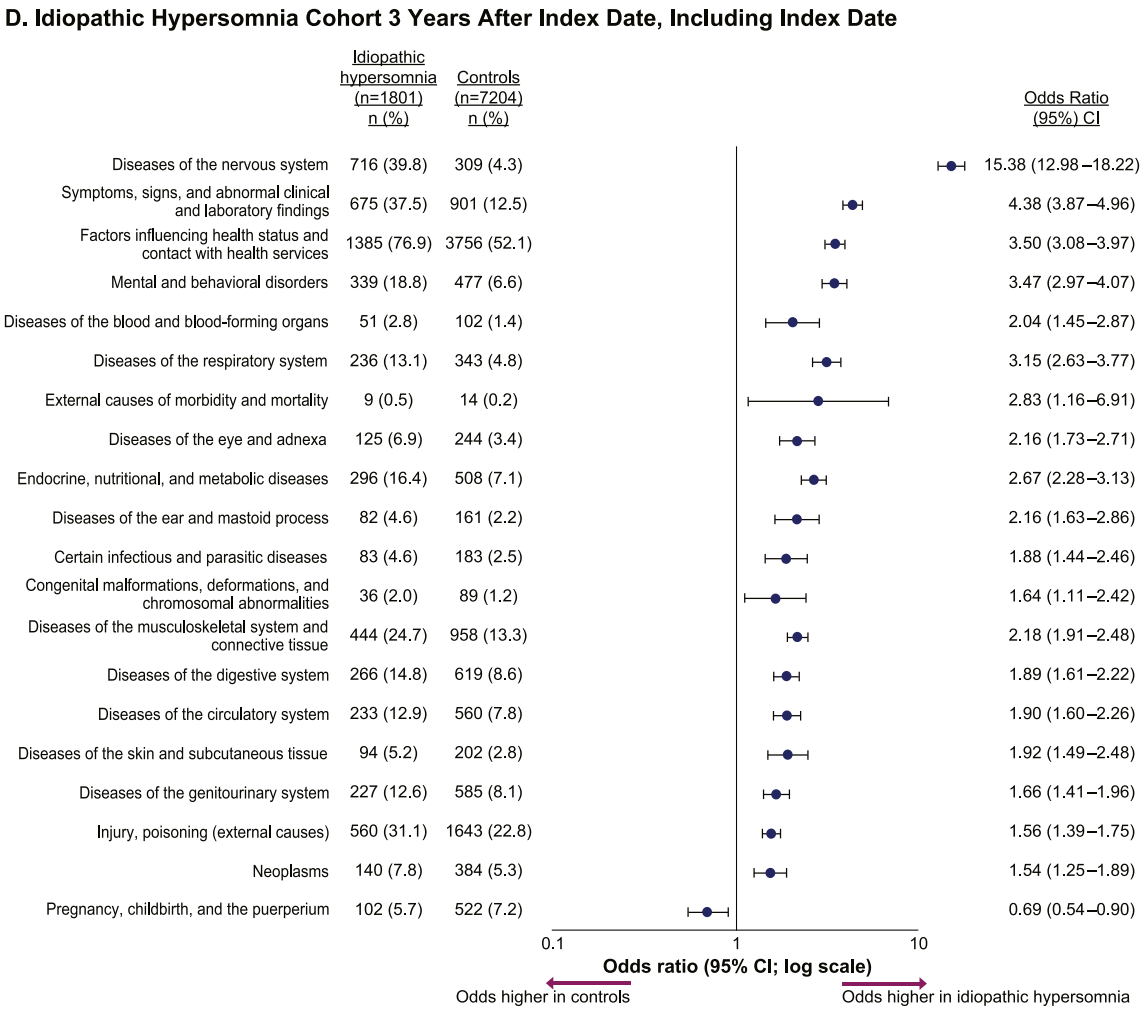


Fig. 2. (*continued*).

and higher healthcare costs. These findings are consistent with previous US-based studies based on participant-reported data from the National Health and Wellness Survey. In those studies, healthcare utilization and healthcare costs were higher for individuals with narcolepsy than for matched controls [8] and higher for individuals with idiopathic hypersomnia than for matched controls [19]. These results suggest similar clinical and socioeconomic burden associated with narcolepsy and idiopathic hypersomnia in Denmark and the United States.

