Burden of Illness and Comorbidity in Narcolepsy with Cataplexy: Findings from the Burden of Narcolepsy Disease (BOND) Study in the United States

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BACKGROUND

- Narcolepsy is a highly disabling condition with substantial impact on quality of life[1-3] and a high rate of medical and psychiatric comorbidity.[4,5]
- Data are lacking on burden of illness and comorbidity prevalence in patients having narcolepsy with cataplexy.
- We accessed a medical claims database of 7.1 million continuously insured persons (2006 to 2010) to evaluate burden of illness and comorbidity patterns in narcolepsy with (N+C) and without cataplexy (N-C).

OBJECTIVE

- To characterize the burden of illness and comorbidity patterns in patients with N+C and N-C

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

- The following were evaluated in N+C and N-C vs matched controls and N+C vs N-C:
  - Healthcare service (admissions/visits) and drug utilization (# filled prescriptions)
  - Population prevalence of comorbidities identified by the appearance of ≥1 ICD9 diagnosis codes in the CCS[6] multilevel (CCSM) or single-level category
  - Usage patterns of narcolepsy drug categories

RESULTS

Study Population

- 55,871 subjects (9312 narcolepsy; 46,559 matched controls)
  - 1890 N+C (mean age, 45.5 years; range 18-90 years; 62% women)
  - 7422 N-C (mean age, 46.3 years; range 18-93 years; 58% women)

Healthcare and Drug Utilization

- N+C and N-C versus their respective controls:
  - Significantly higher healthcare utilization (**Figs. 1 and 2**)
- N+C versus N-C:
  - Total healthcare service utilization not different (**Fig. 1**)
  - Total health plan costs not different (**Fig. 2**)
  - Narcolepsy drug usage patterns similar (**Fig. 3**)

Comorbidity Prevalence

- Prevalence of 18 CCS level 1 category comorbidities[6] was similar between N+C and N-C (**Table 1**)
- Targeted comorbidity prevalence higher in N+C and N-C vs controls (**Fig. 4**)
  - Comorbidity prevalence not different by cataplexy status, except sleep apnea more commonly diagnosed in N-C (**Fig. 4**)

CONCLUSIONS

- **Narcolepsy patients with or without cataplexy show patterns of service utilization, cost, and comorbid conditions that are significantly higher than matched controls without narcolepsy.**
- **In narcolepsy patients, the presence or absence of cataplexy is not associated with measurable differences in most treatments or patient outcomes examined in this study.**
- **All narcolepsy patients, regardless of cataplexy status, should be evaluated regularly for comorbid illnesses.**

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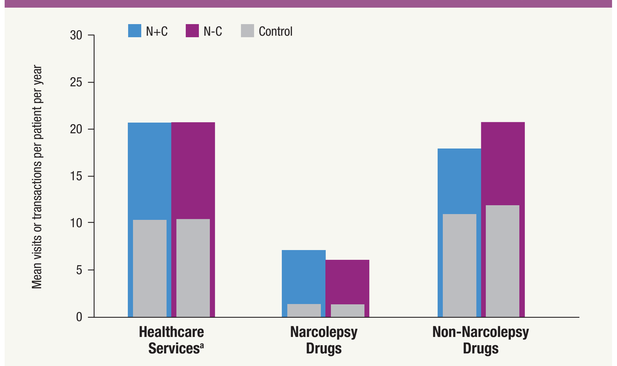
* ICD9 codes: 347.0, 347.00, 347.01, 347.1, 347.10 or 347.11; N+C identified by any occurrence of 347.01 or 347.11

Table 1. Population prevalence of all 18 CCSM level 1 categories in narcolepsy patients by cataplexy status (% of patients)

CCSM Category[a]	N+C, % (N=1890)	N-C, % (N=7422)
01 Infectious and parasitic diseases	65.5	68.4
02 Neoplasms	56.2	55.6
03 Endocrine; nutritional; and metabolic diseases and immunity disorders	80.5	82.0
04 Diseases of the blood and blood-forming organs	30.0	30.9
05 Mental illness	60.7	62.7
06x Diseases of the nervous system/sense organs, excepting narcolepsy	87.2	87.6
07 Diseases of the circulatory system	80.7	81.0
08 Diseases of the respiratory system	88.8	91.4 *
09 Diseases of the digestive system	75.2	73.6
10 Diseases of the genitourinary system	78.1	77.3
11 Complications of pregnancy; childbirth; and the puerperium	12.9	10.9
12 Diseases of skin and subcutaneous tissue	62.5	64.0
13 Diseases of the musculoskeletal system and connective tissue	87.7	90.0
14 Congenital anomalies	13.0	14.2
15 Certain conditions originating in the perinatal period	1.3	1.8
16 Injury and poisoning	71.5	72.3
17 Symptoms; signs; and ill-defined conditions and factors influencing health status	96.5	97.1
18 Residual codes; unclassified; all E codes	87.9	91.2 *

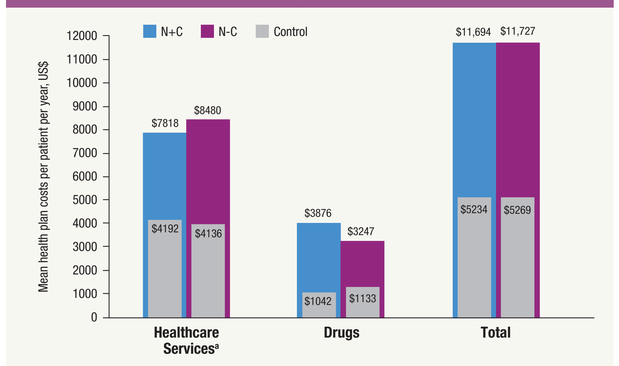
* P<0.05 by Chi-square test; adjusted using the Bonferroni method to correct for multiple testing; [a] CCSM=Clinical Classification Software for ICD-9 diagnosis codes, multi-level[6]; Note: Comparative prevalence of each CCSM category was significantly higher in narcolepsy compared to controls (p<0.0001), except CCSM 11 and 15 (difference not significant)

