Narcolepsy: A Clinical Perspective.

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A Case Example From My Clinic.

A 35-year-old woman with daytime sleepiness for 20 years.

Weakness in the jaw and neck with laughter in the past.

Seeking medical attention now because moved to the US from Europe.

Day of the Study

Getting married that weekend.

PSG normal, TST 470 minutes, REM latency 12 minutes.

MSLT MSL 4 minutes and 2 SOREMPs.

Recommendations.
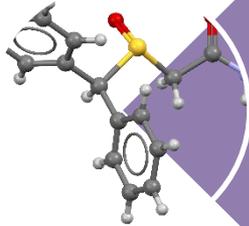

Modafinil

Napping

Avoid drowsy driving

Stigmas

Characteristics	Narcolepsy (n = 122)	Control (n = 93)	Mann-Whitney U*P* value
Perceived Stigma (SSIS) Total Score	52.3 ± 14.4	30.9 ± 10.5	<0.001
Social Rejection	17.8 ± 5.8	10.7 ± 3.4	<0.001
Financial Insecurity	7.3 ± 2.8	4.1 ± 1.8	<0.001
Internalized Shame	10.2 ± 3.4	7.0 ± 2.8	<0.001
Social Isolation	17.1 ± 5.3	9.2 ± 3.7	<0.001
Disclosure Concerns	23.8 ± 7.7	15.6 ± 5.8	<0.001
HADS Anxiety	8.2 ± 4.3	6.7 ± 3.9	0.011
HADS Depression	7.1 ± 4.4	3.2 ± 2.9	<0.001
SF36 QOL (norm-based)			
Physical Function (PF)	49.2 ± 10.4	54.9 ± 4.0	<0.001
Bodily Pain (BP)	49.3 ± 10.9	53.1 ± 6.6	0.027
Role Physical (RP)	39.5 ± 10.4	53.5 ± 6.1	<0.001
General Health (GH)	43.8 ± 10.7	52.4 ± 8.4	<0.001
Vitality (V)	37.0 ± 8.7	48.2 ± 7.6	<0.001
Social Functioning (SF)	36.5 ± 13.7	49.7 ± 7.6	<0.001
Role Emotional (RE)	42.4 ± 12.8	47.1 ± 11.3	0.006
Mental Health (MH)	42.4 ± 10.9	47.5 ± 8.3	<0.001
FOSQ Total Score	13.3 ± 3.0	18.4 ± 1.9	<0.001
Activity Level	2.3 ± 0.7	3.6 ± 0.4	<0.001
Vigilance	2.4 ± 0.7	3.5 ± 0.6	<0.001
Productivity	2.7 ± 0.7	3.8 ± 0.3	<0.001
Intimacy & Sexual Relationship	3.0 ± 0.8	3.6 ± 0.6	<0.001
Social Outcome	2.8 ± 0.9	3.8 ± 0.4	<0.001
ESS Score	16.0 ± 4.6	7.7 ± 4.4	<0.001
PSQI Global Score	14.9 ± 7.1	10.4 ± 5.8	<0.001

Analyses are reported as mean ± SD. SSIS-Stigma and Social Impact Scale, HADS-Hospital Anxiety and Depression Scale, SF36—Short Form Health Survey, QOL- Quality of Life, FOSQ—Functional Outcomes of Sleep Questionnaire, ESS- Epworth Sleepiness Scale, PSQI-Pittsburgh Sleep Quality Index.

doi:10.1371/journal.pone.0122478.t002

Kapella MC, Berger BE, Vern BA, Vispute S, Prasad B, Carley DW. Health-related stigma as a determinant of functioning in young adults with narcolepsy. PLoS One. 2015;10(4): e0122478. doi:10.1371/journal.pone.0122478

# Follow Up.
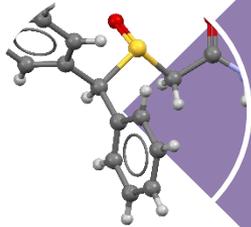
Modafinil

Napping
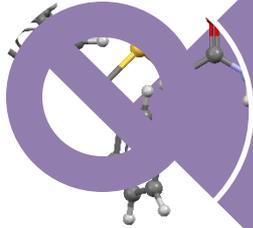
Avoid drowsy driving

Modafinil

Napping

Avoid drowsy driving

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Husband

Is narcolepsy real? Anyway you don't have it.

Don't embarrass me in front of my family.

Just stay awake. You have control.

