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Supplemental Materials

Supplemental Table 1. Prevalence of baseline risk factors

	≥2 diagnosis codes definition ^{a,b}	≥1 diagnosis code definition ^{b,c}
	Narcolepsy cohort N = 29,317	Narcolepsy cohort N = 29,317
Narcolepsy		
Number of risk factors, N (%)		
0	12,090 (41.2%)	9030 (30.8%)
≥ 1	17,227 (58.8%)	20,287 (69.2%)
≥ 2	10,056 (34.3%)	13,216 (45.1%)
≥ 3	6133 (20.9%)	8665 (29.6%)
Risk factors, N (%)		
Any cardiovascular comorbidities	11,013 (37.6%)	11,954 (40.8%)
Hypertension	10,791 (36.8%)	11,513 (39.3%)
Atherosclerosis	1251 (4.3%)	1939 (6.6%)
Heart failure	666 (2.3%)	968 (3.3%)
Atrial fibrillation	558 (1.9%)	721 (2.5%)
Stroke	278 (0.9%)	478 (1.6%)
Transient ischemic attack	151 (0.5%)	320 (1.1%)
Myocardial infarction	102 (0.3%)	176 (0.6%)
Unstable angina	33 (0.1%)	86 (0.3%)
Cardiac arrest	18 (0.1%)	26 (0.1%)
Any cardiometabolic comorbidities	11,219 (38.3%)	14,627 (49.9%)
Diabetes/obesity	8073 (27.5%)	11,233 (38.3%)
Hyperlipidemia	6997 (23.9%)	8834 (30.1%)
Edema	1116 (3.8%)	2260 (7.7%)
Metabolic syndrome	172 (0.6%)	366 (1.2%)
Any renal comorbidities	1010 (3.4%)	1542 (5.3%)
Chronic kidney disease	750 (2.6%)	1055 (3.6%)
Kidney failure	369 (1.3%)	547 (1.9%)
Proteinuria	151 (0.5%)	316 (1.1%)
Liver cirrhosis	85 (0.3%)	120 (0.4%)
Sleep apnea	7449 (25.4%)	10,452 (35.7%)
	≥2 diagnosis codes definition ^{a,b}	≥1 diagnosis code definition ^{b,c}
	Idiopathic hypersomnia cohort N = 11,951	Idiopathic hypersomnia cohort N = 11,951
Idiopathic hypersomnia		
Number of risk factors, N (%)		
0	4409 (36.9%)	3054 (25.6%)
≥ 1	7542 (63.1%)	8897 (74.4%)
≥ 2	4321 (36.2%)	5780 (48.4%)
≥ 3	2540 (21.3%)	3702 (31.0%)
Risk factors, N (%)		
Any cardiovascular comorbidities	4467 (37.4%)	4805 (40.2%)
Hypertension	4380 (36.6%)	4635 (38.8%)
Atherosclerosis	433 (3.6%)	699 (5.8%)
Heart failure	214 (1.8%)	330 (2.8%)
Atrial fibrillation	255 (2.1%)	326 (2.7%)
Stroke	74 (0.6%)	138 (1.2%)
Transient ischemic attack	55 (0.5%)	98 (0.8%)
Myocardial infarction	28 (0.2%)	49 (0.4%)
Unstable angina	18 (0.2%)	34 (0.3%)
Cardiac arrest	4 (0.0%)	10 (0.1%)
Any cardiometabolic comorbidities	4738 (39.6%)	6185 (51.8%)
Diabetes/obesity	3346 (28.0%)	4738 (39.6%)
Hyperlipidemia	2912 (24.4%)	3664 (30.7%)
Edema	330 (2.8%)	803 (6.7%)
Metabolic syndrome	109 (0.9%)	179 (1.5%)
Any renal comorbidities	315 (2.6%)	506 (4.2%)
Chronic kidney disease	247 (2.1%)	339 (2.8%)
Kidney failure	91 (0.8%)	163 (1.4%)
Proteinuria	45 (0.4%)	90 (0.8%)
Liver cirrhosis	20 (0.2%)	36 (0.3%)
Sleep apnea	3770 (31.5%)	5540 (46.4%)

^aRisk factors were identified by requiring ≥2 diagnosis codes for the comorbidity on distinct dates during the baseline period. ^bFor hypertension, hyperlipidemia, and diabetes/obesity, prescription fills for related medications were also considered an indicator of the risk factor. ^cRisk factors were identified by requiring ≥1 diagnosis code for the comorbidity during the baseline period.

