IN PARTNERSHIP WITH Sleep Research Society Foundation

Psych Congress MasterClass

Treatment-Resistant or Something Else?

Finding Hypersomnolence Disorders in Psychiatric Practice and Managing them with Heart-Healthy Strategies

Supported by an independent educational grant from Jazz Pharmaceuticals

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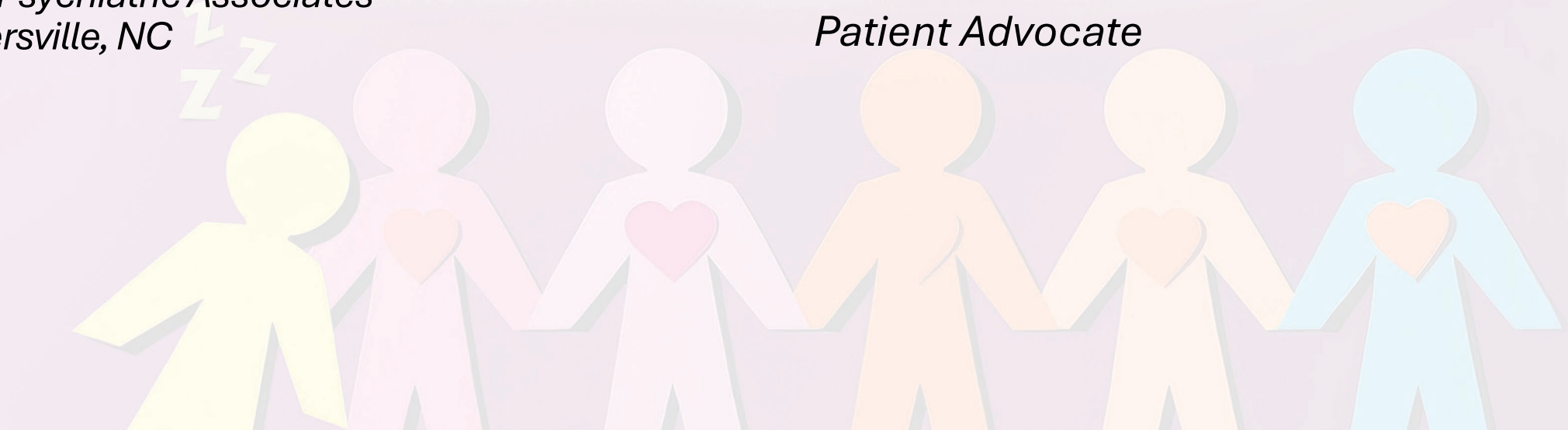


Faculty Disclosures

- **Dr. Chepke:** Advisory Board: AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Corium, Eli Lilly, Idorsia, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Takeda, Teva; Advisory Board (spouse): Bristol Myers Squibb, Otsuka; Consultant: AbbVie, Acadia, Alkermes, Axsome, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Corium, Eli Lilly, Intra-Cellular, Johnson & Johnson, Lundbeck, MedinCell, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Supernus, Takeda, Teva; Research/Grant Support: Acadia, Axsome, Harmony, Neurocrine, Teva; Speaker's Bureau: AbbVie, Acadia, Alkermes, Axsome, Boehringer Ingelheim, Bristol Myers Squibb, Corium, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, Luye, Merck, Neurocrine, Otsuka, Sumitomo, Takeda, Teva;
- **Dr. Winter:** Advisory Board–Avadel Pharma, Axsome Therapeutics, Harmony Biosciences, Jazz Pharma; Consultant–Avadel Pharma, Axsome Therapeutics, Harmony Biosciences, Jazz Pharma; Speaker's Bureau–Avadel Pharma, Axsome Therapeutics, Harmony Biosciences, Jazz Pharma
- **Laney Geismar:** Has no financial relationships to disclose

Learning Objectives

- Describe the prevalence and common presentations of hypersomnolence among patients with mental illness and the role of psychiatry clinicians in assessing hypersomnolence
- Apply strategies for assessing hypersomnolence in patients with mental illness, including the optimal use of screening tools/tests and referrals to sleep specialists
- Differentiate between sleep-wake disorders underlying hypersomnolence, including OSA, NT1, NT2, and IH, in patients with mental illness
- Evaluate clinical safety and efficacy data associated with traditional/off-label treatments versus newer/emerging treatments for narcolepsy and IH, with a focus on cardiovascular health

Introduction to Hypersomnolence

Craig Chepke, MD, DFAPA

Case Study: 31-year-old man seeking treatment for previously diagnosed ADHD and depression

Clinical Presentation

- Experienced EDS since childhood
- Feeling sleepiness “beyond belief,” with only brief relief from stimulants
- Mind fog and difficulty remaining awake while driving
- Some cataplexy and some hypnagogic and hypnopompic hallucinations
- Prescribed multiple antidepressants and stimulants with little clinical benefit

Referral to sleep specialist confirmed the suspected diagnosis of **narcolepsy type 1**

Initial Treatment

Started low-sodium oxybate 2.25 g, twice nightly for 1 week, titrated to 3.75 g, twice nightly

EDS=Excessive daytime sleepiness.

Chepke C. *J Psychiatry Neurosci*. 2023;48(6):E472-E473.

Case Study: 31-year-old man seeking treatment for previously diagnosed ADHD and depression

After 6 weeks of treatment:

Symptomatic Improvement	• ESS improved from 22 at diagnosis to 7 • Patient reported no napping, anxiety, depression, or cataplexy
Functional Improvement	• Significant improvements in **concentration, work performance,** and **family relationships** • Discontinued stimulant and anti-depressant use
Familial Improvement	• Father and sister subsequently received diagnoses for narcolepsy and responded well to low-sodium oxybate

EDS=Excessive daytime sleepiness; ESS=Epworth Sleepiness Scale

Chepke C. *J Psychiatry Neurosci*. 2023;48(6):E472-E473.

Hypersomnolence Disorders Run in the Same Circles as Psychiatric Conditions

While narcolepsy and IH are considered rare disorders, there are high rates of psychiatric comorbidities, and therefore, these individuals may concentrate in our clinics

While no studies have evaluated IH prevalence *in individuals with psychiatric disorders,*

Compared with matched controls, people with narcolepsy in a survey study were:

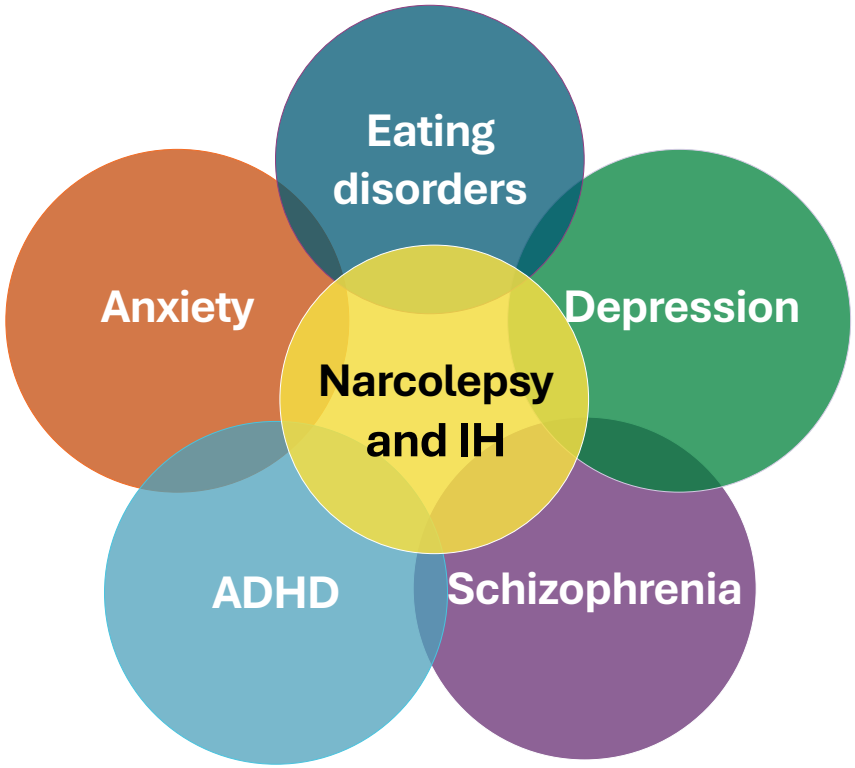
2.7x more likely to have MDD;
3.3x more likely to have GAD;
4.6x more likely to have bipolar disorder

Subjective EDS (ESS>10) is common in retrospective & cross-sectional studies:

50.8% of people with MDD;
40% of people with bipolar disorder;
47% of adults with ADHD

Hypersomnolence is often unrecognized and underdiagnosed; Narcolepsy is often diagnosed **10-15 years after symptom onset**

60% of people with narcolepsy were initially misdiagnosed, 31% of them with depression, in an HCP survey and retrospective chart review (n=252)



EDS=Excessive Daytime Sleepiness; ESS=Epworth Sleepiness Scale; IH=Idiopathic Hypersomnia; ADHD=Attnetion Deficit Hyperactivity Disorder; MDD=Major Depressive Disorder; GAD=Generalized Anxiety Disorder

Chepke C, et al. J Clin Psychiatry 86.3 (2025): 24nr15718. Morse AM & K Sanjeev. Med. Sci 6.1 (2018): 16. Saad R, et al. Nat. Sci. Sleep (2025): 1809-1823. Thorpy MJ & AC Krieger. *Sleep Med.* 2014;15(5):502-507. Carter, LP, et al. Postgrad Med 126.3 (2014): 216-224. Ohayon MM. Sleep Med 14.6 (2013): 488-492.

Differentiating Hypersomnolence Disorders from ADHD and Difficult-to-Treat MDD

Overlap of Psychiatric Diagnoses and Hypersomnolence Disorders

Overlap of MDD and Hypersomnolence

- Patients may say they feel "fatigued", "low energy"/ "low motivation", or even "depressed" when they mean "sleepy".
- Depression may make people *feel* sleepy without increased sleep propensity

Overlap of ADHD and Hypersomnolence

- The cognitive fog and under-arousal in narcolepsy can look like inattention
- Hyperactivity in ADHD can be a *compensatory* response to sleepiness
- Stimulant response creates the perception of an ADHD diagnosis

Clues that Favor Hypersomnolence Disorders

- When depression/anxiety seems unusually refractory despite good treatment.
- Irresistible dozing in passive situations or massive over-caffeination
- Habitual total sleep ≥10 -11h (**Long sleep time in IH)**
- Prolonged confusion and irritability with a strong pull to return to sleep on awakening (**Sleep inertia/"sleep drunkenness" in IH)**
- Emotion-triggered brief weakness: knee buckling, jaw slackening, dysarthria, grip loss **(Cataplexy in NT1)**

