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

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BACKGROUND

- Narcolepsy is a treatable condition characterized by profound excessive daytime sleepiness commonly presenting as tiredness and/or fatigue.
- While various medical comorbidities have been reported to be associated with narcolepsy in case series and smaller studies[1-5], the full scope of concomitant illness in this population has not been well characterized.
- We accessed a medical claims database of 7.1 million continuously insured persons (2006 to 2010) to evaluate medical comorbidity in narcolepsy.

OBJECTIVE

- To characterize medical comorbidity in patients with 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

- Comorbidity prevalence (1 or more occurrences during study period), narcolepsy versus controls
  - CCS level 1 (CCSM)[6] categories
  - Targeted diagnoses (previously associated with narcolepsy)
- Selected diagnoses and procedures supported by objective criteria (e.g., confirmatory laboratory and/or diagnostic testing)

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

Comorbidity Patterns

- Narcolepsy patients versus controls:
  - All CCSM categories were more prevalent (p<0.0001), except perinatal conditions and complications of pregnancy and childbirth (p=NS) (**Figure 1**).
  - All targeted diagnoses were more prevalent (p<0.0001) (**Figure 2**).
  - Select diagnoses/procedures supported by objective criteria were more frequent (all p<0.02) (**Figure 3**).
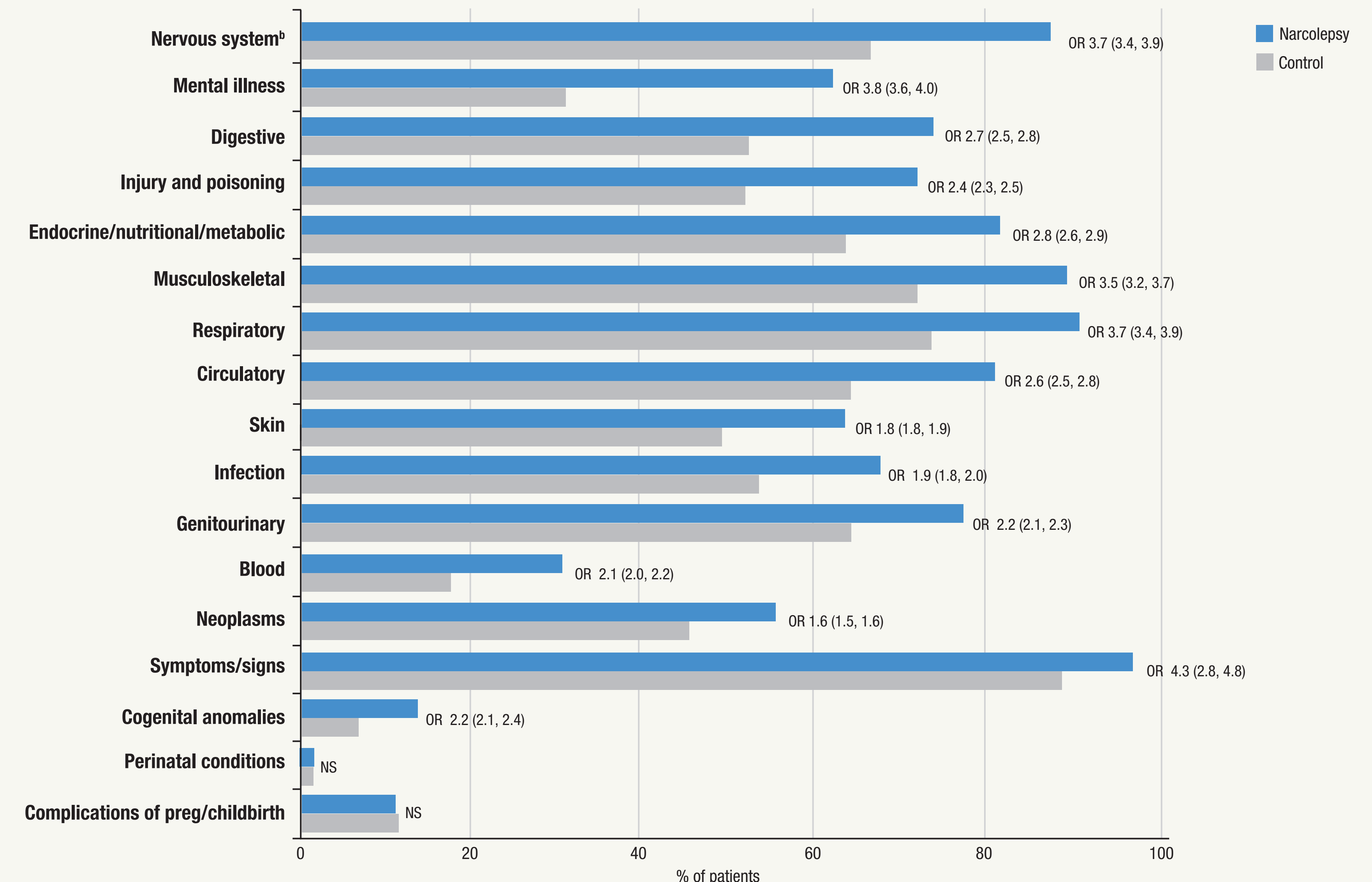
CONCLUSIONS