Don't say you are too drowsy to drive.
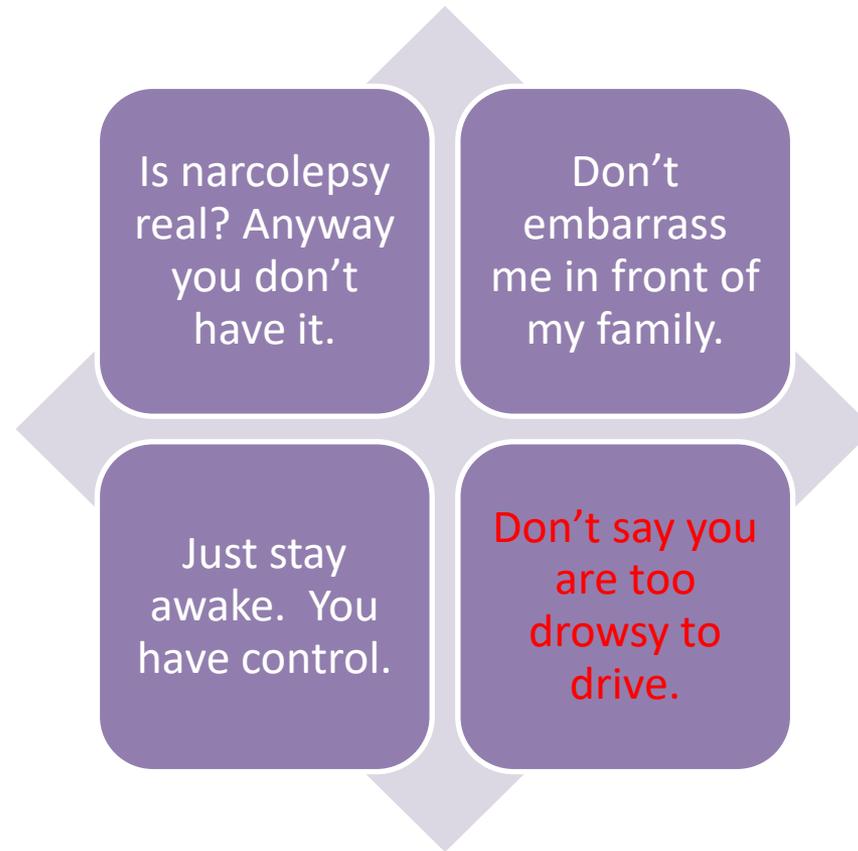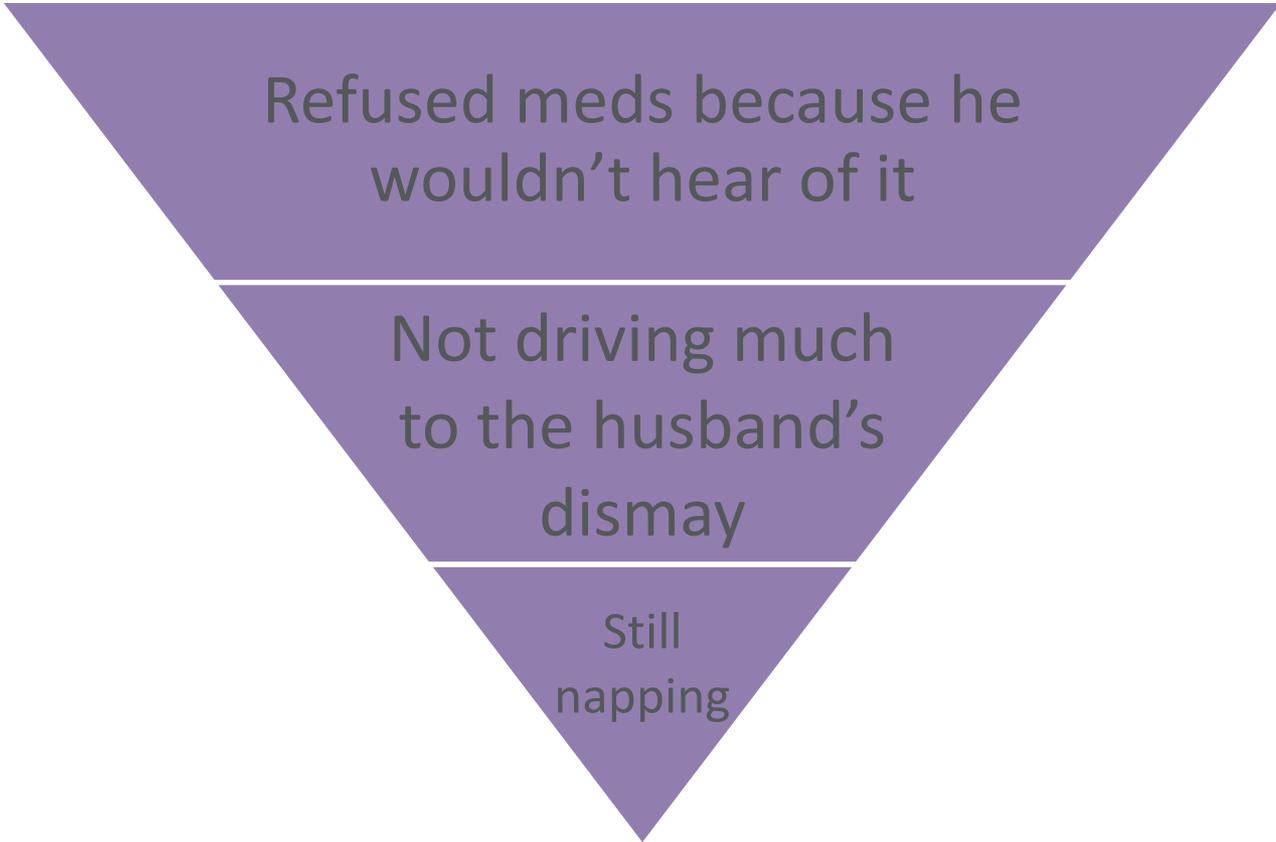
Another Case example

A 28-year-old woman with daytime sleepiness for 7 years.

+Cataplexy twice a week on average +Frequent SP and HH

PSG/MSLT ordered

Insurance Struggles: testing.

Denied	Need to rule out sleep apnea. P2P not helpful

Six weeks later

HSAT done: No OSA	Denied. Need to rule out sleep apnea by a PSG P2P not helpful.