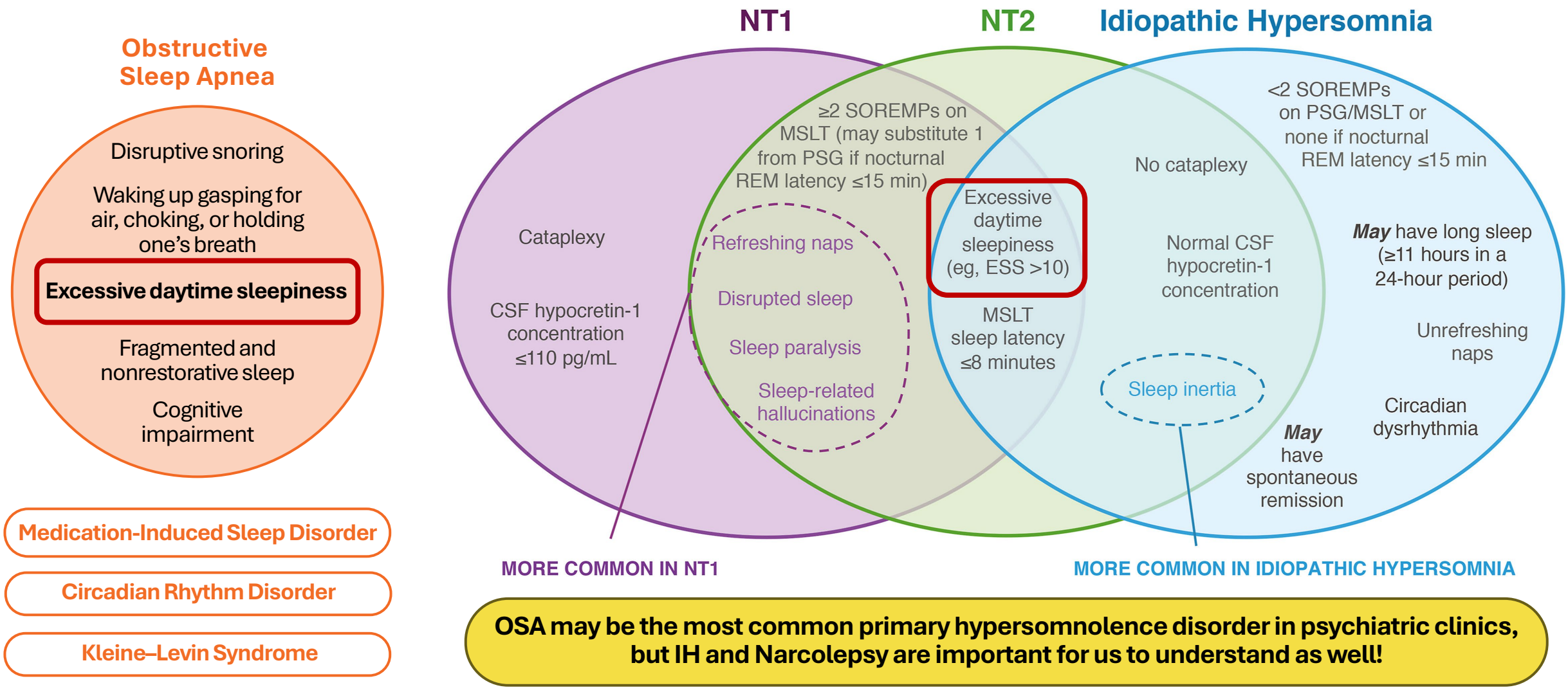
Quick Questions to Surface Red Flags

- Do you fight sleep most days? When you say tired, do you mean sleepy, like nodding off, or just exhausted? (**Excessive Sleepiness**)
- When you laugh or feel excited/angry, does your jaw get slack, words get slurred, do your knees buckle, or do you drop objects? **(Cataplexy)**
- How long until you can think or function after waking? **(Morning inertia)**
- Do you ever "zone out "or "go on autopilot" and then realize you kept doing what you were doing (working, cooking, driving) but don't remember doing it? (**Automatic Behaviors)**
- Have you ever woken up unable to move or speak for a period of time, even though you're fully aware? (**Sleep Paralysis)**
- As you're drifting off or waking up, do you ever see vivid images, hear voices/sounds, or feel a presence in the room? (**Hypnagogic/Hypnopompic events**)

ADHD=Attention Deficit Hyperactivity Disorder; MDD=Major Depresive Disorder

Chepke C, et al. J Clin Psychiatry 86.3 (2025): 24nr15718. Morse AM & K Sanjeev. Med. Sci 6.1 (2018): 16. Dunne L, et al. Sleep and Breathing 20.4 (2016): 1277-1284. Thorpy M and AM Morse. Sleep Medicine Clinics 12.1 (2017): 61-71. Morse AM, et al. CNS drugs (2025): 1-14. Moderie C, and DB Boivin. Sleep Medicine 124 (2024): 462-470. Chepke C. J Psychiatry Neurosci. 2023;48(6):E472-E473

Differential Diagnosis of Hypersomnolence



OSA may be the most common primary hypersomnolence disorder in psychiatric clinics, but IH and Narcolepsy are important for us to understand as well!

OSA=Obstructive Sleep Apnea; NT1=Narcolepsy Type 1; NT2=Narcolepsy Type 2; IH=Idiopathic Hypersomnia

Dauvilliers Y, et al. *Sleep Med Rev*. 2022;66:101709. Chepke C, et al. J Clin Psychiatry 86.3 (2025): 24nr15718.

Key Learning Points

- While narcolepsy and IH are considered rare disorders, there are high rates of psychiatric comorbidities, and therefore, these individuals may concentrate in our clinics
- Hypersomnolence is often unrecognized and underdiagnosed; Narcolepsy is often diagnosed 10-15 years after symptom onset
- Hypersomnolence may masquerade as other psychiatric conditions and cloud the clinical picture, so always keep hypersomnolence disorders on your differential diagnosis

Assessment of Hypersomnolence in Patients with Mental Illness

W. Christopher Winter, MD, DABSM, DABPN, FAASM

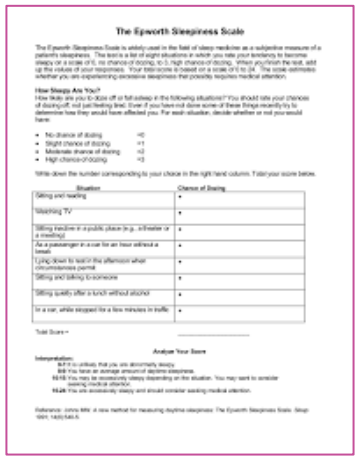
Photo: AI Generated (Gemini)

"I'm Tired."

- How do we begin to assess hypersomnolence in our patient population?
- What does a patient mean when they report feeling "tired?"
- **Excessive daytime sleepiness (EDS)** could affect 50-80% of patients in a typical psychiatric practice.
- **Fatigue** could affect as many as 47% of stable psychiatric patients.
- Start by differentiating the two

Zou S, et al. *Global Health*. 2020;16(1):119.

Assessments



The Epworth Sleepiness Scale

The Epworth Sleepiness Scale is widely used in the field of sleep medicine as a subjective measure of a patient's sleepiness. The test is a list of eight situations in which you rate your tendency to become sleepy on a scale of 0, no chance of dozing, to 3, high chance of dozing. When you finish the test, add up the values of your responses. Your total score is based on a scale of 0 to 24. The scale estimates whether you are experiencing excessive sleepiness that possibly requires medical attention.

How Sleepy Are You?

How likely are you to doze off or fall asleep in the following situations? You should rate your chances of dozing off, not just feeling tired. Even if you have not done some of these things recently try to determine how they would have affected you. For each situation, decide whether or not you would have:

- No chance of dozing =0
- Slight chance of dozing =1
- Moderate chance of dozing =2
- High chance of dozing =3

Write down the number corresponding to your choice in the right hand column. Total your score below.

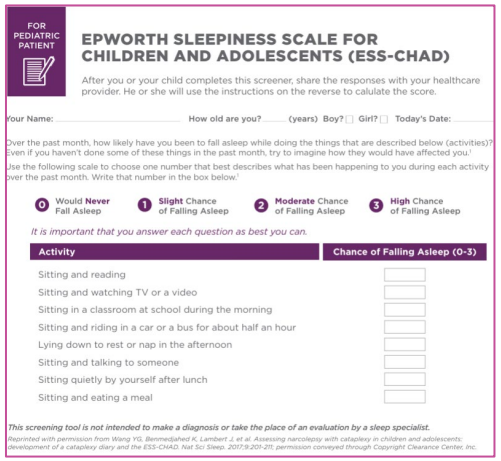
Situation	Chance of Dozing
Sitting and reading	
Watching TV	
Sitting inactive in a public place (e.g., a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in traffic	

Total Score=

Analyse Your Score

Interpretation:

Reference: Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1991; 14(6):540-5.



FOR PEDIATRIC PATIENT

EPWORTH SLEEPINESS SCALE FOR CHILDREN AND ADOLESCENTS (ESS-CHAD)

After you or your child completes this screener, share the responses with your healthcare provider. He or she will use the instructions on the reverse to calculate the score.

Your Name: _____ How old are you? _____ (years) Boy? ☐ Girl? ☐ Today's Date: _____

Over the past month, how likely have you been to fall asleep while doing the things that are described below (activities)? Even if you haven't done some of these things in the past month, try to imagine how they would have affected you.[1]

Use the following scale to choose one number that best describes what has been happening to you during each activity over the past month. Write that number in the box below.[1]

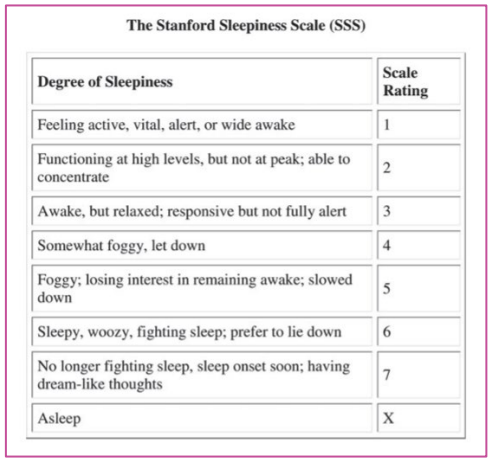
0 Would Never Fall Asleep 1 Slight Chance of Falling Asleep 2 Moderate Chance of Falling Asleep 3 High Chance of Falling Asleep

It is important that you answer each question as best you can.

Activity	Chance of Falling Asleep (0-3)
Sitting and reading	
Sitting and watching TV or a video	
Sitting in a classroom at school during the morning	
Sitting and riding in a car or a bus for about half an hour	
Lying down to rest or nap in the afternoon	
Sitting and talking to someone	
Sitting quietly by yourself after lunch	
Sitting and eating a meal	

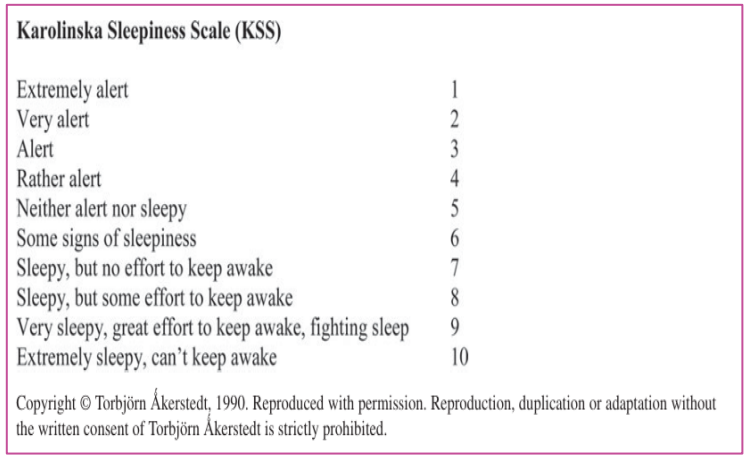
This screening tool is not intended to make a diagnosis or take the place of an evaluation by a sleep specialist.

Reprinted with permission from Wang YG, Bermejofahed K, Lambert J, et al. Assessing narcolepsy with cataplexy in children and adolescents: development of a cataplexy diary and the ESS-CHAD. Nat Sci Sleep. 2017;9:201-211; permission conveyed through Copyright Clearance Center, Inc.