Figure 1. Healthcare service and drug utilization in narcolepsy patients by cataplexy status vs controls. All comparisons versus respective controls p<0.0001. N+C versus N-C non-significant for healthcare services; drug comparisons, p<0.01



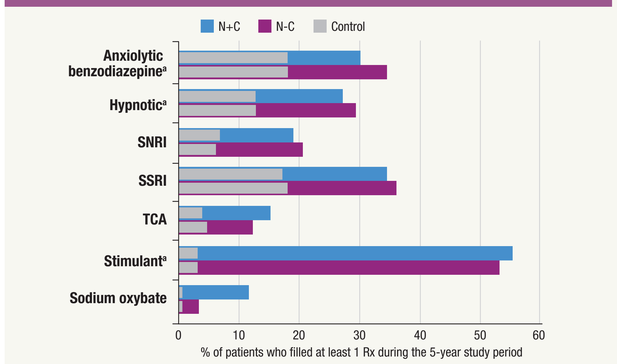
[a] Healthcare services include: Inpatient admissions; emergency department visits; outpatient visits (hospital and other); physician visits

Figure 2. Mean annualized health plan costs in narcolepsy patients by cataplexy status vs controls. All comparisons versus respective controls, p<0.0001. N+C versus N-C, non-significant for total costs; other comparisons p<0.05



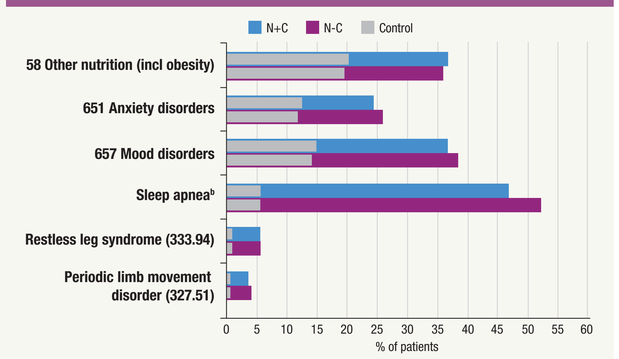
[a] Healthcare services include: Inpatient admissions; emergency department visits; outpatient visits (hospital and other); physician visits

Figure 3. Narcolepsy drug exposure in narcolepsy patients by cataplexy status vs controls. All comparisons versus respective controls, p<0.0001. N+C versus N-C, p<0.05 for anxiolytic benzodiazepines, TCAs, and sodium oxybate



[a] **Anxiolytic benzodiazepines:** Alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, flurazepam, lorazepam, oxazepam; **Hypnotics:** Estazolam, quarazepam, temazepam, triazolam, mirtazapine, trazadone, chloral hydrate, eszopiclone, ramelteon, zaleplon, zolpidem; **Stimulants:** amphetamine, armodafinil, benzphetamine, dexmethylphenidate, dextroamphetamine, diethylpropion, lisdexamfetamine, methamphetamine, methylphenidate, modafanil, pemoline, phendimetrazine, phentermine, atomexetine

Figure 4. Population prevalence of targeted comorbidities[a] in narcolepsy patients by cataplexy status vs controls. All comparisons versus respective controls, p<0.0001. N+C versus N-C, p<0.01 for sleep apnea



[a] Conditions defined by single-level CCS category[6] or ICD-9 diagnosis codes
[b] Sleep apnea, ICD-9 codes 327.20, 327.21, 327.23, 327.27, 327.29

ABSTRACT

INTRODUCTION: There is a lack of data on burden of illness and comorbidity prevalence in patients having narcolepsy with cataplexy (N+C).

METHODS: Truven Health Analytics MarketScan® Research Databases were accessed to identify individuals >18 years of age, continuously insured between 2006 and 2010, with at least one diagnosis code for narcolepsy with cataplexy (347.01, 347.11) in any claim during the 5-year study period. Control subjects without narcolepsy were matched 5:1 on age, sex, region, and payer. Extensive sub-analyses were conducted to determine the validity of the narcolepsy definitions.

RESULTS: A total of 1890 subjects with N+C were identified (average age, 45.5 years; 62% female). Compared with 9450 matched controls, N+C patients had significantly (p<0.0001) higher mean (SD) rates of annual healthcare and drug utilization, including inpatient admissions (0.14 [0.27] vs 0.08 [0.19]), ED visits (0.3 [0.7] vs 0.2 [0.4]), hospital outpatient visits (2.4 [3.0] vs 1.3 [2.5]), other outpatient services (7.2 [9.8] vs 3.3 [6.8]), physician visits (11.2 [9.4] vs 5.6 [5.9]), and drug transactions (24.6 [26.0] vs 12.7 [17.2]). Mean annualized total healthcare costs per patient were $11,603 in N+C patients vs $5,233 in controls (difference, 122%). Compared with controls, patients with N+C cost health insurers an additional $2,744 on drugs, $1,211 on outpatient hospital visits, $847 on physician visits, and $719 on inpatient admissions per year (all p<0.0001). Across a wide range of comorbidities as measured by Clinical Classification System (CCS), patients with N+C showed higher frequencies of disease compared to controls, including sleep apnea, cardiovascular disease and pulmonary conditions (p<0.001).

CONCLUSIONS: Narcolepsy + cataplexy is associated with higher frequency of comorbid disease and significantly higher rates of healthcare utilization and medical costs compared with the non-narcolepsy population.

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