- **Narcolepsy is associated with a surprising range and significantly high rate of comorbid medical illnesses.**
- **The consistency across objectively measured conditions (e.g., renal failure, cardiac arrest) and more symptomatic conditions (e.g., headache) suggests that observed comorbidity patterns cannot be attributed primarily to care-seeking behavior.**
- **The potential presence of narcolepsy and other sleep disorders should be investigated in patients who present with other conditions and have sleep-related complaints to facilitate earlier diagnosis and treatment.**
- **Narcolepsy patients should be evaluated regularly for comorbid illnesses.**

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

Figure 1. Population prevalence of CCSM[a] categories, narcolepsy versus controls. All comparisons versus controls, p<0.0001 except perinatal conditions and complications of pregnancy and childbirth.

Categories (with Narcolepsy vs Control bars):
- Nervous system[b] — OR 3.7 (3.4, 3.9)
- Mental illness — OR 3.8 (3.6, 4.0)
- Digestive — OR 2.7 (2.5, 2.8)
- Injury and poisoning — OR 2.4 (2.3, 2.5)
- Endocrine/nutritional/metabolic — OR 2.8 (2.6, 2.9)
- Musculoskeletal — OR 3.5 (3.2, 3.7)
- Respiratory — OR 3.7 (3.4, 3.9)
- Circulatory — OR 2.6 (2.5, 2.8)
- Skin — OR 1.8 (1.8, 1.9)
- Infection — OR 1.9 (1.8, 2.0)
- Genitourinary — OR 2.2 (2.1, 2.3)
- Blood — OR 2.1 (2.0, 2.2)
- Neoplasms — OR 1.6 (1.5, 1.6)
- Symptoms/signs — OR 4.3 (2.8, 4.8)
- Cogenital anomalies — OR 2.2 (2.1, 2.4)
- Perinatal conditions — NS
- Complications of preg/childbirth — NS

x-axis: % of patients

[a] CCSM = Clinical Classifications Software multilevel; category 18 (Residual codes/unclassified) excluded for being too divergent to be useful; [b] Excluding narcolepsy; NS=not significant

Figure 2. Population prevalence of targeted diagnoses, narcolepsy versus control. All comparisons versus controls, p<0.0001