The DNPR is a valuable population-based registry that provides detailed longitudinal data and complete coverage for all outpatient, inpatient, and emergency department contacts made by the Danish population dating from 1978 [23]. DNPR's link with several other Statistics Denmark registers allowed for comprehensive assessment of longitudinal sociodemographic information, including education, income, public transfers, employment status, immigration/emigration, and death, and thus comprehensive understanding of each cohort's demographics, clinical and socioeconomic conditions. To ensure a more representative sample, controls were randomly selected from the total Danish population, excluding individuals with a narcolepsy or idiopathic hypersomnia diagnosis. While individuals with narcolepsy and individuals with idiopathic hypersomnia were examined separately, the comparison of both cohorts' results with those of their respective matched controls allows for greater understanding of the challenges experienced by individuals with central disorders of hypersomnolence. The 3-year periods before and after diagnosis were utilized to demonstrate accumulated disease prevalence before diagnosis and continuing disease burden after diagnosis while maintaining a robust study population size. Both narcolepsy and idiopathic hypersomnia are commonly associated with significant diagnostic delay [1,28]; this analysis underscores the disease burden that accrues in the pre-diagnostic period.

Despite these strengths, there were several study limitations. Inclusion in the narcolepsy or idiopathic hypersomnia cohort required only one diagnosis code for either condition; it is possible that conditions were misclassified, given the challenges in diagnosing these conditions [28]. This limitation is mitigated by the Danish requirement for multiple sleep latency testing, polysomnographic monitoring, and, for NT1, assessment of hypocretin levels to diagnose these central disorders of hypersomnolence [1]. The higher ORs for clinical comorbidities reported in the 3 years after diagnosis compared with the 3 years before diagnosis may be attributable to more frequent medical professional visits among individuals with either condition compared with their controls; this increased contact with medical professionals may create opportunities for identifying comorbidities in individuals with narcolepsy or idiopathic hypersomnia. Although this study used Danish registry data that may limit generalizability to populations outside Denmark, the results of this analysis align with the clinical and economic burden reported for US populations [2,5,7,27].

5. Conclusions

The clinical comorbidity and socioeconomic burden were greater in individuals with narcolepsy or idiopathic hypersomnia than in their respective matched controls. These findings corroborate the known

