High Rates of Psychiatric Comorbidity in Narcolepsy: Findings from the Burden of Narcolepsy Disease (BOND) Study of 9,312 Patients in the United States

Chad Ruoff, MD; Nancy L. Reaven, MA; Susan E. Funk, MBA; Karen McGaughey, PhD; Maurice Ohayon, MD, DSc, PhD; Christian Guilleminault, MD; Jed Black, MD

BACKGROUND

- Narcolepsy is a treatable condition characterized by profound excessive daytime sleepiness commonly presenting as tiredness and/or fatigue.
- Psychiatric conditions historically associated with narcolepsy include depression, anxiety, and schizophrenia[1-3].
- We accessed a medical claims database of 7.1 million continuously insured persons (2006 to 2010) to evaluate psychiatric comorbidity in narcolepsy.

OBJECTIVE

- To characterize psychiatric comorbidity in narcolepsy

METHODS

Subject selection

- Truven Health Analytics MarketScan® Research Databases
- Patients ≥18 years of age with at least one diagnosis code for narcolepsy ± cataplexy*
- Controls without narcolepsy matched 5:1 on age, sex, region, and payer
- Extensive subgroup analyses validated the population (see handout)

Analysis

- Psychiatric comorbid condition prevalence evaluated in:
  - Narcolepsy vs matched controls
  - Narcolepsy with and without cataplexy
  - Men and women
- Comorbidity prevalence measured using CCS[4] level 1 (CCSM) categories
- Psychiatric medication use, narcolepsy vs. matched controls
- Annualized health plan costs, narcolepsy vs. matched controls

RESULTS

Study Population

- 55,871 subjects
  - 9,312 narcolepsy (20.3% with cataplexy; 59.2% women)
  - 46,559 matched controls
  - Mean (SD) age, 46.1 (13.3) years; range 18-93 years

Psychiatric Comorbidity: Narcolepsy vs. Controls

- Depressive and anxiety disorders demonstrated the greatest excess prevalence (**Figure 1**).
- All Mental Illness categories were more prevalent (**Table 1**).
- The excess prevalence of comorbid mental illness was independent of cataplexy status and occurred in both men and women (data not shown).

Psychiatric Medication Usage and Specialist Utilization: Narcolepsy vs. Controls

- Psychiatric medication usage was significantly higher (**Figure 2**).
  - Psychiatric medication usage was similar among patients with and without cataplexy (data not shown).
- Psychiatry office visits were more frequent (0.53 visits/patient/year vs 0.12 visits/patient/year).
- Costs for mental illness-related services were higher ($314/patient/year vs $85/patient/year).

CONCLUSIONS

- **High rates of depression and anxiety were seen among patients with narcolepsy.**
- **These findings may help explain the frequent misdiagnosis of narcolepsy[5] and long diagnostic delays (≥10 years) reported elsewhere[6,7].**
- **Narcolepsy should be included in the differential diagnosis of mood and anxiety disorders, particularly in patients with fatigue or daytime sleepiness and in those unresponsive to standard treatment.**

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* ICD9 codes: 347.0, 347.00, 347.01, 347.1, 347.10 or 347.11

Figure 1. Top mental illness comorbidities by excess prevalence in the data set (narcolepsy % - controls %), showing odds ratios (95% CI). All comparisons p<0.0001, narcolepsy vs controls