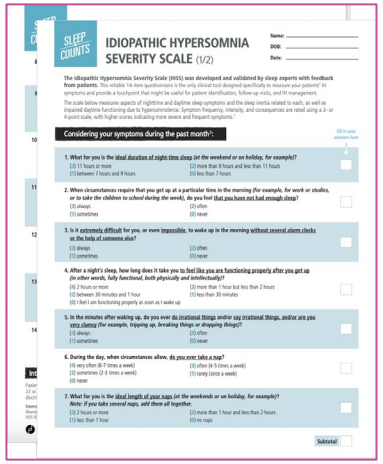
The Stanford Sleepiness Scale (SSS)

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X



Karolinska Sleepiness Scale (KSS)

Extremely alert	1
Very alert	2
Alert	3
Rather alert	4
Neither alert nor sleepy	5
Some signs of sleepiness	6
Sleepy, but no effort to keep awake	7
Sleepy, but some effort to keep awake	8
Very sleepy, great effort to keep awake, fighting sleep	9
Extremely sleepy, can't keep awake	10



SLEEP COUNTS

IDIOPATHIC HYPERSOMNIA SEVERITY SCALE (1/2)

Name: _____
DOB: _____
Date: _____

The idiopathic hypersomnia Severity Scale (IHSS) was developed and validated by sleep experts with feedback from patients. This reliable 14-item questionnaire is the only clinical tool designed specifically to measure your patients' IH symptoms and provide a touchpoint that might be useful for patient identification, follow-up visits, and IH management.

The scale below measures aspects of nighttime and daytime sleep symptoms and the sleep inertia related to each, as well as impaired daytime functioning due to hypersomnolence. Symptom frequency, intensity, and consequences are rated using a 3- or 4-point scale, with higher scores indicating more severe and frequent symptoms.[1]

Considering your symptoms during the past month:

Fill in your answers here

1. **What for you is the ideal duration of night-time sleep** *(at the weekend or on holiday, for example)*?
(2) 11 hours or more (2) more than 9 hours and less than 11 hours
(1) between 7 hours and 9 hours (0) less than 7 hours

2. **When circumstances require that you get up at a particular time in the morning** *(for example, for work or studies, or to take the children to school during the week)*, **do you feel that you have not had enough sleep?**
(3) always (2) often
(1) sometimes (0) never

3. **Is it extremely difficult for you, or even impossible, to wake up in the morning without several alarm clocks or the help of someone else?**
(3) always (2) often
(1) sometimes (0) never

4. **After a night's sleep, how long does it take you to feel like you are functioning properly after you get up** *(in other words, fully functional, both physically and intellectually)*?
(4) 2 hours or more (3) more than 1 hour but less than 2 hours
(2) between 30 minutes and 1 hour (1) less than 30 minutes
(0) I feel I am functioning properly as soon as I wake up

5. **In the minutes after waking up, do you ever do irrational things and/or say irrational things, and/or are you very clumsy** *(for example, tripping up, breaking things or dropping things)*?
(3) always (2) often
(1) sometimes (0) never

6. **During the day, when circumstances allow, do you ever take a nap?**
(4) very often (6-7 times a week) (3) often (4-5 times a week)
(2) sometimes (2-3 times a week) (1) rarely (once a week)
(0) never

7. **What for you is the ideal length of your nap** *(at the weekends or on holiday, for example)*?
Note: if you take several naps, add them all together.
(3) 2 hours or more (2) more than 1 hour and less than 2 hours
(1) less than 1 hour (0) no naps

Subtotal

Fatigue Assessment Inventory

Instructions:
Below are a series of statements regarding your Fatigue. By Fatigue we mean a sense of tiredness, lack of energy or total body give-out. Please read each statement and choose a number from 1 to 7, where #1 indicates you completely disagree with the statement and #7 indicates you completely agree. Please answer these questions as they apply to the past TWO WEEKS.

Circle the appropriate number on the answer sheet!

Questions:

	Completely Disagree						Completely agree
1. I feel drowsy when I am fatigued.	1	2	3	4	5	6	7
2. When I am fatigued, I lose my patience.	1	2	3	4	5	6	7
3. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
4. When I am fatigued, I have difficulty concentrating.	1	2	3	4	5	6	7
5. Exercise brings on my fatigue.	1	2	3	4	5	6	7
6. Heat brings on my fatigue.	1	2	3	4	5	6	7
7. Long periods of inactivity bring on my fatigue	1	2	3	4	5	6	7
8. Stress brings on my fatigue.	1	2	3	4	5	6	7
9. Depression brings on my fatigue.	1	2	3	4	5	6	7
10. Work brings on fatigue.	1	2	3	4	5	6	7
11. My fatigue is worse in the afternoon.	1	2	3	4	5	6	7
12. My fatigue is worse in the morning.	1	2	3	4	5	6	7
13. Performance of routine daily activities increases my fatigue.	1	2	3	4	5	6	7
14. Resting lessens my fatigue.	1	2	3	4	5	6	7
15. Sleeping lessens my fatigue.	1	2	3	4	5	6	7
16. Cool temperatures lessen my fatigue.	1	2	3	4	5	6	7
17. Positive experiences lessen my fatigue.	1	2	3	4	5	6	7
18. I am easily fatigued.	1	2	3	4	5	6	7
19. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
20. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
21. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
22. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
23. Fatigue predated other symptoms of my condition.	1	2	3	4	5	6	7
24. Fatigue is my most disabling symptom	1	2	3	4	5	6	7
25. Fatigue is among my 3 most disabling symptoms.	1	2	3	4	5	6	7
26. Fatigue interferes with my work, family or social life.	1	2	3	4	5	6	7
27. Fatigue makes other symptoms worse.	1	2	3	4	5	6	7
28. Fatigue that I now experience is different in quality or severity than the fatigue I experienced before I developed this condition	1	2	3	4	5	6	7
29. I experienced prolonged fatigue after exercise.	1	2	3	4	5	6	7

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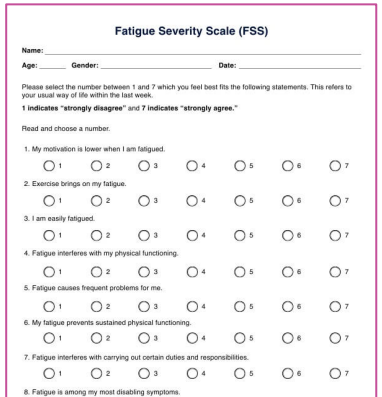

Fatigue Severity Scale (FSS)

Name: _____

Age: _____ Gender: _____ Date: _____

Please select the number between 1 and 7 which you feel best fits the following statements. This refers to your usual way of life within the last week.

1 indicates "strongly disagree" and **7 indicates "strongly agree."**

Read and choose a number.

1. My motivation is lower when I am fatigued.
○1 ○2 ○3 ○4 ○5 ○6 ○7

2. Exercise brings on my fatigue.
○1 ○2 ○3 ○4 ○5 ○6 ○7

3. I am easily fatigued.
○1 ○2 ○3 ○4 ○5 ○6 ○7

4. Fatigue interferes with my physical functioning.
○1 ○2 ○3 ○4 ○5 ○6 ○7

5. Fatigue causes frequent problems for me.
○1 ○2 ○3 ○4 ○5 ○6 ○7

6. My fatigue prevents sustained physical functioning.
○1 ○2 ○3 ○4 ○5 ○6 ○7

7. Fatigue interferes with carrying out certain duties and responsibilities.
○1 ○2 ○3 ○4 ○5 ○6 ○7

8. Fatigue is among my most disabling symptoms.
○1 ○2 ○3 ○4 ○5 ○6 ○7

9. Fatigue interferes with my work, family, or social life.
○1 ○2 ○3 ○4 ○5 ○6 ○7

Krupp, L. B., LaRocca, N. G., Muir-Nash, J., & Steinberg, A. D. (1989). Fatigue Severity Scale (FSS) [Database record]. APA PsycTests. https://doi.org/10.1037/t25491-000

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Fatigue Assessment Scale (FAS)

The following 10 statements refer to how you usually feel. For each statement you can choose one out of five answer categories, varying from *never* to *always*. 1 = *never*; 2 = *sometimes*; 3 = *regularly*; 4 = *often*; 5 = *always*.

	Never	Sometimes	Regularly	Often	Always
1. I am bothered by fatigue (WHOQOL)	1	2	3	4	5
2. I get tired very quickly (CIS)	1	2	3	4	5
3. I don't do much during the day (CIS)	1	2	3	4	5
4. I have enough energy for everyday life (WHOQOL)	1	2	3	4	5
5. Physically, I feel exhausted (CIS)	1	2	3	4	5
6. I have problems starting things (FS)	1	2	3	4	5
7. I have problems thinking clearly (FS)	1	2	3	4	5
8. I feel no desire to do anything (CIS)	1	2	3	4	5
9. Mentally, I feel exhausted	1	2	3	4	5
10. When I am doing something, I can concentrate quite well (CIS)	1	2	3	4	5

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Note: The abbreviations after the items indicate the scale from which the items has been abstracted. The following are the scales:
CIS - Checklist Individual Strength
WHOQOL - World Health Organization Quality of Life assessment instrument
FS - Fatigue Scale

Daily Fatigue Impact Scale

Fatigue is a feeling of physical tiredness and lack of energy that many people experience from time to time. In certain medical conditions, feelings of fatigue can be more frequent and more of a problem than usual. The following questionnaire has been designed to help us understand how you experience fatigue and how it has affected your life. Below is a list of statements that describe how fatigue may cause problems in people's lives. Please read each statement carefully and place an 'X' in the box that indicates best HOW MUCH OF A PROBLEM FATIGUE HAS BEEN FOR YOU TODAY. Please check ONE box for each statement and do not skip any items.

	No problem 0	Small problem 1	Moderate problem 2	Big problem 3	Extreme problem 4
1. Because of fatigue, I feel less alert.					
2. Because of fatigue, I have to reduce my workload or responsibilities.					
3. Because of fatigue, I am less motivated to do anything that requires physical effort.					
4. Because of fatigue, I have trouble maintaining physical effort for long periods.					
5. Because of fatigue, I find it difficult to make decisions					
6. Because of fatigue, I am less able to finish tasks that require thinking.					
7. Because of fatigue, I feel slowed down in my thinking.					
8. Because of fatigue, I have to limit my physical activities.					

With kind permission from Springer Science+Business media: John et al. [3], Appendix A.

Fatigue Symptom Inventory (FSI)

For each of the following, circle the one number that best indicates how that item applies to you.