Two months later

PSG done: No OSA	Finally, PSG MSLT approved. Completed 3 months later. Consistent with Narcolepsy
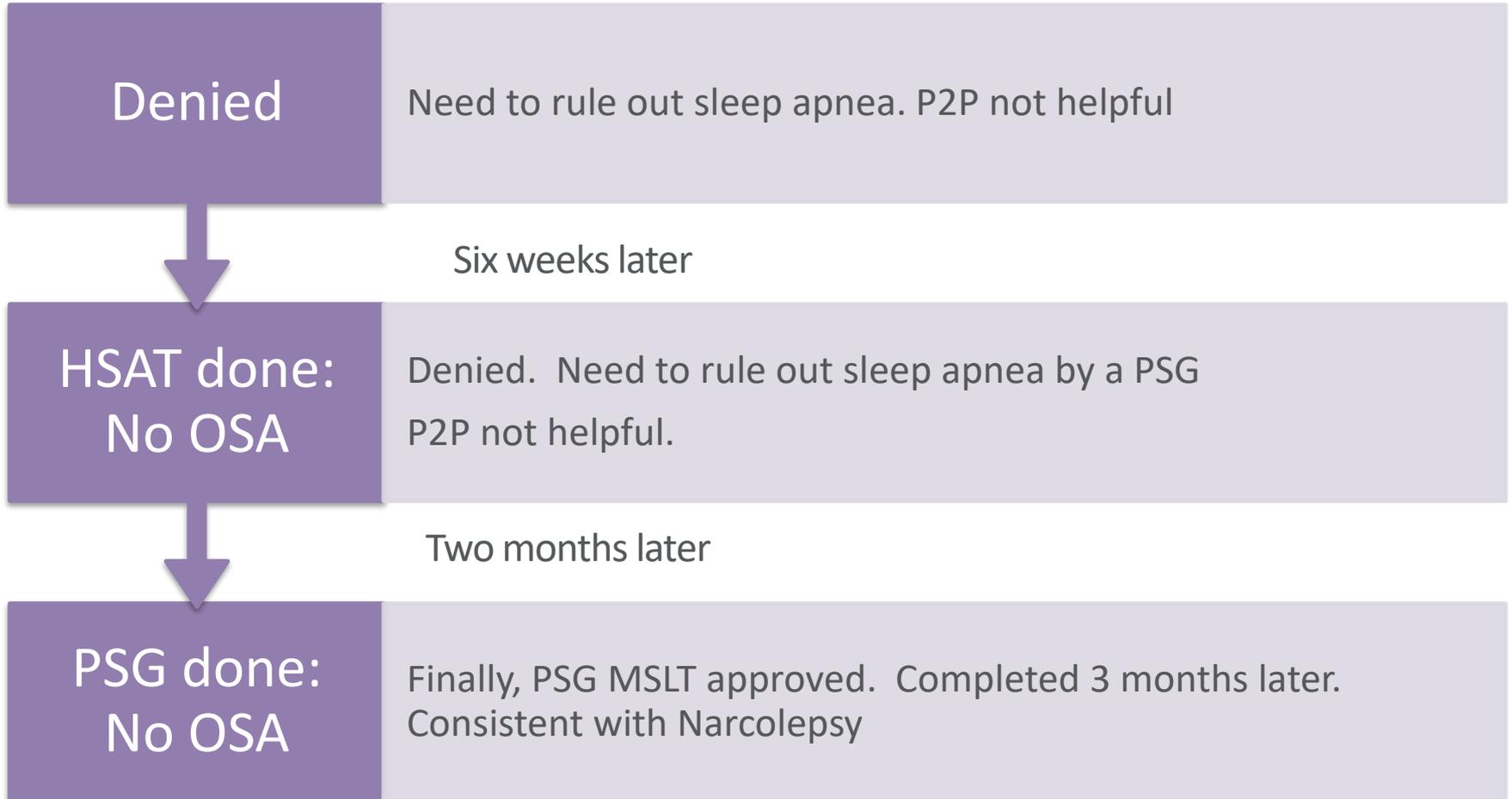
Insurance Struggles: Treatment

|	
Modafinil	Denied. Needs to fail a stimulant
Stimulant	Denied. Doesn't have indication for Narcolepsy. Only Modafinil does.
Stimulant tried and failed	Patient paid OOP for the stimulant. Modafinil finally approved.
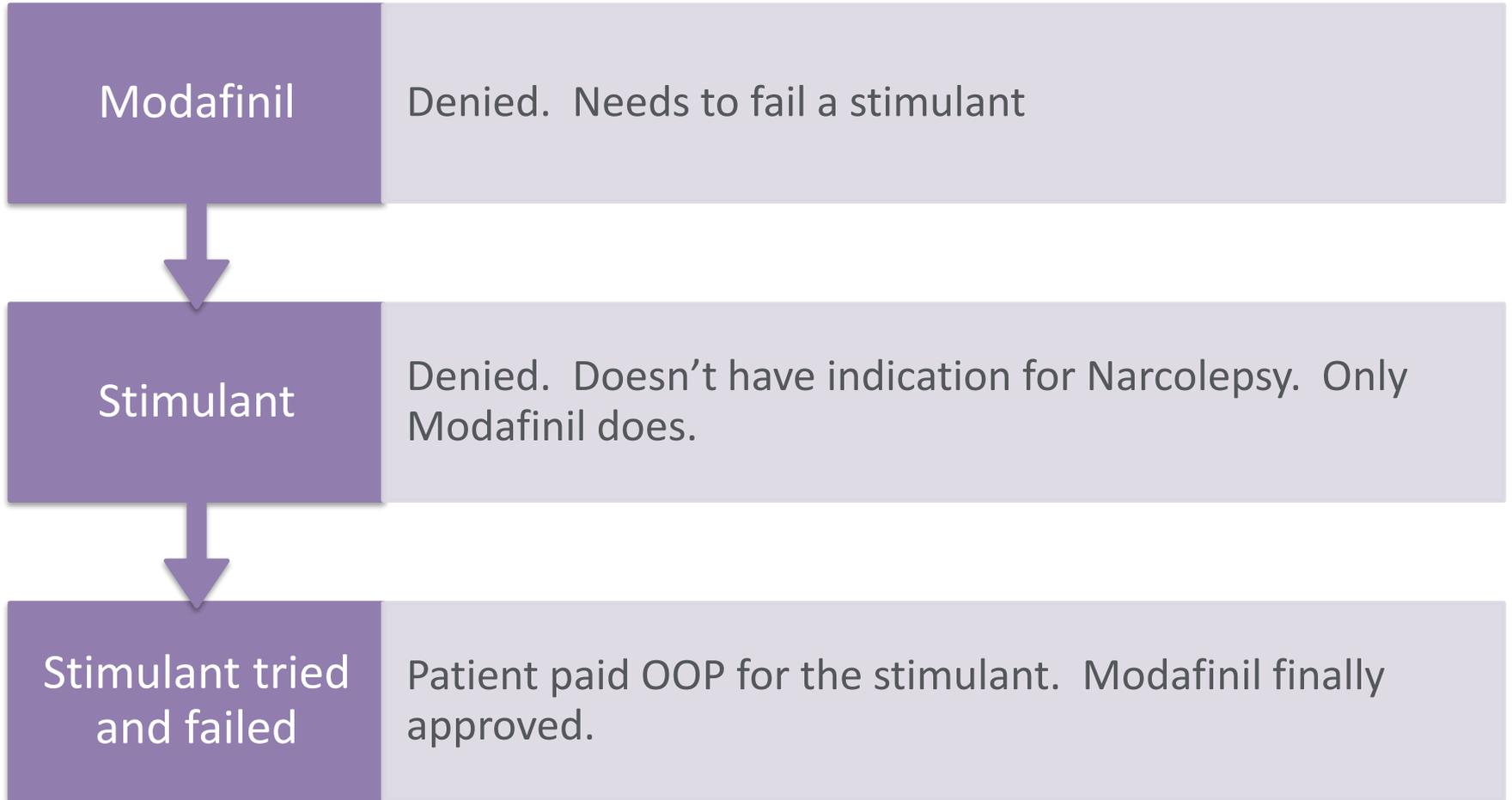
Health Care Utilization.