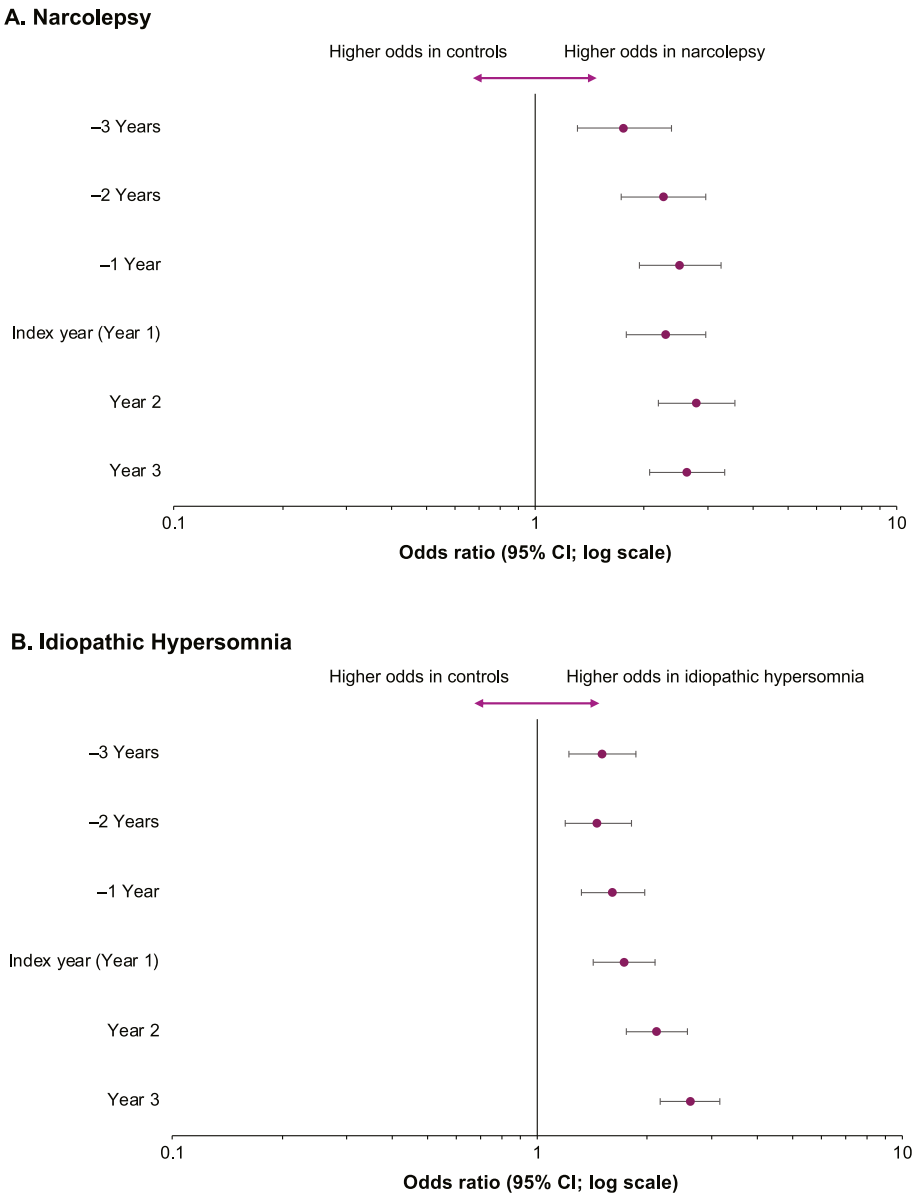


Fig. 3. Odds ratios and 95 % confidence intervals of unemployment before and after diagnosis.
CI, confidence interval.

clinical and socioeconomic burden experienced by people with narcolepsy or idiopathic hypersomnia and provide increased awareness of the comorbidities and potential negative social outcomes associated with these conditions. Future research topics may include the evaluation of disease-related costs to provide a clearer understanding of the sources of disease burden, an assessment of the impact of age and sex on disease burden to better inform intervention, and a comparison between treated and untreated individuals to promote early identification and treatment. During treatment selection, careful consideration of the substantial comorbidity burden of these populations may prevent or limit exacerbation of underlying risk.

CRediT authorship contribution statement

Poul Jørgen Jennum: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Michael Ibsen:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sam Mettam:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Sarah C. Markt:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Conceptualization. **Douglas S. Fuller:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Jessica K. Alexander:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Rikke Ibsen:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jakob Kjellberg:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Caroleen Drachenberg:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization.

Data sharing statement

All relevant data are provided within the manuscript and supporting files.



Fig. 4. Mean income from employment per person-year before and after diagnosis.
[a]Income weighted by person-year and reported in 2020 prices.
*$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