1. Rate your level of fatigue on the day you felt most fatigued during the past week.
0 1 2 3 4 5 6 7 8 9 10
Not at all Fatigued — As fatigued as I could be

2. Rate your level of fatigue on the day you felt least fatigued during the past week.
0 1 2 3 4 5 6 7 8 9 10
Not at all fatigued — As fatigued as I could be

3. Rate your level of fatigue on the average in the last week.
0 1 2 3 4 5 6 7 8 9 10
Not at all fatigued — As fatigued as I could be

4. Rate your level of fatigue right now.
0 1 2 3 4 5 6 7 8 9 10
Not at all fatigued — As fatigued as I could be

5. Rate how much, in the past week, fatigue interfered with your general level of activity.
0 1 2 3 4 5 6 7 8 9 10
No interference — Extreme interference

6. Rate how much, in the past week, fatigue interfered with your ability to bathe and dress yourself.
0 1 2 3 4 5 6 7 8 9 10
No interference — Extreme interference

7. Rate how much, in the past week, fatigue interfered with your normal work activity (includes both work outside the home and housework).
0 1 2 3 4 5 6 7 8 9 10
No Interference — Extreme Interference

8. Rate how much, in the past week, fatigue interfered with your ability to concentrate.
0 1 2 3 4 5 6 7 8 9 10
No Interference — Extreme Interference

9. Rate how much, in the past week, fatigue interfered with your relations with other people.
0 1 2 3 4 5 6 7 8 9 10
No Interference — Extreme Interference

10. Rate how much, in the past week, fatigue interfered with your enjoyment of life.
0 1 2 3 4 5 6 7 8 9 10
No Interference — Extreme Interference

11. Rate how much, in the past week, fatigue interfered with your mood:
0 1 2 3 4 5 6 7 8 9 10
No Interference — Extreme Interference

12. Indicate how many days, in the past week, you felt fatigued for any part of the day.
0 1 2 3 4 5 6 7
Days — Days

13. Rate how much of the day, on average you felt fatigued in the past week.
0 1 2 3 4 5 6 7 8 9 10
None of the day — The entire day

With kind permission from Springer Science+Business Media: Hann et al. [2], Table 1.

Epworth Sleepiness Scale

Situation	Chance of dozing (0-3)			
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive in a public place—for example, a theater or meeting	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch (when you've had no alcohol)	0	1	2	3
In a car, while stopped in traffic	0	1	2	3
Total Score				

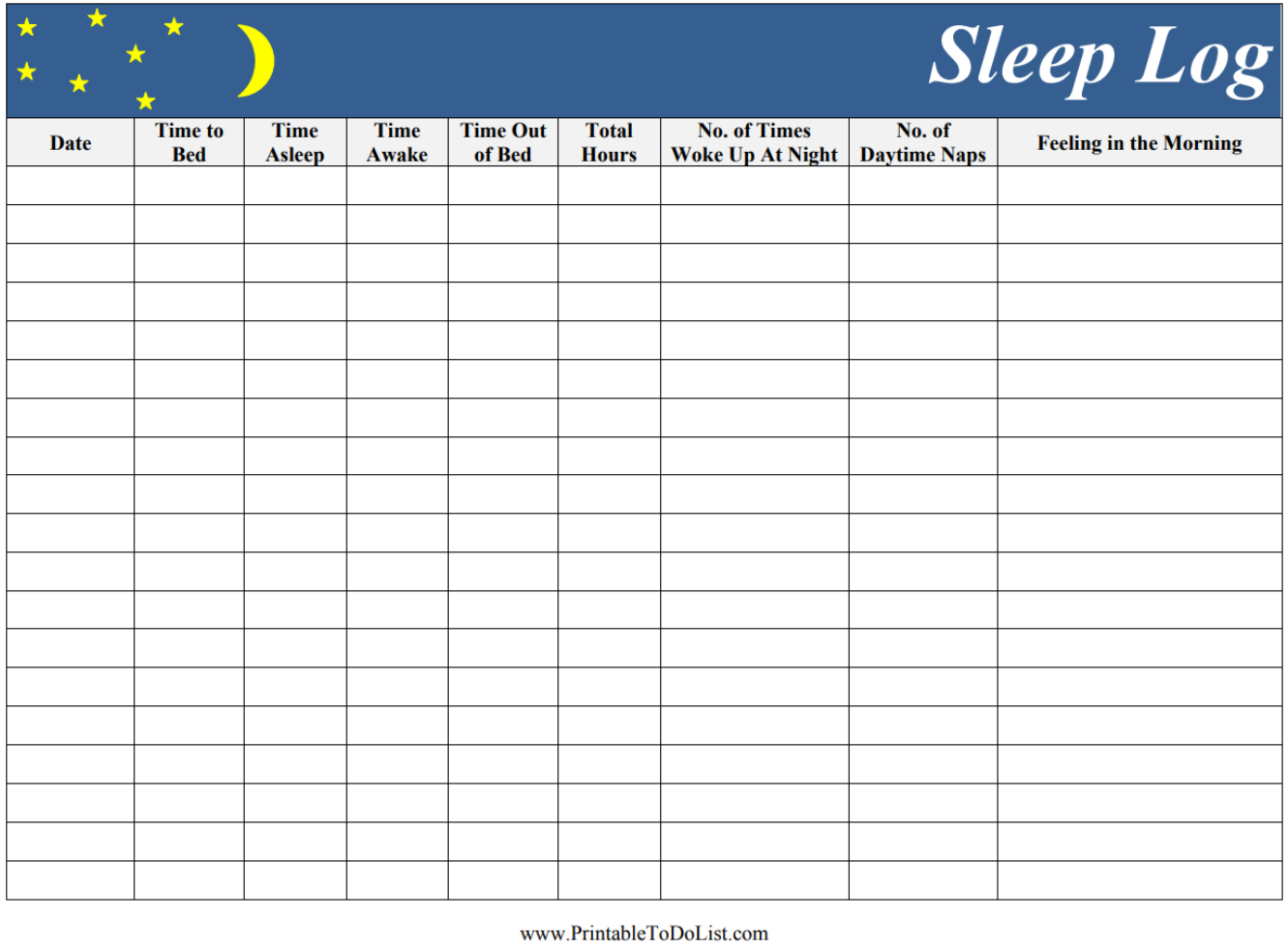
0 = would never doze, 1 = slight chance of dozing, 2 = moderate chance of dozing, 3 = high chance of dozing

- The Epworth is a clinically validated tool for helping quantify EDS in an adult population.
- Subjects are properly asked "Do you fall asleep?" not "Could you fall asleep?"
- 0-9 is generally considered normal with scores greater than ten suggestive of EDS.

EDS=Excessive Daytime Sleepiness

Johns MW. Sleep (1991).

Sleep History/Sleep Log



Sleep Log

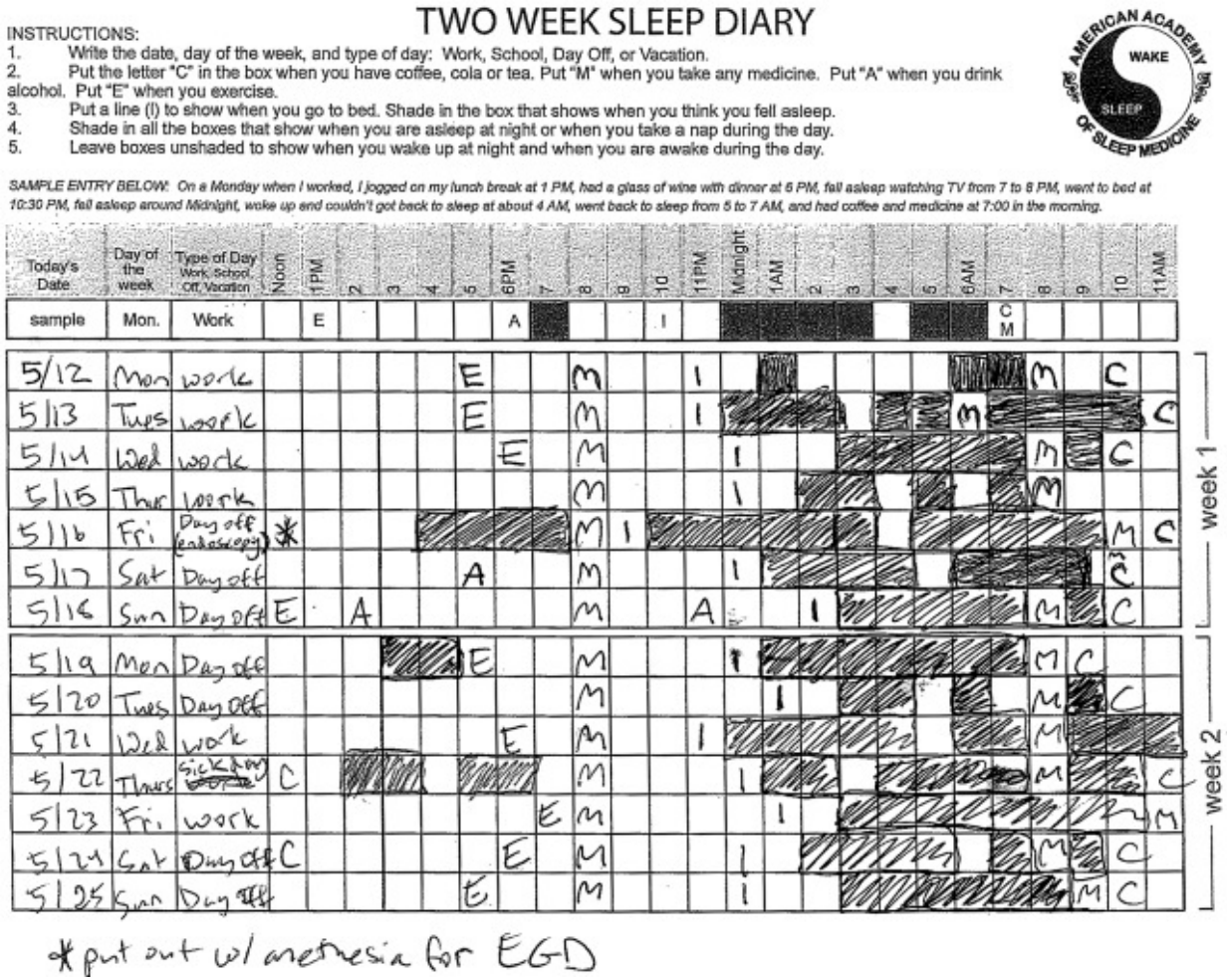
Date	Time to Bed	Time Asleep	Time Awake	Time Out of Bed	Total Hours	No. of Times Woke Up At Night	No. of Daytime Naps	Feeling in the Morning

www.PrintableToDoList.com

- Taking a baseline sleep history is essential for any patient visit
- This history will mirror a sleep log
- The log begins at a time of day (e.g. bedtime) and will survey an entire 24-hour period.
- While soliciting partner/parental observation is helpful, it should be made clear to the patient that they are to record what they feel is happening during the night/day
- This log can lay the foundation for various future conversations:
  - Paradoxical insomnia (perception<reality)
  - Inadequate sleep (perception>reality)

Cossa G, et al. Austin J Sleep Disord. 2017;4(1).

Sleep History/Sleep Log



TWO WEEK SLEEP DIARY

INSTRUCTIONS:
1. Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation.
2. Put the letter "C" in the box when you have coffee, cola or tea. Put "M" when you take any medicine. Put "A" when you drink alcohol. Put "E" when you exercise.
3. Put a line (|) to show when you go to bed. Shade in the box that shows when you think you fell asleep.
4. Shade in all the boxes that show when you are asleep at night or when you take a nap during the day.
5. Leave boxes unshaded to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn't get back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7:00 in the morning.

Today's Date | Day of the week | Type of Day Work, School, Off, Vacation | Noon | 1PM | 2 | 3 | 4 | 5 | 6PM | 7 | 8 | 9 | 10 | 11PM | Midnight | 1AM | 2 | 3 | 4 | 5 | 6AM | 7 | 8 | 9 | 10 | 11AM

week 1

week 2

* put out w/ anesthesia for EGD

Steele TA, et al. *Neurotherapeutics*. 2021;18(1):53-74.