- Other nutritional (inc. obesity) — OR 2.4 (2.3, 2.5)
- Headache/migraine — OR 2.9 (2.8, 3.1)
- Mood disorders — OR 4.0 (3.8, 4.2)
- Anxiety disorders — OR 2.5 (2.4, 2.7)
- Depressive disorders — OR 3.9 (3.7, 4.1)
- Sleep apnea — OR 18.7 (17.5, 20.0)
- Hypersomnia — OR 80.1 (62.6, 102.5)
- Restless leg — OR 8.9 (7.7, 10.3)
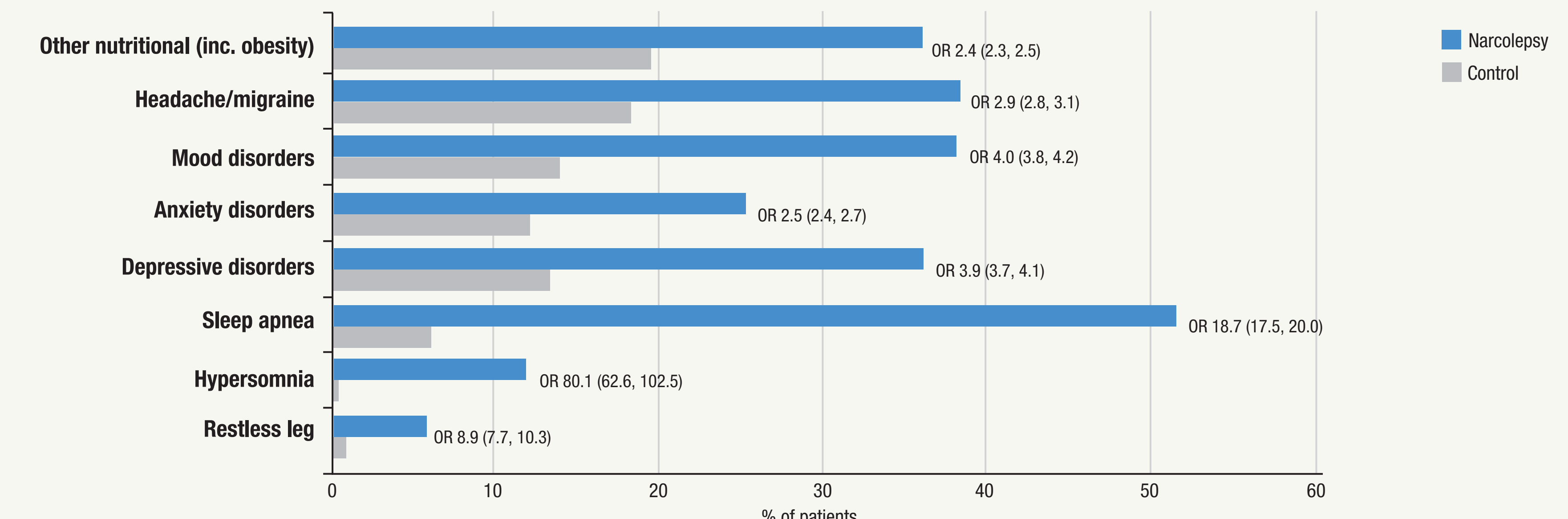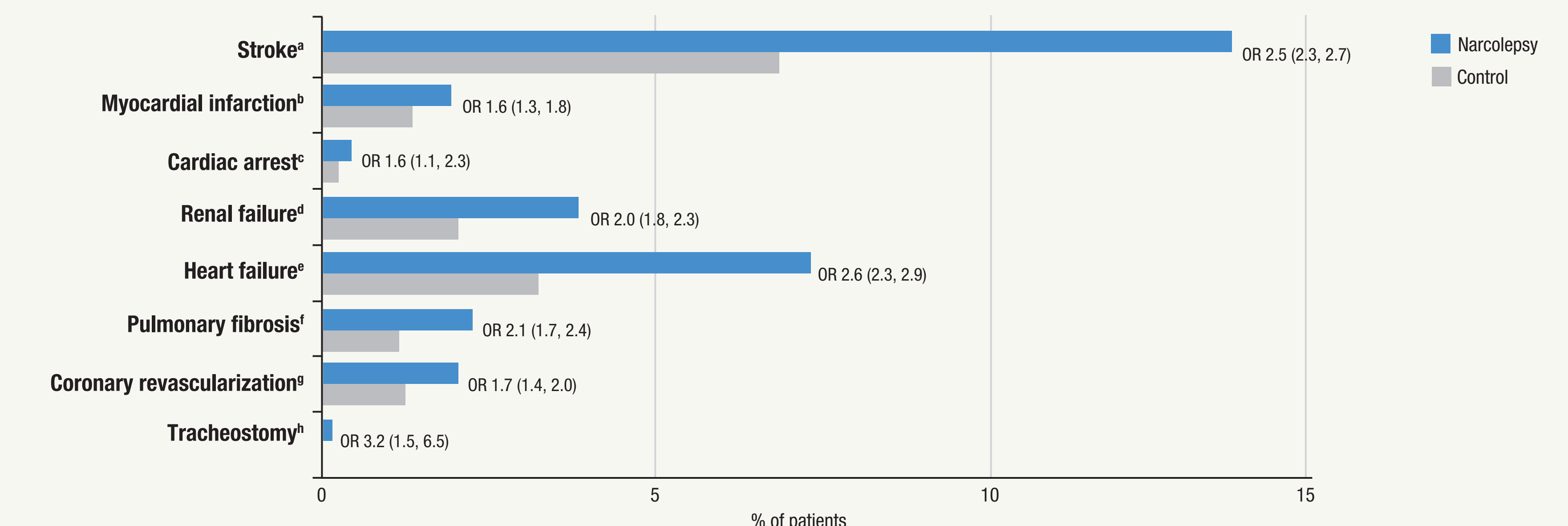
x-axis: % of patients