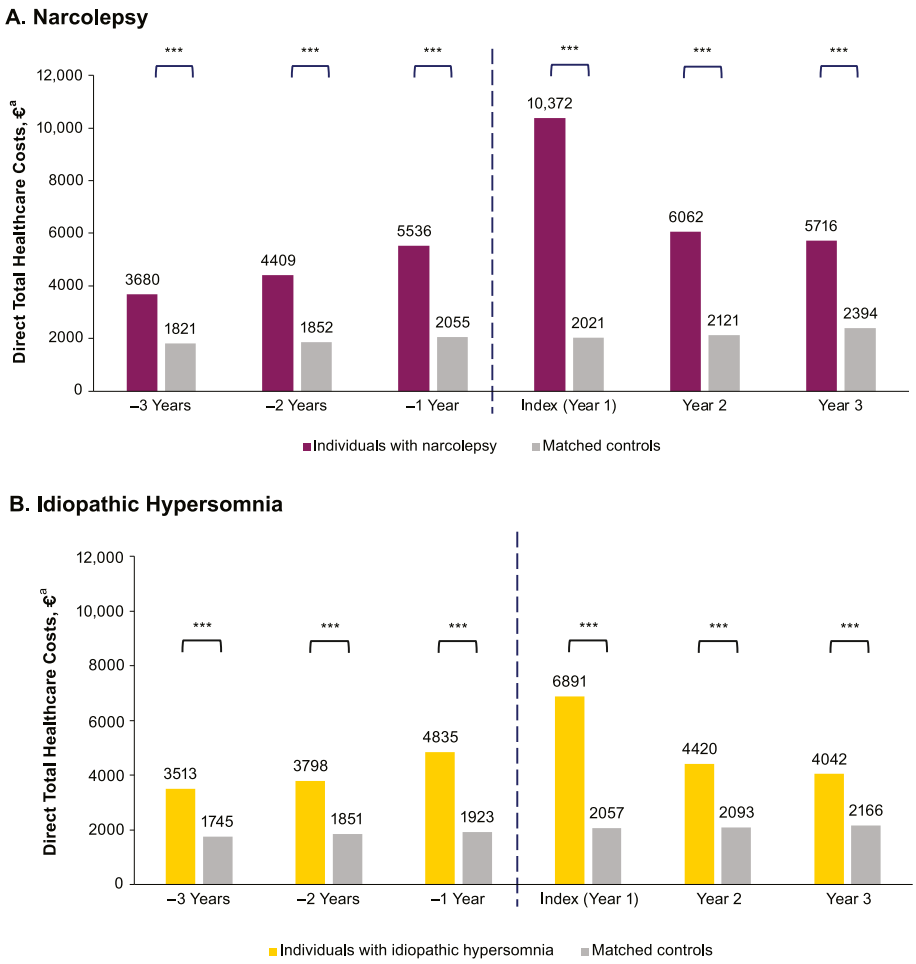


Fig. 5. Mean healthcare costs per person-year before and after diagnosis.
[a]Costs weighted by person-year and reported in 2020 prices.
$^{***}P < 0.001$.

Funding source

This study was sponsored by Jazz Pharmaceuticals.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **PJ Jennum, M Ibsen, R Ibsen,** and **J Kjellberg** have nothing to disclose. **S Mettam, SC Markt, DS Fuller, JK Alexander,** and **C Drachenberg** are full-time employees of Jazz Pharmaceuticals who, in the course of this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

Acknowledgements

This study was sponsored by Jazz Pharmaceuticals. Under the direction of the authors, Peloton Advantage, LLC (an OPEN Health company) employees Joseph Mansonet, MPH, Hannah Ritchie, PhD, and Nicole Boyer, PhD, provided medical writing support and Christopher Jaworski provided editorial support, which were funded by Jazz Pharmaceuticals.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2025.108690.

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] Lipford MC, Ip W, Awasthi S, et al. Demographic characteristics and comorbidities of patients with narcolepsy: a propensity-matched cohort study. Sleep Adv 2024;5(1):zpae067. https://doi.org/10.1093/sleepadvances/zpae067.
[3] Ben-Joseph RH, Somers VK, Black J, et al. Increased risk of new-onset hypertension in patients with narcolepsy initiating sodium oxybate: a real-world study. Mayo Clin Proc 2024;99(11):1710–21. https://doi.org/10.1016/j.mayocp.2024.05.029.
[4] Ben-Joseph RH, Saad R, Black J, et al. Cardiovascular Burden of Narcolepsy Disease (CV-BOND): a real-world evidence study. Sleep 2023;46(10):zsad161. https://doi.org/10.1093/sleep/zsad161.
[5] Black J, Reaven NL, Funk SE, et al. Medical comorbidity in narcolepsy: findings from the Burden of Narcolepsy Disease (BOND) study. Sleep Med 2017;33:13–8. https://doi.org/10.1016/j.sleep.2016.04.004.
[6] Jennum P, Thorstensen EW, Pickering L, et al. Morbidity and mortality of middle-aged and elderly narcoleptics. Sleep Med 2017;36:23–8. https://doi.org/10.1016/j.sleep.2017.03.029.
[7] Ohayon MM. Narcolepsy is complicated by high medical and psychiatric comorbidities: a comparison with the general population. Sleep Med 2013;14(6):488–92. https://doi.org/10.1016/j.sleep.2013.03.002.
[8] Flores NM, Villa KF, Black J, et al. The humanistic and economic burden of narcolepsy. J Clin Sleep Med 2016;12(3):401–7. https://doi.org/10.5664/jcsm.5594.
[9] Gauffin H, Fast T, Komkova A, et al. Narcolepsy treatment in Sweden: an observational study. Acta Neurol Scand 2022;145(2):185–92. https://doi.org/10.1111/ane.13532.
[10] Black J, Reaven NL, Funk SE, et al. The Burden of Narcolepsy Disease (BOND) study: health-care utilization and cost findings. Sleep Med 2014;15(5):522–9. https://doi.org/10.1016/j.sleep.2014.02.001.
[11] Jennum P, Ibsen R, Petersen ER, et al. Health, social, and economic consequences of narcolepsy: a controlled national study evaluating the societal effect on patients