- Grid diaries can be more useful for patients and practitioners alike to visualize sleep amounts and patterns
- These can be very useful in the tracking of circadian disorders, shift work, social jet lag, etc.
- These diaries are useful when sleep consolidation therapies are utilized

Sleep Trackers

- With the rise of consumer sleep tracking devices, more clinics are utilizing their data
- Many patient will already be tracking this information
- Thoughtful pairing with sleep logs/diaries can create a powerful clinical tool.

de Zambotti et al. *Sleep*. 2019;42(12):zsz254.

Causes of EDS: Quantity vs. Quality

Poor Sleep Quality

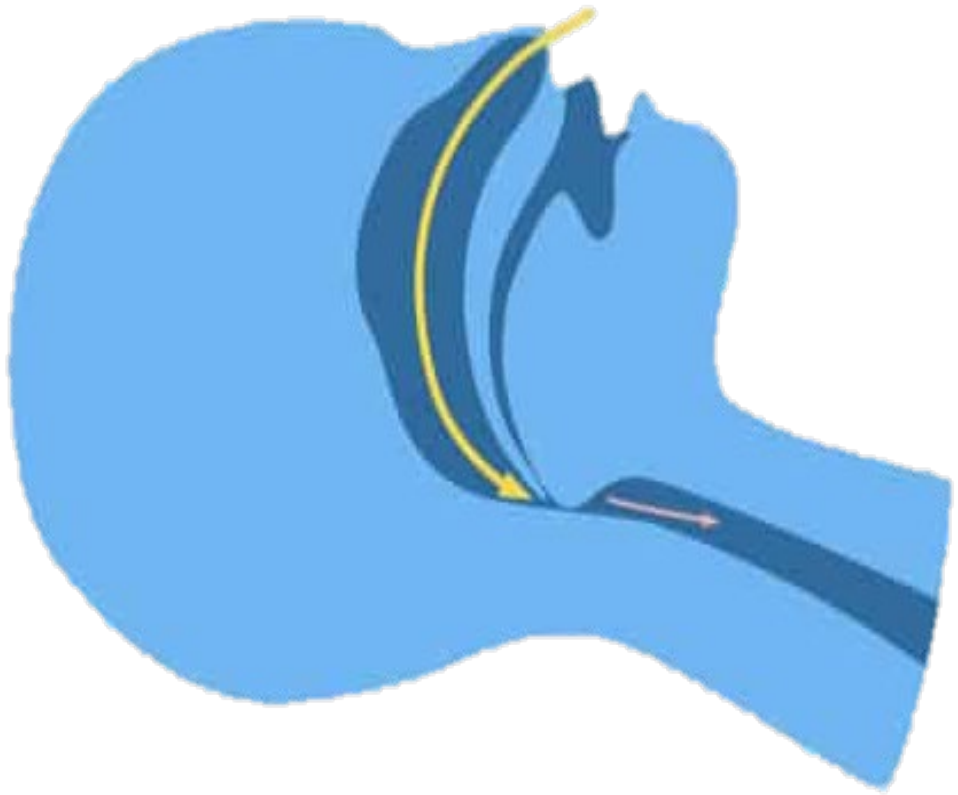
Poor Sleep Quantity

- A high EDS typically indicates one of both are present.
- Generally, it is most practical to begin with assessing for inadequate sleep quantity:
  - Sleep history
  - Sleep diary/log
  - Sleep tracker

Shantakumari N, etl. Oman Med J. 2024 Mar 31;39(2):e612.

Poor Sleep Quality

Sleep Apnea



- Obstructive sleep apnea is the most common cause of excessive daytime sleepiness in adult psychiatric practices
- Easily diagnosed with home sleep testing (HST) or in-lab polysomnograms
- While HST are quite accurate, when in error, they tend to underestimate disease severity:

$$\frac{\#\ \text{Respiratory Events (accurate)}}{\text{Total Sleep Time (overestimate)}} = \text{Events/h (underestimate)}$$

Punjabi Mn et al. Sleep, 2000. Ahmed IM, Thorpy MJ. Sleepiness Causes, Consequences, and Treatments, 2011.

Sleep Apnea Assessment

STOP		
Do you SNORE loudly (louder than talking or loud enough to be heard through closed doors)?	Yes	No
Do you often feel TIRED, fatigued, or sleepy during daytime?	Yes	No
Has anyone OBSERVED you stop breathing during your sleep?	Yes	No
Do you have or are you being treated for high blood PRESSURE?	Yes	No

BANG		
BMI more than 35kg/m2?	Yes	No
AGE over 50 years old?	Yes	No
NECK circumference > 16 inches (40cm)?	Yes	No
GENDER: Male?	Yes	No

TOTAL SCORE		

High risk of OSA: Yes 5 - 8

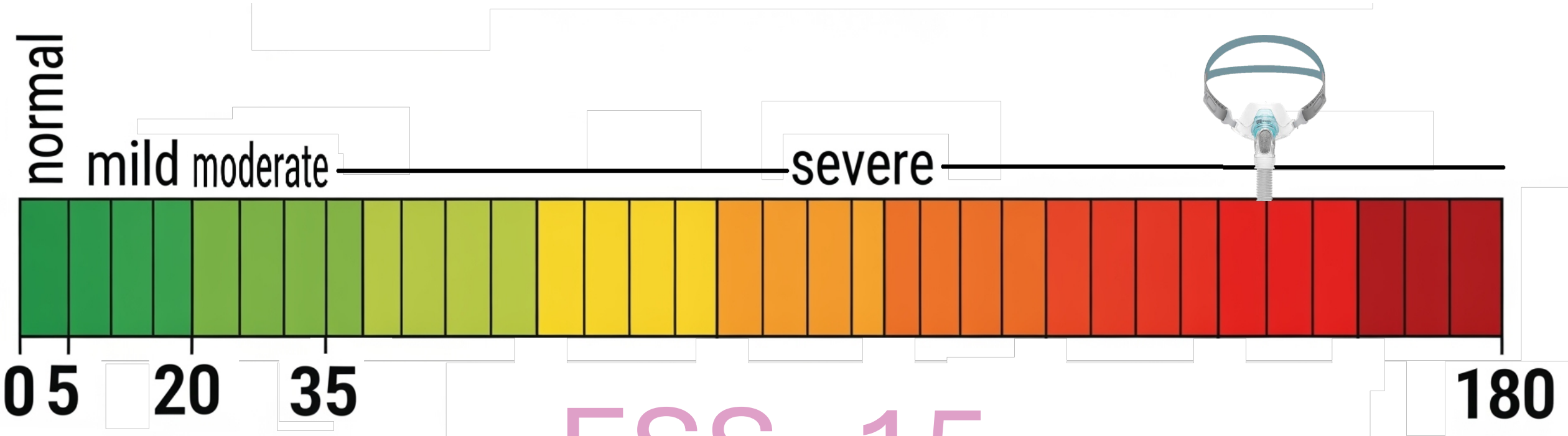
Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

- 26% of adults between the ages of 30-70 have sleep apnea.
- That's about 25 million adults in the United States
- Your clinic is full of sleep apnea patients

Iannella G, et al. *Diagnostics (Basel)*. 2025;15(9):1088

Sleep Apnea Assessment



ESS=15

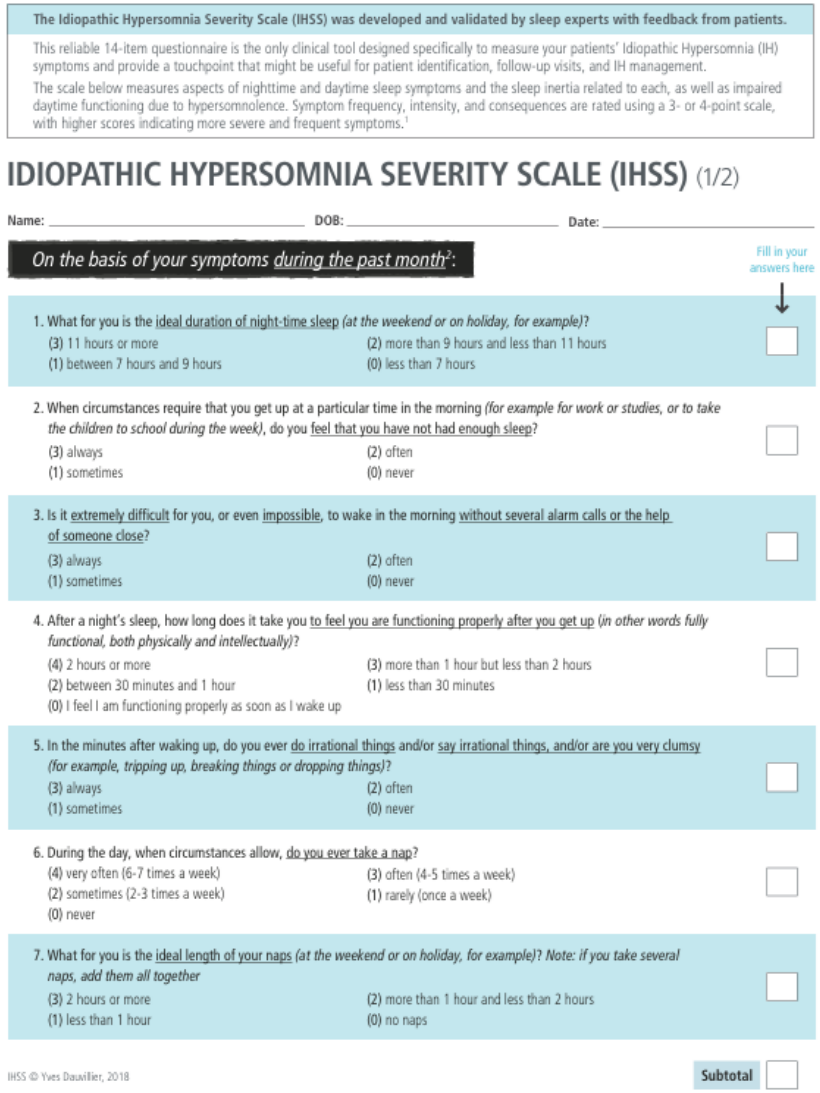
"What's Really Going On?"

ESS=Epworth Sleepiness Scale

Hudgel DW. Sleep. 2016;39(5):1165-1166.

Hypersomnias

Idiopathic Hypersomnia Severity Scale



The Idiopathic Hypersomnia Severity Scale (IHSS) was developed and validated by sleep experts with feedback from patients.

This reliable 14-item questionnaire is the only clinical tool designed specifically to measure your patients' Idiopathic Hypersomnia (IH) symptoms and provide a touchpoint that might be useful for patient identification, follow-up visits, and IH management.