Figure 3—Health care resource use in the year prior to narcolepsy diagnosis, 2013–2018.
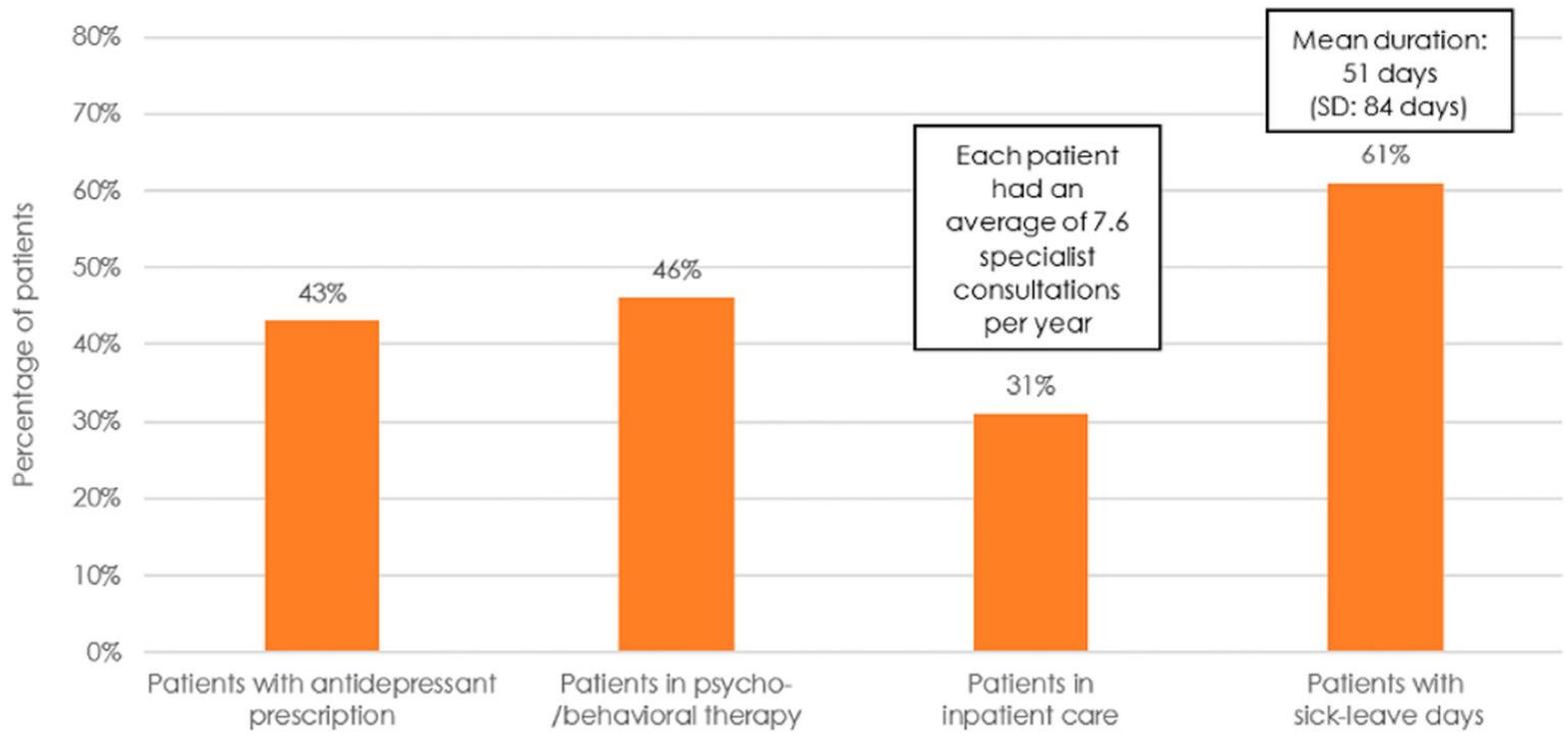
Sick leave days are related to employees in the sense of social security (n = 229). Number of specialist consultations is related to all patients and patients treated as non-inpatients. SD = standard deviation.

Kallweit U, Nilius G, Trümper D, Vogelmann T, Schubert T. Prevalence, incidence, and health care utilization of patients with narcolepsy: a population-representative study. J Clin Sleep Med. 2022;18(6):1531-1537. doi: 10.5664/jcsm.9910.