Figure 3. Frequency of selected diagnoses and procedures supported by objective criteria, narcolepsy versus control. All comparisons versus controls, p<0.001

- Stroke[a] — OR 2.5 (2.3, 2.7)
- Myocardial infarction[b] — OR 1.6 (1.3, 1.8)
- Cardiac arrest[c] — OR 1.6 (1.1, 2.3)
- Renal failure[d] — OR 2.0 (1.8, 2.3)
- Heart failure[e] — OR 2.6 (2.3, 2.9)
- Pulmonary fibrosis[f] — OR 2.1 (1.7, 2.4)
- Coronary revascularization[g] — OR 1.7 (1.4, 2.0)
- Tracheostomy[h] — OR 3.2 (1.5, 6.5)

x-axis: % of patients

[a] CCS 109 Acute cerebrovascular disease, CCS 110 Occlusion or stenosis of precerebral arteries; [b] CCS 100 Acute myocardial infarction; [c] CCS 107 Cardiac arrest and ventricular fibrillation; [d] CCS 158 Chronic renal failure; [e] CCS 108 Congestive heart failure; nonhypertensive; [f] ICD-9 diagnosis code 515, Postinflammatory Pulmonary Fibrosis; [g] CCS 44 Coronary Artery Bypass Graft, CCS 45 Percutaneous Transluminal Coronary Angioplasty; [h] CCS 34 Tracheostomy

ABSTRACT

INTRODUCTION: While narcolepsy is known to be associated with medical comorbidities, the full scope of concomitant illness in this population has not been well characterized.

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 the narcolepsy definitions.

Narcolepsy and control subjects were compared for frequency of comorbid conditions, identified by the appearance of >1 diagnosis code(s) mapped to a Clinical Classification System (CCS) level 1 category any time during the study period, and on specific subcategories, including recognized narcolepsy comorbidities of obstructive sleep apnea (OSA) and depression.

RESULTS: The final population included 9,312 narcolepsy subjects and 46,559 controls (each group, average age of 46.1 years and 59% female). Compared with controls, narcolepsy patients had significantly higher frequencies of the following CCS categories: respiratory (90.9% vs 73.5%), musculoskeletal (89.5% vs 72.0%), endocrine (81.7% vs 63.8%), circulatory (80.9% vs 64.3%), genitourinary (77.5% vs 64.3%), digestive system (73.9% vs 52.5%), injury (72.1% vs 51.9%), infectious disease (67.8% vs 53.6%), skin (63.7% vs 49.3%), mental illness (62.3% vs 31.2%), neoplasms (55.7% vs 45.4%), blood diseases (30.7% vs 17.7%), and congenital anomalies (13.9% vs 6.9%) (all p<0.0001). High excess frequency was observed for OSA (51.4% vs 5.7%; OR 18.7; 95% CI 17.5, 20.0) and depressive disorders (35.8% vs 13.0%; OR 3.9; 95% CI 3.7,4.1) (p<0.0001). No excess frequency was observed in conditions arising perinatally (1.7% vs 1.6%; p=0.68) or obstetrical conditions (11.3% vs 11.7%; p=0.30).

CONCLUSIONS: Narcolepsy is associated with a significantly high rate of comorbid medical illness burden.