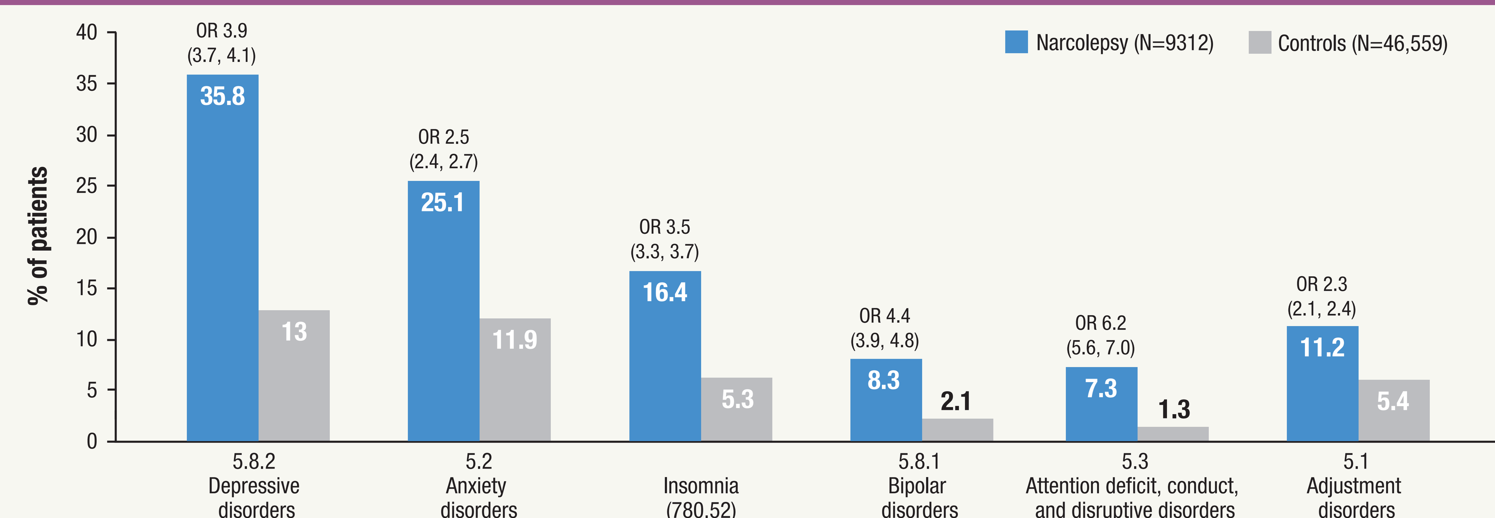
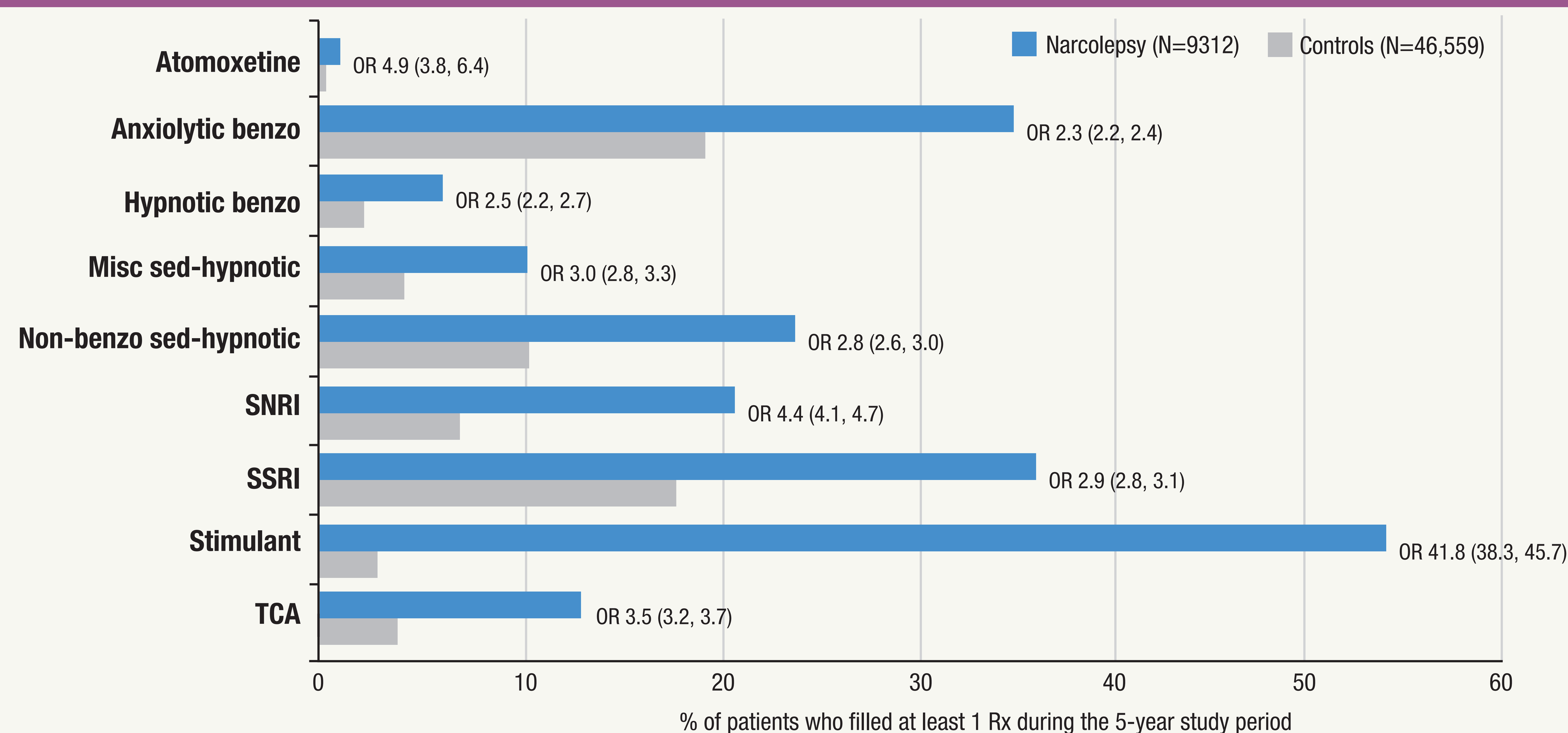