Insurance Denials.
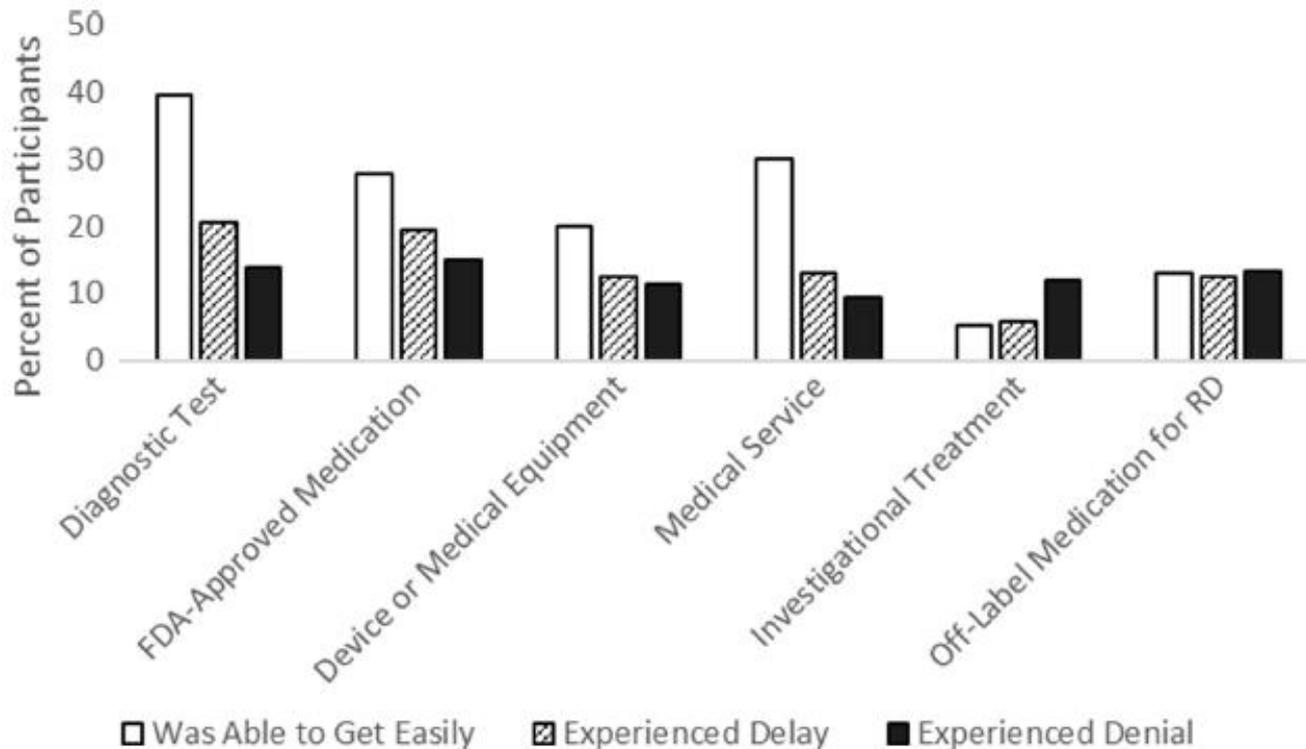
Fig. 4 Experiences with US health insurance approvals, delays, and denials for RD tests, medications, treatments, and services

Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P; Chloe Barnes Advisory Council on Rare Diseases. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022 May 12;17(1):196

OOP Expenses.
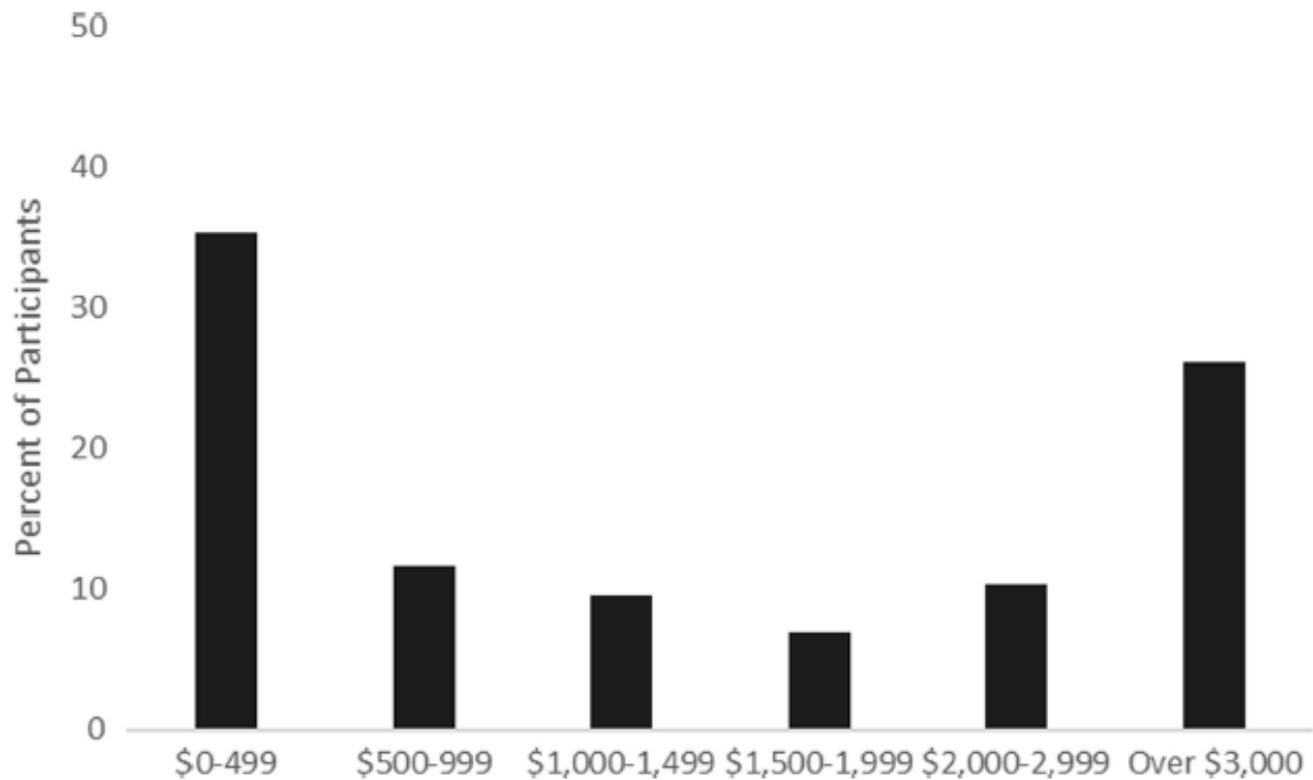
Fig. 3 Self-reported out-of-pocket expenses for health claims in 2019 (USD)

Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P; Chloe Barnes Advisory Council on Rare Diseases. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022 May 12;17(1):196

Final Case Example.