The scale below measures aspects of nighttime and daytime sleep symptoms and the sleep inertia related to each, as well as impaired daytime functioning due to hypersomnolence. Symptom frequency, intensity, and consequences are rated using a 3- or 4-point scale, with higher scores indicating more severe and frequent symptoms.[1]

IDIOPATHIC HYPERSOMNIA SEVERITY SCALE (IHSS) (1/2)

Name: _____ DOB: _____ Date: _____

On the basis of your symptoms during the past month[2]:

Fill in your answers here

1. What for you is the ideal duration of night-time sleep *(at the weekend or on holiday, for example)*?
   (3) 11 hours or more
   (2) more than 9 hours and less than 11 hours
   (1) between 7 hours and 9 hours
   (0) less than 7 hours

2. When circumstances require that you get up at a particular time in the morning *(for example for work or studies, or to take the children to school during the week)*, do you feel that you have not had enough sleep?
   (3) always
   (2) often
   (1) sometimes
   (0) never

3. Is it extremely difficult for you, or even impossible, to wake in the morning without several alarm calls or the help of someone close?
   (3) always
   (2) often
   (1) sometimes
   (0) never

4. After a night's sleep, how long does it take you to feel you are functioning properly after you get up *(in other words fully functional, both physically and intellectually)*?
   (4) 2 hours or more
   (3) more than 1 hour but less than 2 hours
   (2) between 30 minutes and 1 hour
   (1) less than 30 minutes
   (0) I feel I am functioning properly as soon as I wake up

5. In the minutes after waking up, do you ever do irrational things and/or say irrational things, and/or are you very clumsy *(for example, tripping up, breaking things or dropping things)*?
   (3) always
   (2) often
   (1) sometimes
   (0) never

6. During the day, when circumstances allow, do you ever take a nap?
   (4) very often (6-7 times a week)
   (3) often (4-5 times a week)
   (2) sometimes (2-3 times a week)
   (1) rarely (once a week)
   (0) never

7. What for you is the ideal length of your naps *(at the weekend or on holiday, for example)*? *Note: if you take several naps, add them all together*
   (3) 2 hours or more
   (2) more than 1 hour and less than 2 hours
   (1) less than 1 hour
   (0) no naps

IHSS © Yves Dauvilliers, 2018

Subtotal

IDIOPATHIC HYPERSOMNIA SEVERITY SCALE (IHSS) (2/2)

8. In general, how do you feel after a nap?
   (3) very sleepy
   (2) sleepy
   (1) awake
   (0) wide awake

9. During the day, while carrying out activities that are not very stimulating, do you ever struggle to stay awake?
   (4) very often (at least twice a day)
   (3) often (4-7 times a week)
   (2) sometimes (2-3 times a week)
   (1) rarely (once a week or less)
   (0) never

10. Do you consider that your hypersomnolence has an impact on your general health *(i.e. lack of energy, no motivation to do things, physical fatigue on exertion, decrease in physical fitness)*?
    (4) very significant
    (3) significant
    (2) moderate
    (1) minor
    (0) no impact

11. Do you consider that your hypersomnolence is a problem in terms of your proper intellectual functioning *(i.e. problems with concentration, memory problems, decrease in your intellectual performance)*?
    (4) very significant
    (3) significant
    (2) moderate
    (1) minor
    (0) no problem

12. Do you consider that your hypersomnolence affects your mood *(for example sadness, anxiety, hypersensitivity, irritability)*?
    (4) very severely
    (3) severely
    (2) moderately
    (1) slightly
    (0) not at all

13. Do you consider that your hypersomnolence prevents you from carrying out daily tasks properly *(family-related or household tasks, school, leisure or job-related tasks)*?
    (4) very significantly
    (3) significantly
    (2) moderately
    (1) slightly
    (0) not at all

14. Do you consider that your hypersomnolence is a problem in terms of your driving a car?
    (4) very significant
    (3) significant
    (2) moderate
    (1) minor
    (0) no problem/I do not drive

Interpreting IHSS Scores

TOTAL SCORE

Patients' IHSS scores will range from 0 to 50, with higher scores indicating more severe IH symptoms. A score of 22 or below is typical for people without any sleep disorder. Additionally, a cutoff score of 26 can reliably discriminate between treated and untreated patients with IH. A 4-point change in the IHSS represents a minimum clinically important difference.[1,3]

For any information on the use of the IHSS, please contact Mapi Research Trust, Lyon, France. Internet: https://eprovide.mapi-trust.org

Sources: 1. Dauvilliers Y, Evangelista E, Barateau L, et al. Measurement of symptoms in idiopathic hypersomnia: the Idiopathic Hypersomnia Severity Scale. *Neurology*. 2019;92(15):e1754-e1762. **2.** Dauvilliers Y. Idiopathic hypersomnia severity scale. 2018. Accessed October 3, 2022. http://links.lww.com/WNL/A854. **3.** Rassu AL, Evangelista E, Barateau L, et al. Idiopathic Hypersomnia Severity Scale to better quantify symptoms severity and their consequences in idiopathic hypersomnia. *J Clin Sleep Med*. 2022;18(2):617-629.

- The IHSS is a brief, validated 14-point scale that looks for the most common signs and symptoms of IH.
- Scoring:
  - MILD: 0-12
  - MODERATE: 13-25
  - SEVERE: 26-38
  - VERY SEVERE: 39-50

Rassu AL, et al. J Clin Sleep Med. 2022;18(2):617-629.

Testing For Hypersomnia

MSLT/MWT

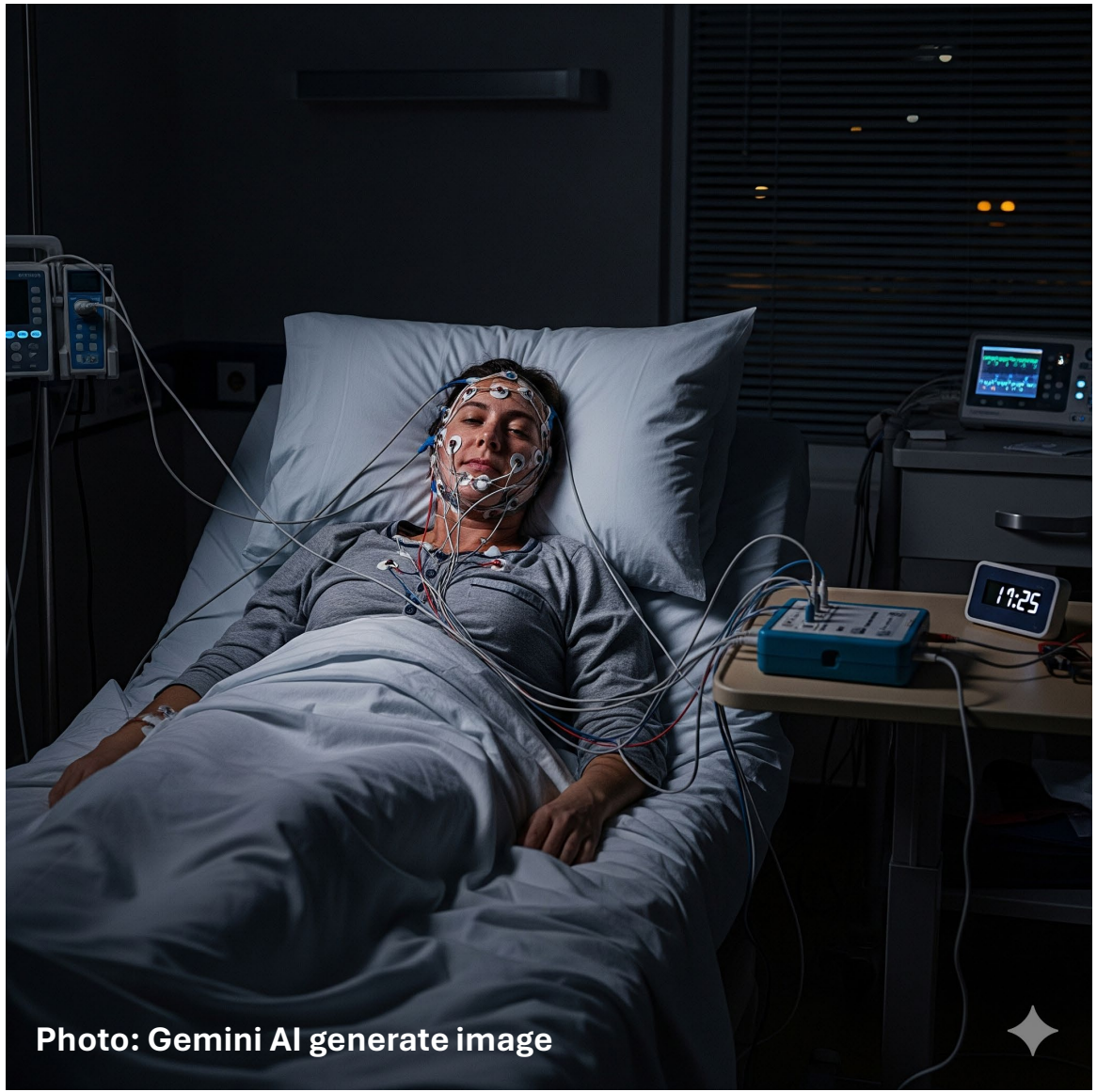


Photo: Gemini AI generate image

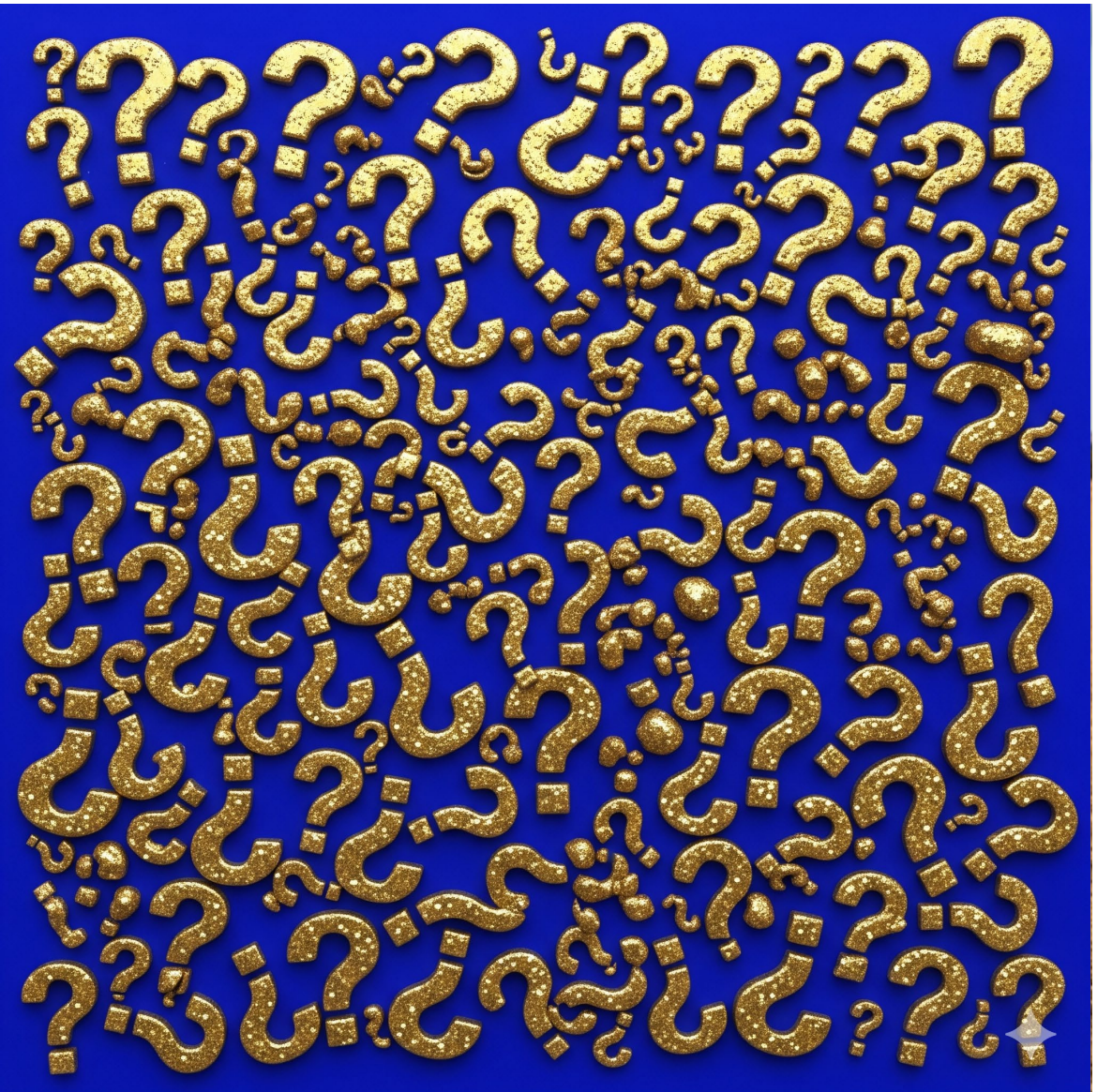
- In-lab polysomnograms followed by multiple sleep latency tests are typically used to diagnose EDS/hypersomnia
- Supportive findings are:
  - Mean sleep latency 8 minutes or less
  - 2 or more sleep-onset REM periods (a reduced REM latency on the overnight PSG can count)
- The MSLT provides supportive information/evidence for the presence of a hypersomnia; it is not diagnostic.
- The false negative rate of the MSLT is roughly 20%, other estimates in IH are as high as 71%.
- What would your diagnosis be for an individual who after a head trauma frequently convulses, bites their tongue/is enuretic, and displays a prolonged postictal period…

…but the in-office EEG was normal?