Supplemental Table 2. All-cause HCRU

Narcolepsy				
	Higher-risk narcolepsy ^a N = 17,227	Lower-risk narcolepsy N = 12,090	IRR [95% CI]	<i>P</i> value
All-cause HCRU PPPY				
OP visits (patients with ≥1 visit), n (%)				
Number of OP visits, mean ± SD [median]	32.2 ± 32.5 [23.5]	19.3 ± 19.8 [13.5]	1.67 [1.63, 1.71]	<0.001
ED visits (patients with ≥1 visit), n (%)				
Number of ED visits, mean ± SD [median]	1.2 ± 4.2 [0.6]	0.8 ± 2.0 [0.4]	1.61 [1.51, 1.72]	<0.001
IP visits (patients with ≥1 visit), n (%)				
Number of IP days, mean ± SD [median]	2.4 ± 13.7 [0.0]	0.6 ± 4.3 [0.0]	4.19 [3.54, 4.94]	<0.001
Idiopathic hypersomnia				
	Higher-risk idiopathic hypersomnia ^a N = 7542	Lower-risk idiopathic hypersomnia N = 4409	IRR [95% CI]	<i>P</i> value
All-cause HCRU PPPY				
OP visits (patients with ≥1 visit), n (%)				
Number of OP visits, mean ± SD [median]	30.3 ± 27.4 [23.6]	20.4 ± 17.7 [15.1]	1.48 [1.44, 1.53]	<0.001
ED visits (patients with ≥1 visit), n (%)				
Number of ED visits, mean ± SD [median]	1.0 ± 3.3 [0.4]	0.6 ± 1.3 [0.3]	1.57 [1.43, 1.72]	<0.001
IP visits (patients with ≥1 visit), n (%)				
Number of IP days, mean ± SD [median]	1.1 ± 6.6 [0.0]	0.3 ± 2.5 [0.0]	3.20 [2.43, 4.23]	<0.001

^aUsing the ≥2 diagnosis codes definition.
CI, confidence interval; ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; IRR, incidence rate ratio; OP, outpatient; PPPY, per-patient-per-year; SD, standard deviation.

Supplemental Table 3. NCO-related HCRU

Narcolepsy				
	Higher-risk narcolepsy ^a N = 17,227	Lower-risk narcolepsy N = 12,090	IRR [95% CI]	<i>P</i> value
NCO-related HCRU PPPY				
OP visits (patients with ≥1 visit), n (%)				
Number of OP visits, mean ± SD [median]	3.7 ± 9.2 [1.0]	1.5 ± 3.4 [0.0]	2.51 [2.37, 2.65]	<0.001
ED visits (patients with ≥1 visit), n (%)				
Number of ED visits, mean ± SD [median]	0.2 ± 0.8 [0.0]	0.0 ± 0.2 [0.0]	5.43 [4.79, 6.16]	<0.001
IP visits (patients with ≥1 visit), n (%)				
Number of IP days, mean ± SD [median]	1.6 ± 11.1 [0.0]	0.2 ± 1.9 [0.0]	10.46 [8.16, 13.41]	<0.001
Idiopathic hypersomnia				
	Higher-risk idiopathic hypersomnia ^a N = 7542	Lower-risk idiopathic hypersomnia N = 4409	IRR [95% CI]	<i>P</i> value
NCO-related HCRU PPPY				
OP visits (patients with ≥1 visit), n (%)				
Number of OP visits, mean ± SD [median]	3.4 ± 7.7 [0.7]	1.5 ± 3.4 [0.0]	2.23 [2.05, 2.42]	<0.001
ED visits (patients with ≥1 visit), n (%)				
Number of ED visits, mean ± SD [median]	0.1 ± 0.4 [0.0]	0.0 ± 0.1 [0.0]	5.04 [4.13, 6.16]	<0.001
IP visits (patients with ≥1 visit), n (%)				
Number of IP days, mean ± SD [median]	0.7 ± 5.9 [0.0]	0.1 ± 0.8 [0.0]	8.80 [5.42, 14.29]	<0.001

^aUsing the ≥2 diagnosis codes definition.
CI, confidence interval; ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; IRR, incidence rate ratio; NCO, negative clinical outcome; OP, outpatient; PPPY, per-patient-per-year; SD, standard deviation.