A 56-year-old man presents because he fell out of bed during dream enactment two months ago.

Always has been sleepy during the day.

Fragmented sleep.

No recollection of cataplexy. Past SP and HH

PSG/MSLT ordered

Day of the Study

PSG shows occasional RSWA.

Otherwise normal, TST 484 minutes, REM latency 76 minutes.

MSLT MSL 3.2 minutes and 4 SOREMPs.

History

Failed grad school due to sleepiness.

Treated for depression several times

Stands at work during meetings

"It's not like I have Narcolepsy"

Labeled as lazy

Skips lunch to nap in his car

Recommendations.

Stimulants
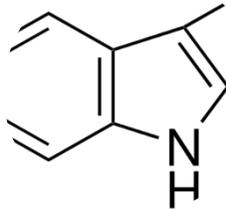
Melatonin

Avoid drowsy driving

Diagnostic Delay

Table 1
Studies reporting a specific duration (mean or median) of the delay between narcolepsy symptom onset and diagnosis.

Study (country)[reference]	Type of study (N)	Age at symptom onset, years		Age at diagnosis, years		Diagnostic delay, years	
		Mean (variance)	Median (range)	Mean (variance)	Median (range)	Mean (variance)	Median (range)
Broughton et al. (Canada) [25]	Clinical trial (75)	–	–	–	–	16 (SD 13)	–
Dauvilliers et al. (France) [26]	Patient survey (300)	23.7 (11.8)	–	42.9 (16.5)	–	20.2 (16.2)	–
Dauvilliers et al. (Canada) [26]	Patient survey (189)	22.9 (12.7)	–	44.0 (15.9)	–	22.1 (16.7)	–
Thorpy et al. (United States) [19]	Patient survey (1035)	19.2 (9.8)	16.0[a]	34.5 (12.6)	–	19.3 (21.4)	–
Morrish et al. (United Kingdom) [17]	Patient survey (219)	–	18 (range 1–68)	36	35	15	10.5 (0–61)
BaHammam et al. (Saudi Arabia) [29]	PSG (47)	20.5 (1.4)	–	28.9 (1.8)	(9–65)	8.4 (1.2)	–
Campbell et al. (New Zealand) [30]	Patient survey (54)	20.7 (9.7)	–	–	–	–	–
Ingravallo et al. (Italy) [13]	Observational (100)	21.0 (10.4)	19.0 (3–48)	29.7 (SD 11.1)	30.0 (10–62)	8.7 (8.5)	6.0 (0–37)
Frauscher et al. (Austria) [32]	PSG (100)	–	20 (6–69)	–	32 (12–74)	12	6.5 (0–39)
Luca et al. (9 European countries) [24]	Retrospective database analysis (1099)	22.7 (11.9) [EDS][b]	20 (3–80) [EDS][b]	36.9 (17.1)[c]	(4–87)	14.6 (14.3)[d]	10.5 (<1–67)
Carter et al. (United States) [31]	Patient chart survey (252)	–	–	–	–	–	1.8 (0–10.5)[e]

EDS, excessive daytime sleepiness; PSG, polysomnogram; SD, standard deviation.

[a] Personal communication.
[b] n = 990.
[c] n = 755.
[d] n = 738.
[e] Conservative estimate because value represents duration between symptoms first reported to a physician and diagnosis.

Thorpy MJ, Krieger AC. Delayed diagnosis of narcolepsy: characterization and impact. Sleep Med. 2014 May;15(5):502-7.

Misdiagnoses

Table 3—Mental disorder diagnoses in narcolepsy cases

| Mental Disorder	Odds ratio	95% lower CL	95% upper CL	Prob
290-294 Organic psychotic conditions	3.00	0.35	25.68	0.2918
295-299 Other psychoses	0.94	0.12	7.06	0.9493
300-316 Nonpsychotic mental disorders	4.47	2.70	7.41	<0.0001
300 Neurotic disorders	2.59	1.35	4.97	0.0025
301 Personality disorders	10.00	1.67	59.85	0.0018
307 Special symptoms or syndromes, NEC	6.67	2.05	21.65	0.0003
309 Adjustment reaction	5.63	1.49	21.20	0.004
311 Depressive disorder, NEC	5.47	2.70	11.08	<0.0001

Table 4—Nervous system disorder diagnoses in narcolepsy cases

Neurological disorder	Odds ratio	95% lower CL	95% upper CL	Prob
340-349 Other disorders of the central nervous system	56.25	24.15	131.03	<0.0001
345 Epilepsy	22.50	3.76	134.65	<0.0001
346 Migraine	1.61	0.36	7.18	0.5301
347 Narcolepsy and cataplexy	93.00	42.14	205.25	<0.0001
340-346, 348-349 Other CNS EXCLUDING narcolepsy	3.74	1.32	10.59	0.0099
350-359 Disorders of the peripheral nervous system	1.07	0.14	8.16	0.9461
360-379 Disorders of the eye and adnexa	1.64	0.89	3.01	0.1123
380-389 Diseases of the ear and mastoid process	1.49	0.70	3.21	0.2967

Legend: The odds ratio and 95% confidence interval of a diagnosis having been made in narcolepsy cases (n=77) compared with N=1155 controls.

Kryger MH, Walid R, Manfreda J. Diagnoses received by narcolepsy patients in the year prior to diagnosis by a sleep specialist. Sleep 2002;25:36–41.