Table 1. Psychiatric comorbidity prevalence for CCSM level 2 categories* and selected subcategories and ICD9 diagnosis codes of interest. All comparisons p<.05, narcolepsy vs controls

	Patients with Comorbidity, n (%)			
CCSM 5 Mental Illness	**Controls N=46,559**	**Narcolepsy N=9312**	**Excess prevalence**	**OR (95% CI)**
5.8 Mood disorders	13.8%	37.9%	**24.1%**	4.0 (3.8, 4.2)
5.2 Anxiety disorders	11.9%	25.1%	**13.1%**	2.5 (2.4, 2.7)
5.15 Other miscellaneous mental disorders	4.0%	14.5%	**10.5%**	4.1 (3.8, 4.4)
5.3 Attention deficit, conduct, and disruptive behavior disorders	1.3%	7.3%	**6.0%**	6.2 (5.6, 7)
5.1 Adjustment disorders	5.4%	11.2%	**5.8%**	2.3 (2.1, 2.4)
5.4 Delirium, dementia, and amnestic and other cognitive disorders	1.5%	4.6%	**3.2%**	3.8 (3.3, 4.3)
5.12 Substance-related disorders	1.2%	4%	**2.8%**	3.5 (3, 4)
5.10 Schizophrenia and other psychotic disorders	0.9%	3.4%	**2.5%**	3.8 (3.3, 4.4)
5.9 Personality disorders	0.2%	1.1%	**0.9%**	5.8 (4.3, 7.7)
5.13 Suicide [attempted] and intentional self-inflicted injury	0.2%	1.0%	**0.8%**	4.1 (3.1, 5.4)
5.11 Alcohol-related disorders	1.3%	1.9%	**0.5%**	1.4 (1.2, 1.7)
5.7 Impulse control disorders not elsewhere classified	0.1%	0.2%	**0.1%**	1.9 (1.1, 3.2)
Selected subcategories				
5.8.2 Depressive disorders	13.0%	35.8%	**22.8%**	3.9 (3.7, 4.1)
5.8.1 Bipolar disorders	2.1%	8.3%	**6.2%**	4.4 (3.9, 4.8)
ICD9 Diagnosis codes of interest				
331 Depressive disorders	8.5%	24.6%	**16.2%**	3.5 (3.3, 3.7)
780.52 Insomnia	5.3%	16.4%	**11.0%**	3.5 (3.3, 3.7)
300.00 Anxiety state	8.2%	17.1%	**9.0%**	2.3 (2.2, 2.5)