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Supplemental Table 4. Risk Factor-Related HCRU

Narcolepsy	
RF-related ^a HCRU PPPY	Higher-risk narcolepsy ^b N = 17,227
OP visits (patients with ≥1 visit), n (%)	14,046 (81.5%)
Number of OP visits, mean ± SD [median]	5.8 ± 12.2 [2.6]
ED visits (patients with ≥1 visit), n (%)	4041 (23.5%)
Number of ED visits, mean ± SD [median]	0.2 ± 1.4 [0.0]
IP visits (patients with ≥1 visit), n (%)	1665 (9.7%)
Number of IP days, mean ± SD [median]	0.6 ± 6.1 [0.0]
Idiopathic hypersomnia	
RF-related ^a HCRU PPPY	Higher-risk idiopathic hypersomnia ^b N = 7542
OP visits (patients with ≥1 visit), n (%)	5928 (78.6%)
Number of OP visits, mean ± SD [median]	5.0 ± 7.8 [2.5]
ED visits (patients with ≥1 visit), n (%)	1417 (18.8%)
Number of ED visits, mean ± SD [median]	0.1 ± 0.6 [0.0]
IP visits (patients with ≥1 visit), n (%)	473 (6.3%)
Number of IP days, mean ± SD [median]	0.2 ± 1.7 [0.0]

^aRF-related HCRU was restricted to higher-risk individuals by design. ^bUsing the ≥2 diagnosis codes definition. ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; OP, outpatient; PPPY, per-patient-per-year; RF, risk factor; SD, standard deviation.

Supplemental Table 5. All-Cause Healthcare Costs

Narcolepsy				
All-cause healthcare costs PPPY (2024 USD)	Higher-risk narcolepsy ^a N = 17,227	Lower-risk narcolepsy N = 12,090	Mean difference [95% CI]	P value
Total healthcare costs (\$), mean ± SD [median]	35,193.0 ± 59,687.0 [17,099.8]	21,341.4 ± 39,281.3 [7815.0]	13,851.6 [12,718.2, 14,985.0]	<0.001
Medical costs	21,564.3 ± 41,950.2 [10,242.8]	10,520.6 ± 19,371.4 [5156.7]	11,043.7 [10,328.4, 11,759.0]	<0.001
IP costs	5705.5 ± 19,666.1 [0.0]	1982.5 ± 8694.7 [0.0]	3722.9 [3390.9, 4055.0]	<0.001
OP costs	14,511.6 ± 31,639.7 [7620.6]	7744.3 ± 15,223.6 [4113.1]	6767.3 [6222.5, 7312.2]	<0.001
ED costs	1347.2 ± 3347.7 [370.1]	793.7 ± 2245.7 [165.1]	553.4 [489.4, 617.5]	<0.001
Pharmacy costs	13,628.7 ± 40,534.9 [2878.7]	10,820.8 ± 33,214.2 [925.4]	2807.9 [1961.2, 3654.6]	<0.001
Idiopathic hypersomnia				
All-cause healthcare costs PPPY (2024 USD)	Higher-risk idiopathic hypersomnia ^a N = 7542	Lower-risk idiopathic hypersomnia N = 4409	Mean difference [95% CI]	P value
Total healthcare costs (\$), mean ± SD [median]	26,201.3 ± 40,903.0 [13,892.1]	15,160.2 ± 25,802.2 [7222.7]	11,041.1 [9844.4, 12,237.8]	<0.001
Medical costs	17,546.4 ± 28,572.7 [9173.8]	10,145.4 ± 17,681.5 [5223.8]	7401.0 [6571.4, 8230.5]	<0.001
IP costs	3748.8 ± 14,434.9 [0.0]	1453.3 ± 8389.7 [0.0]	2295.4 [1886.2, 2704.6]	<0.001
OP costs	12,683.3 ± 20,570.2 [7328.4]	8058.9 ± 13,840.6 [4381.8]	4624.3 [4006.0, 5242.7]	<0.001
ED costs	1114.3 ± 3656.7 [230.5]	633.1 ± 1563.5 [104.2]	481.2 [386.7, 575.8]	<0.001
Pharmacy costs	8654.9 ± 24,739.7 [1924.6]	5014.8 ± 17,212.8 [852.0]	3640.1 [2885.3, 4395.0]	<0.001

^aUsing the ≥2 diagnosis codes definition. CI, confidence interval; ED, emergency department; IP, inpatient; OP, outpatient; PPPY, per-patient-per-year; SD, standard deviation; USD, United States dollar.