Comorbidities
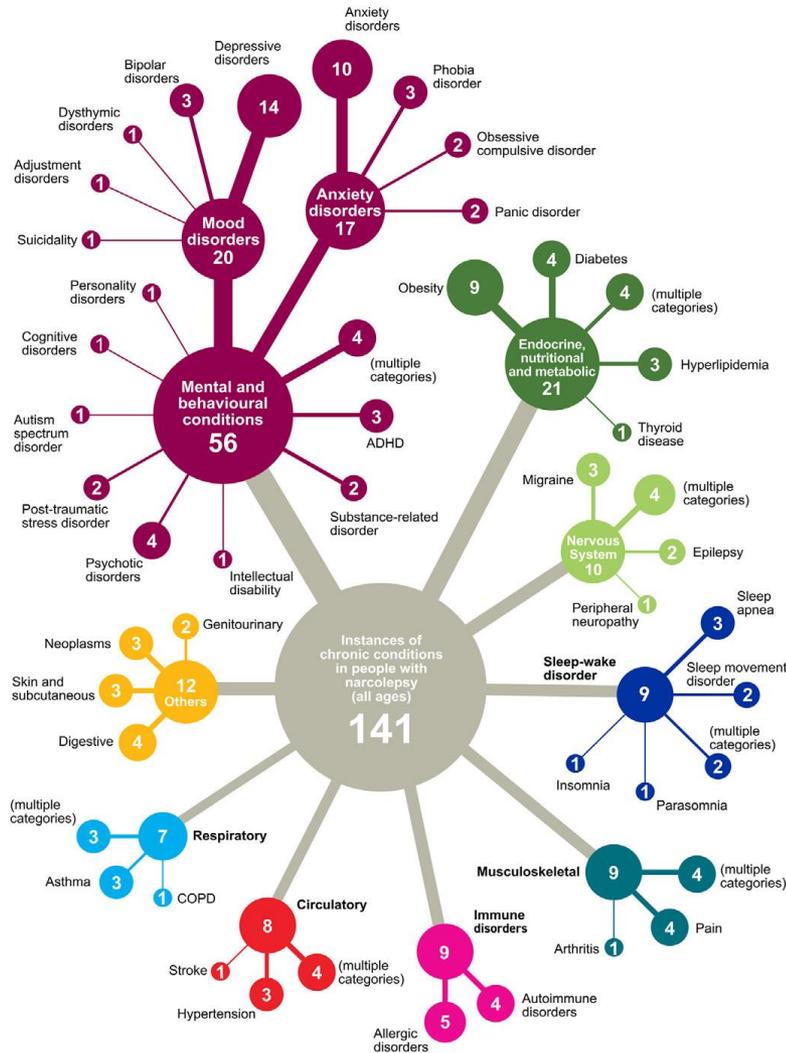
Gudka S, Haynes E, Scotney J, Mukherjee S, Frenkel S, Sivam S, Swieca J, Chamula K, Cunnington D, Saini B. Narcolepsy: Comorbidities, complexities and future directions. Sleep Med Rev. 2022;65:101669

CBT-H

**Table 1—Summary of CBT modules and activities.**

Module	Key Concepts/Activities	Suggested Session
Education about CDH	Provide education about the prevalence and etiology of narcolepsy and/or IH (as appropriate for the patient). Discuss the patient's experience with the emergence of symptoms, the journey to getting diagnosed, and the perception of others about having narcolepsy. Provide resources for learning more about narcolepsy or IH (as appropriate).	Session 1
Self-identity and self-image	Discuss self-identity and changes that have developed as the result of CDH symptoms. This includes strategies for active acceptance and value-congruent living.	Session 2
Structured daytime activities	Use of sleep/wake diaries to develop a personalized structure for scheduled naps (as appropriate) and waking activities in small segments throughout the day (Pomodoro technique). Explain the nurturing/depleting activity to evaluate energy transactions throughout the day.	Session 3
Structured nighttime activities	Use of sleep/wake diaries to develop a structure for regulating bedtime and waketime and to practice good sleep hygiene.	Session 4
Coping skills and emotion-regulation	Discuss problem-focused and emotion-focused coping strategies to manage the unpredictability and/or constancy of CDH symptoms. This include cognitive flexibility for dealing with limitations or setting a structured worry time to manage anxiety.	Session 5
Social support	Explain the importance of support from family and friends and connecting with others through patient organizations for people with CDH.	Session 5
Medical, legal, and occupational issues	Discuss disability accommodations at work/school (if applicable), disclosing CDH diagnosis at work/school, and preparing for doctor's visits.	Session 6
Other topics	Discuss topics as appropriate: (1) managing the unpredictability of cataplexy; (2) medication adherence; (3) impact of CDH symptoms on family relationships; (4) using service or emotional support animals	Optional

This table provides a summary of the CBT modules and key concepts and activities within each module. CDH including narcolepsy type 1, narcolepsy type 2, and IH. CBT = cognitive behavioral therapy, CDH = central disorders of hypersomnolence, IH = idiopathic hypersomnia.

Ong JC, Dawson SC, Mundt JM, Moore C. Developing a cognitive behavioral therapy for hypersomnia using telehealth: a feasibility study. J Clin Sleep Med. 2020;16(12):2047-2062.

On Par With other Rare Disorders.