MSLT=Multiple Sleep Latency Test; MWT=Maintenance of Wakefulness Test

Ohayon MM, et al. Sleep Med. 2019;53:88-93; Ruoff C, et al. J Clin Sleep Med. 2018;14(1):65-74.

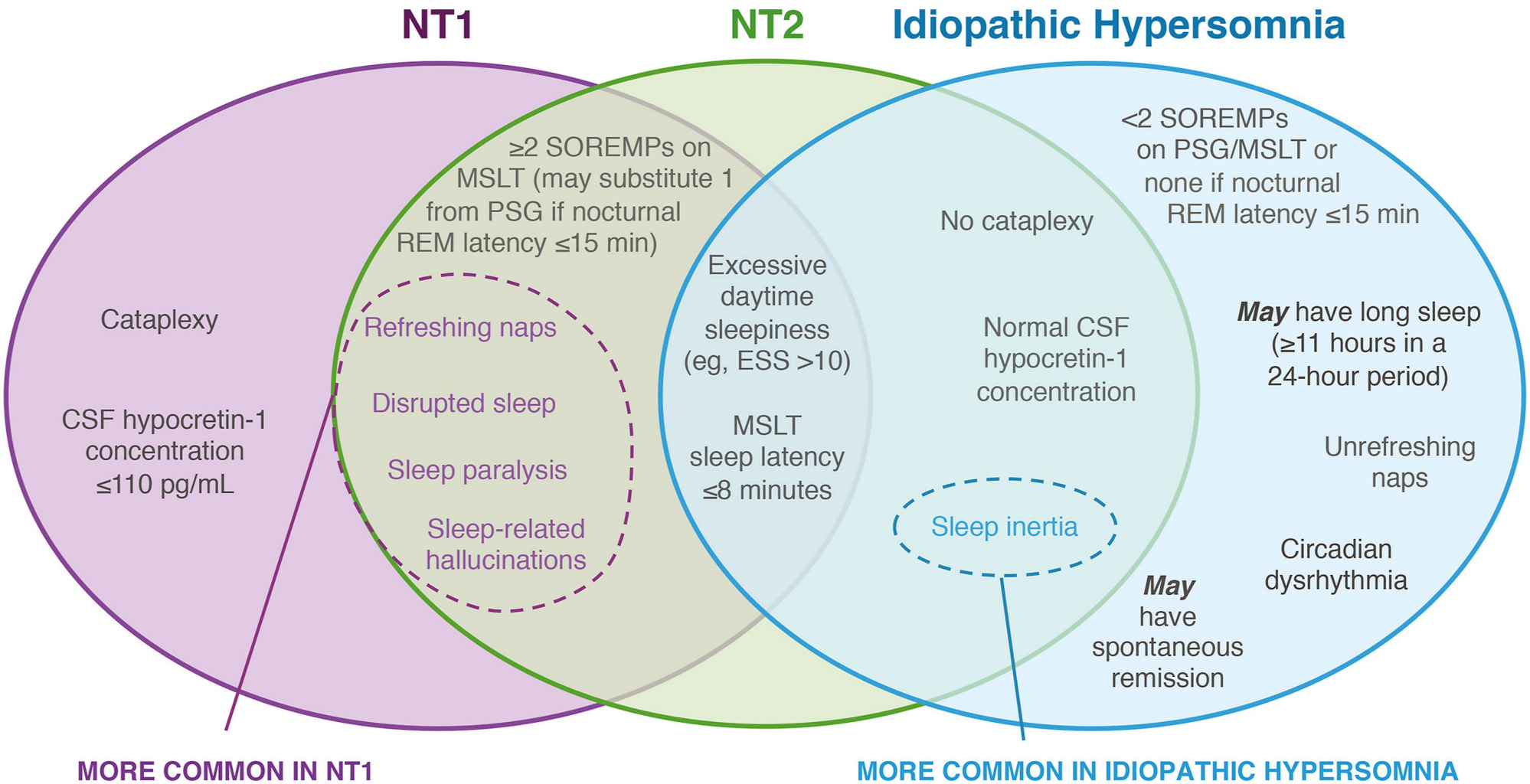
Name This Animal



- It’s very large
- It’s typically gray
- It has big ears
- It can have tusks
- It has a long trunk
- It is often associated with circuses
- It travels in packs
- It is the symbol of the Republican party
- Notable examples include Dumbo and Horton
- It does not have a tail

Don’t throw the elephant out with the bathwater.

Hypersomnias



NT1=Narcolepsy Type 1, NT2=Narcolepsy Type 2.

Dauvilliers Y, et al. Sleep Med Rev. 2022;66:101709.

Disorders of EDS/Hypersomnia Are A Significant Category of Sleep Disorders

- Circadian Rhythm Disorders
- Sleep Related Breathing
- Sleep-Related Movement Disorders/RLS/PLMD
- Parasomnias
- Hypersomnias
- Insomnia
- Curses/Horcruxes/ Spells/Incantations
- Other

RLS=Restless Leg Syndrome; PLMD=Periodic Limb Movement Disorder

Be Careful with This Approach

- Circadian Rhythm Disorders
- Hypersomnias
- Insomnia
- Sleep-Related Movement Disorders/RLS/ PLMD
- Parasomnias
- Other

Sleep Related Breathing

Key Learning Points

- Separate sleepiness and fatigue. Avoid “tired”.

- Regarding ESS:
  - Low ESS is not supportive of “sleepy.”
  - High ESS: Is it poor quality, inadequate quality, or both?
  - Question a High ESS and a low AHI sleep apnea patient.

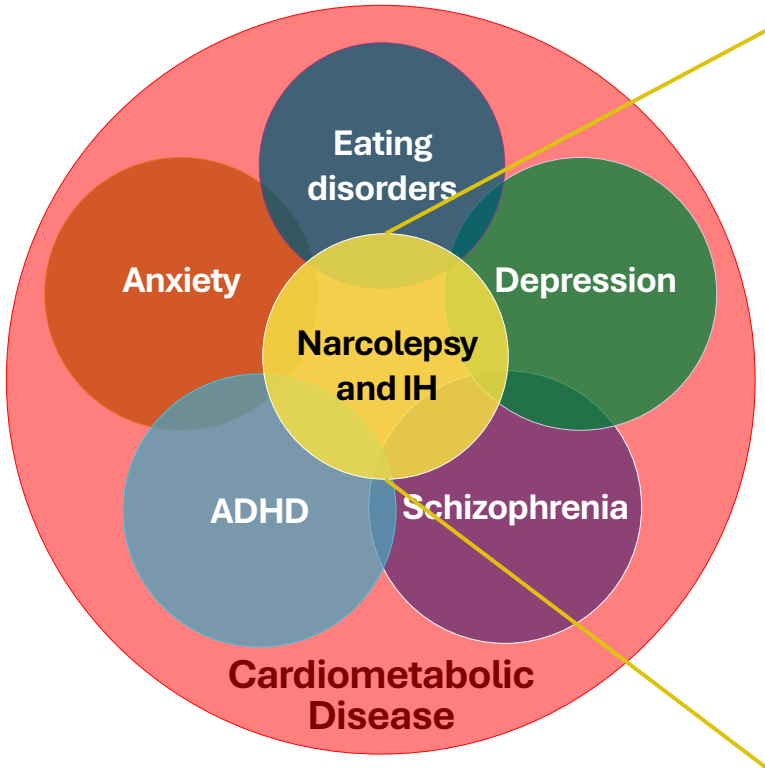
- The IHSS is a brief, validated 14-point scale that looks for the most common signs and symptoms of IH. (MILD: 0-12 | MODERATE: 13-25 | SEVERE: 26-38 | VERY SEVERE: 39-50)

- The MSLT is one piece of information.

The Role of Sodium in Cardiovascular Health

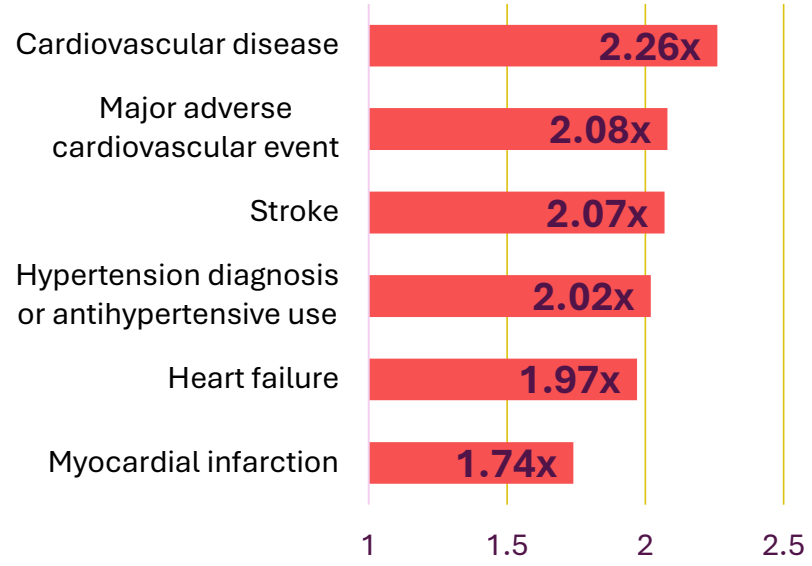
Craig Chepke, MD, DFAPA

Narcolepsy, IH, and Psychiatric Conditions also Run in the Same Circles as Cardiometabolic Disease



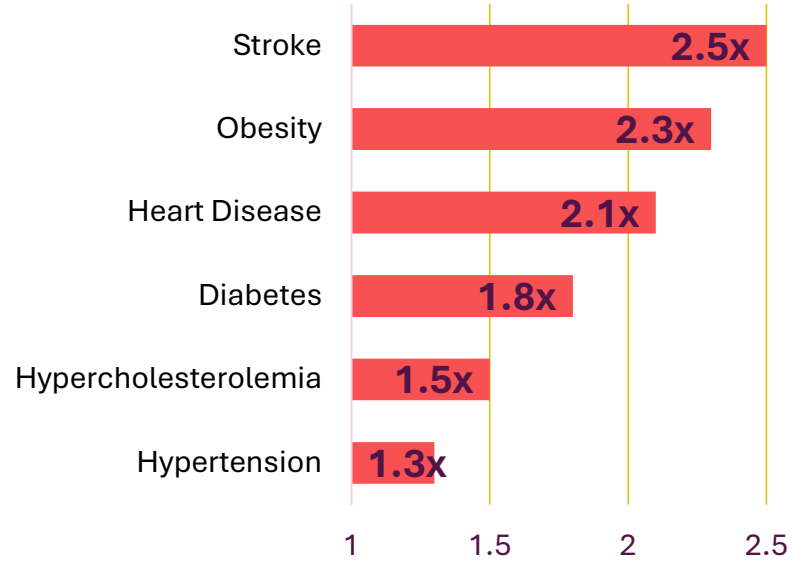
IDEOPATHIC HYPERSOMNIA

Compared to matched controls, **patients with IH had an increased odds of all cardiovascular conditions**



NARCOLEPSY

Increased risk of comorbid conditions in patients with narcolepsy vs controls



IH=Idiopathic Hypersomnia; ADHD=Attention-Deficit Hyperactivity Disorder

Chepke C, et al. J Clin Psychiatry 86.3 (2025): 24nr15718. Morse AM & K Sanjeev. Med. Sci 6.1 (2018): 16. Saad R, et al. Nat. Sci. Sleep (2025): 1809-1823. Black J, et al. Sleep Med. (2017);33:13-18. Ohayon MM. Sleep Med. (2013);14(6):488-492.