Supplemental Table 6. NCO-Related Healthcare Costs

Narcolepsy				
NCO-related healthcare costs PPPY (2024 USD)	Higher-risk narcolepsy ^a N = 17,227	Lower-risk narcolepsy N = 12,090	Mean difference [95% CI]	P value
Total healthcare costs (\$), mean ± SD [median]	6671.8 ± 19,830.6 [458.2]	1738.7 ± 7116.5 [3.8]	4933.1 [4610.9, 5255.2]	<0.001
Medical costs	6074.6 ± 19,251.0 [368.0]	1641.0 ± 6940.4 [0.0]	4433.6 [4120.6, 4746.5]	<0.001
IP costs	3409.8 ± 15,469.3 [0.0]	661.9 ± 5532.4 [0.0]	2747.9 [2496.7, 2999.1]	<0.001
OP costs	2379.5 ± 7211.9 [259.5]	921.5 ± 3248.5 [0.0]	1458.1 [1335.8, 1580.3]	<0.001
ED costs	285.2 ± 1343.0 [0.0]	57.6 ± 479.9 [0.0]	227.6 [205.8, 249.4]	<0.001
Pharmacy costs	597.2 ± 2189.9 [6.9]	97.7 ± 795.0 [0.0]	499.5 [463.9, 535.2]	<0.001
Idiopathic hypersomnia				
NCO-related healthcare costs PPPY (2024 USD)	Higher-risk idiopathic hypersomnia ^a N = 7542	Lower-risk idiopathic hypersomnia N = 4409	Mean difference [95% CI]	P value
Total healthcare costs (\$), mean ± SD [median]	5052.7 ± 15,817.0 [246.2]	1324.0 ± 5213.0 [0.0]	3728.6 [3339.9, 4117.3]	<0.001
Medical costs	4597.6 ± 15,293.7 [198.2]	1257.4 ± 5123.0 [0.0]	3340.2 [2963.4, 3717.0]	<0.001
IP costs	2166.7 ± 11,404.6 [0.0]	336.6 ± 3620.8 [0.0]	1830.1 [1551.4, 2108.8]	<0.001
OP costs	2220.9 ± 7138.0 [159.4]	871.5 ± 2986.0 [0.0]	1349.4 [1165.8, 1533.1]	<0.001
ED costs	210.0 ± 1263.9 [0.0]	49.4 ± 664.4 [0.0]	160.6 [126.0, 195.3]	<0.001
Pharmacy costs	455.0 ± 1717.4 [2.7]	66.6 ± 456.3 [0.0]	388.4 [347.4, 429.5]	<0.001

^aUsing the ≥2 diagnosis codes definition. CI, confidence interval; ED, emergency department; IP, inpatient; NCO, negative clinical outcome; OP, outpatient; PPPY, per-patient-per-year; SD, standard deviation; USD, United States dollar.

Supplemental Table 7. Risk Factor-Related Healthcare Costs

Narcolepsy	
RF-related ^a healthcare costs PPPY (2024 USD)	Higher-risk narcolepsy ^b N = 17,227
Total healthcare costs (\$), mean ± SD [median]	6182.2 ± 17,904.3 [1326.1]
Medical costs	5020.1 ± 17,034.5 [979.3]
IP costs	1511.6 ± 8605.5 [0.0]
OP costs	3157.3 ± 13,256.5 [763.6]
ED costs	351.2 ± 1800.3 [0.0]
Pharmacy costs	1162.1 ± 3862.7 [72.9]
Idiopathic hypersomnia	
RF-related ^a healthcare costs PPPY (2024 USD)	Higher-risk idiopathic hypersomnia N = 7542 ^b
Total healthcare costs (\$), mean ± SD [median]	4762.2 ± 10,994.5 [1127.2]
Medical costs	3820.6 ± 9600.1 [856.7]
IP costs	957.8 ± 5793.9 [0.0]
OP costs	2600.4 ± 6163.7 [710.8]
ED costs	262.4 ± 1825.4 [0.0]
Pharmacy costs	941.5 ± 3798.4 [59.1]

^aRF-related costs were restricted to higher-risk individuals by design. ^bUsing the ≥2 diagnosis codes definition. ED, emergency department; IP, inpatient; PPPY, per-patient-per-year; OP, outpatient; RF, risk factor; SD, standard deviation; USD, United States dollar.