Percent of Participants

	50
	40
	30
	20
	10
	0

0-6 Months · 7-11 Months · 1-3 Years · 4-6 Years · 7-9 Years · 10+ Years · Still Undiagnosed · Don't Know
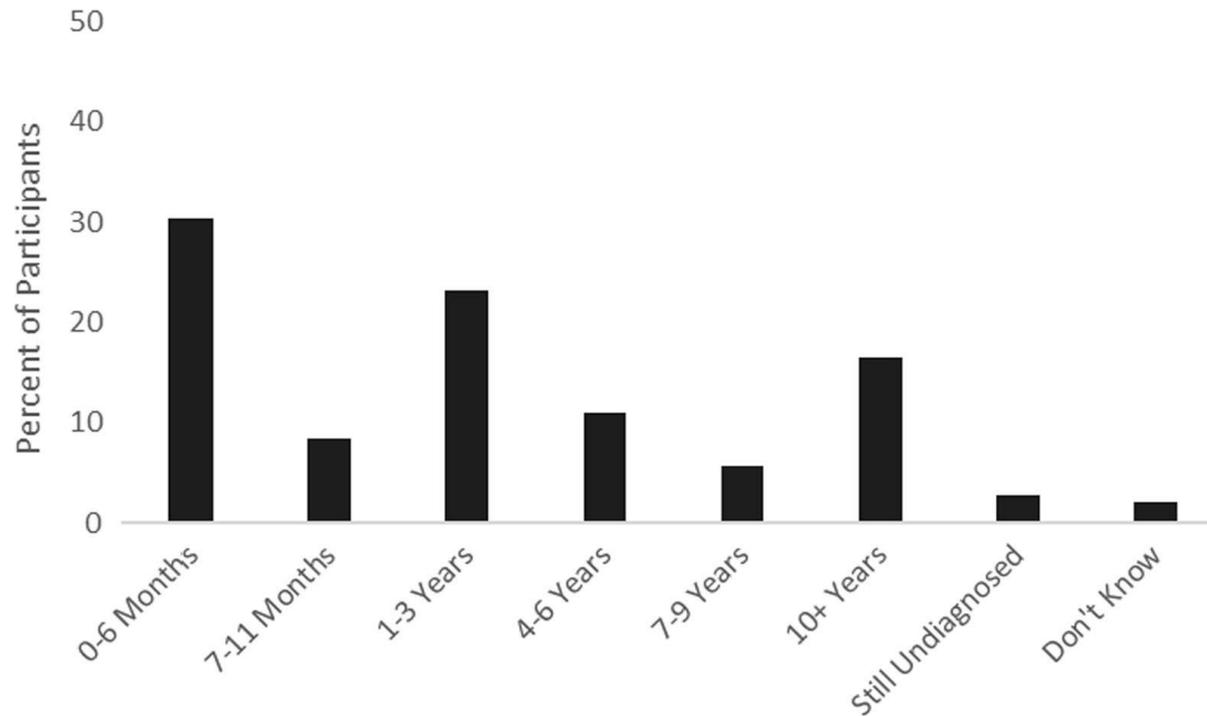
Number of doctors seen to get a diagnosis

1	152 (16%)
2–3	360 (38%)
4–5	231 (24%)
6–10	123 (13%)
11–15	31 (3%)
More than 15	43 (5%)

Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P; Chloe Barnes Advisory Council on Rare Diseases. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022 May 12;17(1):196

What to do?
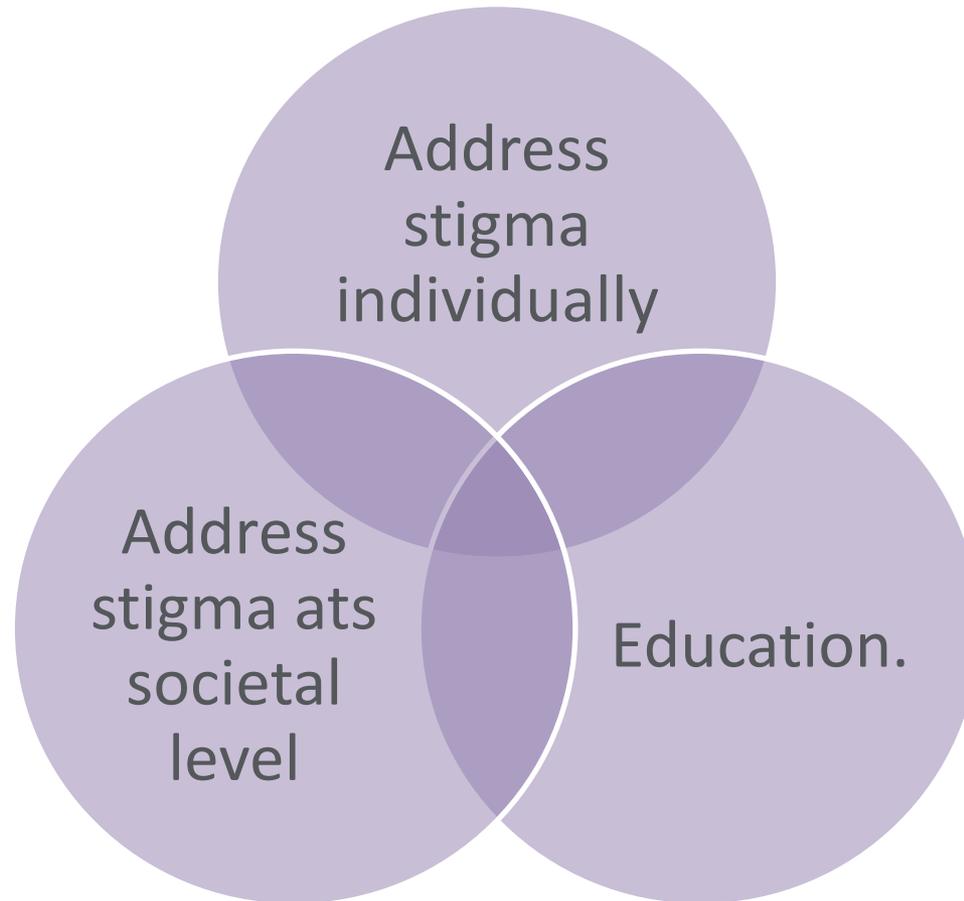
Barker EC, Flygare J, Paruthi S, Sharkey KM. Living with Narcolepsy: Current Management Strategies, Future Prospects, and Overlooked Real-Life Concerns. Nat Sci Sleep. 2020 Jul 16;12:453-466

Questions?