and their partners. Sleep Med 2012;13(8):1086–93. https://doi.org/10.1016/j.sleep.2012.06.006.
[12] Jennum P, Ibsen R, Knudsen S, et al. Comorbidity and mortality of narcolepsy: a controlled retro- and prospective national study. Sleep 2013;36(6):835–40. https://doi.org/10.5665/sleep.2706.
[13] Jennum P, Knudsen S, Kjellberg J. The economic consequences of narcolepsy. J Clin Sleep Med 2009;5(3):240–5.
[14] Schneider LD, Morse AM, Strunc MJ, et al. Long-term treatment of narcolepsy and idiopathic hypersomnia with low-sodium oxybate. Nat Sci Sleep 2023;15:663–75.
[15] Stevens J, Schneider LD, Husain A, et al. Impairment in functioning and quality of life in patients with idiopathic hypersomnia: the real world idiopathic Hypersomnia Outcomes study (ARISE). Nat Sci Sleep 2023;15:593–606.
[16] Lillaney P, Saad R, Profant D, et al. Real-world idiopathic hypersomnia Total Health Model (RHYTHM): clinical burden of patients with idiopathic hypersomnia [poster 250]. In: Annual Meet Assoc Profess Sleep Soc. IN: Indianapolis; 2023.
[17] Drachenberg C, Cambron-Mellott MJ, Yang L, et al. The clinical and humanistic burden of idiopathic hypersomnia in the United States: analysis of the National Health and Wellness Survey [poster 434]. Annual Sci Meet Associated Profess Sleep Soc. TX: Houston; 2024.
[18] Saad R, Prince P, Taylor B, et al. Characteristics of adults newly diagnosed with idiopathic hypersomnia in the United States. Sleep Epidemiol 2023;3:100059. https://doi.org/10.1016/j.sleepe.2023.100059.
[19] Drachenberg C, Cambron-Mellott MJ, Yang L, et al. The economic burden of idiopathic hypersomnia in the United States: analysis of the national health and wellness survey [poster 436]. Annual Sci Meet Associated Profess Sleep Soc. TX: Houston; 2024.
[20] Jennum P, Ibsen R, Avlund K, et al. Health, social and economic consequences of hypersomnia: a controlled national study from a national registry evaluating the societal effect on patients and their partners. Eur J Health Econ 2014;15(3):303–11. https://doi.org/10.1007/s10198-013-0491-2.
[21] Jennum P, Kjellberg J. The socio-economical burden of hypersomnia. Acta Neurol Scand 2010;121(4):265–70. https://doi.org/10.1111/j.1600-0404.2009.01227.x.
[22] von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med 2007;4(10):e296. https://doi.org/10.1371/journal.pmed.0040296.
[23] Schmidt M, Schmidt SA, Sandegaard JL, et al. The Danish national patient registry: a review of content, data quality, and research potential. Clin Epidemiol 2015;7:449–90. https://doi.org/10.2147/clep.s91125.
[24] Classifications. sundhedsdata-styrelsen. Available at: https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/classifications. [Accessed 10 December 2024].
[25] Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? Comparing methods of modeling medicare expenditures. J Health Econ 2004;23(3):525–42. https://doi.org/10.1016/j.jhealeco.2003.10.005.
[26] Jennum P, Ibsen R, Kjellberg J. Social consequences of sleep disordered breathing on patients and their partners: a controlled national study. Eur Respir J 2014;43(1):134–44. https://doi.org/10.1183/09031936.00169212.
[27] Cohen A, Mandrekar J, St Louis EK, et al. Comorbidities in a community sample of narcolepsy. Sleep Med 2018;43:14–8. https://doi.org/10.1016/j.sleep.2017.11.1125.
[28] Boulanger T, Pigeon P, Crawford S. Diagnostic challenges and burden of idiopathic hypersomnia: a systematic literature review. Sleep Adv 2024;5(1):zpae059. https://doi.org/10.1093/sleepadvances/zpae059.