* CCSM categories 5.5 (Developmental disorders) and 5.6 (Disorders usually diagnosed in infancy, childhood, or adolescence) were excluded. CCSM=Clinical Classification Software for ICD-9 diagnosis codes, multi-level.[4]

Figure 2. Psychiatric drug exposure, narcolepsy patients vs controls. Data represent percentage of patients who filled at least 1 prescription for a drug in the category during the 5-year study period. All comparisons p<0.0001, narcolepsy vs controls. Values shown on graph depict odds ratio (95% CI)



ABSTRACT

OBJECTIVE: To evaluate psychiatric comorbidity patterns in narcolepsy patients in the United States.

BACKGROUND: While narcolepsy is known to be associated with medical comorbidity, the burden of concomitant psychiatric illness in this population has not been well characterized.

DESIGN/METHODS: Truven Health Analytics MarketScan® Research Databases were accessed to identify individuals >18 years of age with at least one diagnosis code for narcolepsy + cataplexy (ICD9 347.0, 347.00, 347.01, 347.1, 347.10 or 347.11) continuously insured between 2006 and 2010, and controls without narcolepsy matched 5:1 on age, sex, region, and payer. Extensive sub-analyses were conducted to confirm the validity of narcolepsy definitions.

Narcolepsy and control subjects were compared for frequencies of psychiatric comorbid conditions, identified by the appearance of >1 psychiatric diagnosis code(s) mapped to a Clinical Classification System (CCS) level 2 category any time during the study period, and on specific subcategories. Patterns of psychiatric medication use were also evaluated.

RESULTS: The final population included 9,312 narcolepsy subjects and 46,559 controls (each group, average age of 46.1 years and 59% female). The CCS categories of anxiety disorders and mood disorders appeared at significantly higher frequencies in narcolepsy patients than controls (**Table 1**).

Table 1. Psychiatric comorbidity frequency, control vs narcolepsy

CCS Level 2 Category	Control (N=46,559) n (%)	Narcolepsy (N=9312) n (%)	P-value*	OR (95% CI)
CCS 5.2, Anxiety disorders	5554 (11.9)	2333 (25.1)	<0.0001	2.5 (2.4, 2.7)
CCS 5.8, Mood disorders	6407 (13.8)	3525 (37.9)	<0.0001	4.0 (3.8, 4.2)

* Conditional Chi-square test; accounts for matching

In particular, high excess frequency was noted for the following specific ICD9 diagnoses in the narcolepsy cohort vs controls: 311 depressive disorders (24.6% vs 8.5%; 16% excess); 780.52 insomnia (16.4% vs 5.3%; 11% excess); and 300.00 anxiety state, nonspecified (17.1% vs 8.2%; 9% excess) (all p<0.0001). The percentage of patients with reported psychiatric medication usage during the study period was higher in the narcolepsy group vs controls in the following categories: SSRIs (36% vs 17%), anxiolytic benzodiazepines (34% vs 19%), non-benzodiazepine sedative-hypnotics (23% vs 10%), SNRIs (21% vs 6%), TCAs (13% vs 4%), miscellaneous sedative-hypnotics (10% vs 4%), and hypnotic benzodiazepines (6% vs 2%) (all p<0.0001).

CONCLUSIONS: Narcolepsy is associated with significant comorbid psychiatric illness burden and a higher rate of psychiatric medication usage compared with the non-narcolepsy population.

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