Physical status assessments:

- ☑ Vital signs: pulse, blood pressure
- ☑ Body weight and height
- ☑ Basic Metabolic Panels
- ☑ Liver Function Tests
- ☑ Hemoglobin A1C
- ☑ Lipid Panels
- ☑ Prolactin
- ☑ EKGs

We've become used to monitoring for and educating about many components of physical health and cardiometabolic risk factors…

…why not sodium?

American Psychiatric Association. *Practice Guideline for the Treatment of Patients With Schizophrenia*. 3rd ed. Washington, DC: American Psychiatric Association Publishing; 2020.

Sodium Intake is a Critical Target for CV Health

AHA recommends daily sodium intake *not to exceed 2,300 mg*, with an ideal limit of **1,500 mg**

The average American consumes **3,400 mg** of sodium per day

About **40% of the sodium consumed by Americans comes from:**

deli meat sandwiches, burgers, pizza, burritos/tacos, soups, pasta mixed dishes, egg dishes, and savory snacks (e.g. chips, crackers, popcorn)

High sodium intake is linked to:

High blood pressure	Reducing sodium intake **lowers systolic blood pressure by ~5 mm Hg**
Kidney problems	Higher frequency of salt use is associated with a higher risk of **chronic kidney disease**
Higher risk of heart failure and CVD	There is a **~6% increase in CVD risk** for every 1000mg of sodium consumed
Higher risk of stroke	Those who consume ≥5g of salt per day have **~20% higher risk of stroke**

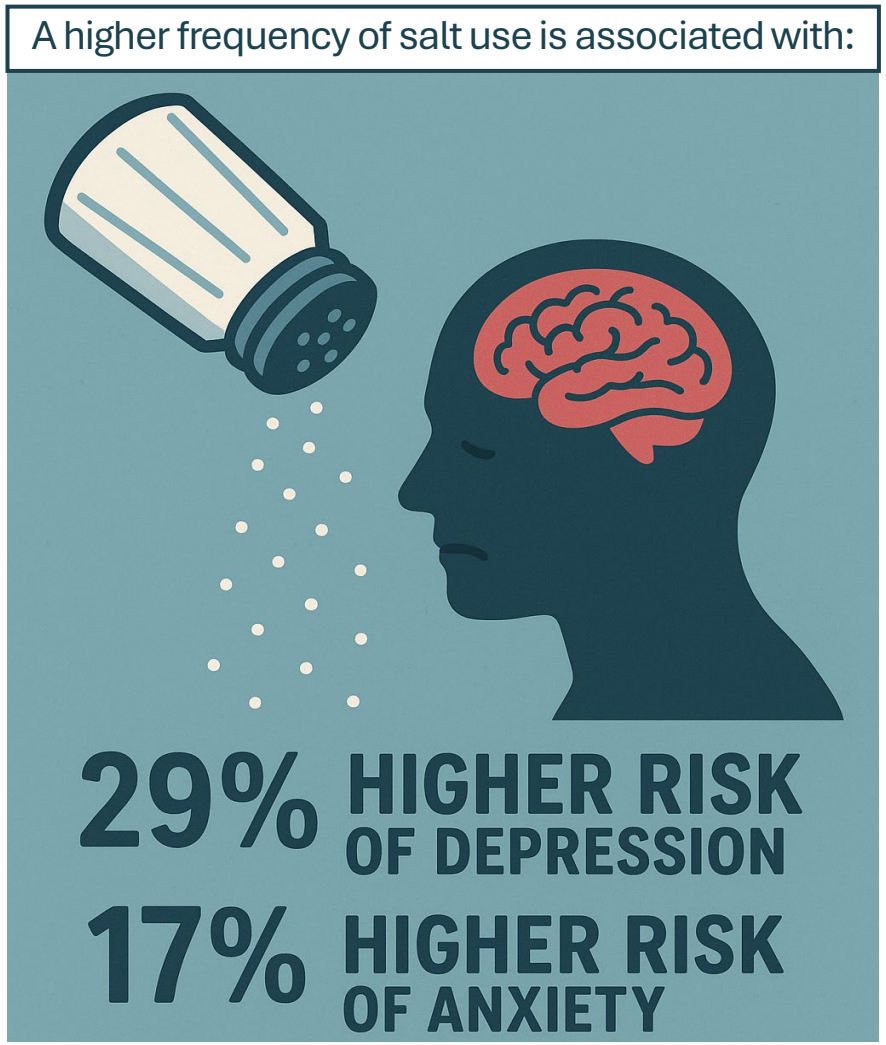
Worse Mental Health Outcomes

AHA=American Heart Association

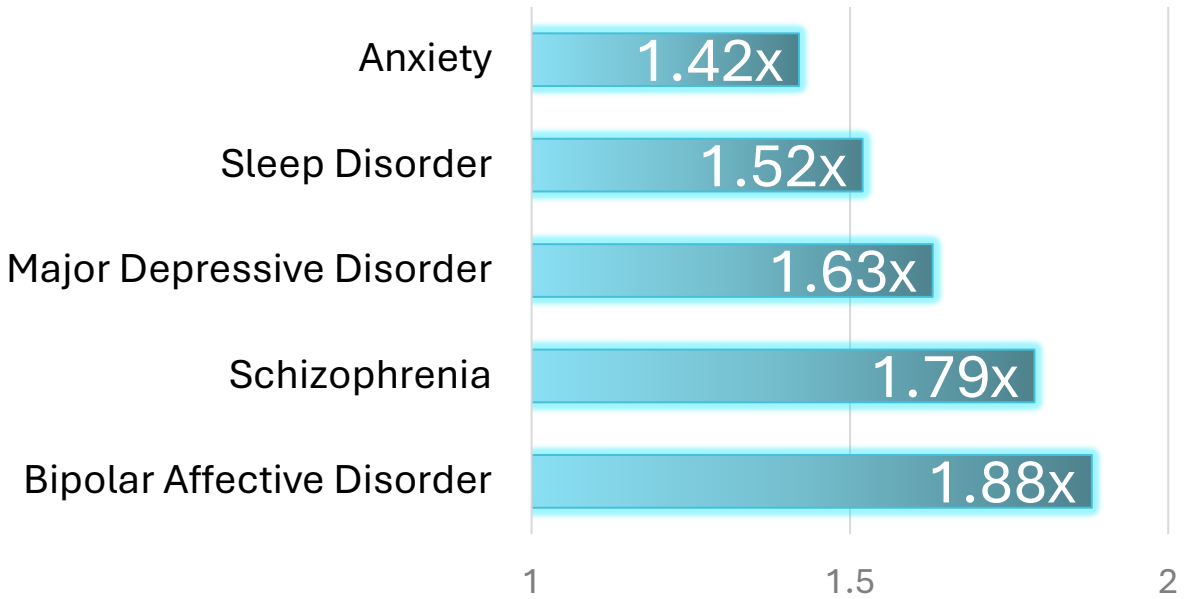
Gupta DK, et al. *JAMA*. 2023;330(23):2258-2266. Tang R, et al. *JAMA Netw Open*. 2023;6(12):e2349930. Wang YJ, et al. *Nutrients*. 2020;12(10):2934. Strazzullo P, et al. *BMJ*. 2009;339:b4567. U.S. Food and Drug Administration. https://www.fda.gov/food/nutrition-education-resources-materials/sodium-your-diet. Accessed September 4, 2025.

...and Linked to Worse Mental Health

A higher frequency of salt use is associated with:



Compared to never/rarely,
always adding salt to food is associated with a
higher risk of the following psychiatric disorders:



In a longitudinal study of adolescents:

Greater sodium excretion and **lower potassium excretion**
(linked to poor diet) predicted
more severe depressive symptoms at follow-up

after controlling for age, sex, BMI, and baseline depressive symptoms

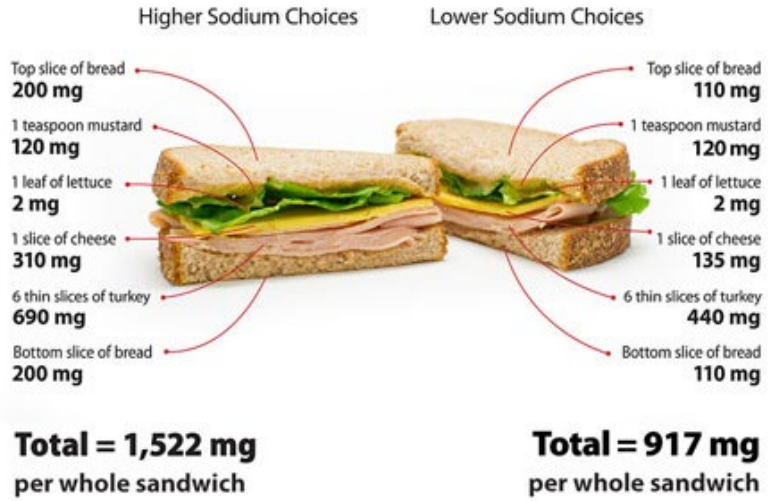
BMI=Body Mass Index.

Mrug S, et al. *Physiol Rep*. 2019;7(16):e14213. Wang W, et al. *BMC Med*. 2025;23(1):32. Yu HH, et al. *J Affect Disord*. 2025;391:119975.

Practical Tips for Sodium Intake Reduction Counseling in Psychiatric Practice

Lifestyle changes to recommend:

- Taste your food before putting extra salt on it
- Try no-salt seasoning blends or herbs and spices instead of salt to add flavor to your food.
- Rinse any canned beans, vegetables, or other foods
- Recognize that foods that don't taste salty can still be high in sodium
- On nutrition labels, ≥20% of DV is considered high



Simply using a salt substitute (75% NaCl ,25% KCl) lowered the risk of major cardiovascular adverse events by 13% (rate ratio 0.87; 95% CI, 0.80 to 0.94; P<0.001)

In an open-label, cluster-randomized trial (n=20,995) with a mean follow-up of 4.75 years

Your advice matters!

People without HTN who received advice about sodium reduction were 55% more likely to reduce their sodium consumption compared to those who did not

in an annual state-based, cross-sectional telephone survey

DV=Daily Value; HTM=Hypertension; Na=Sodium, Cl=Chloride; K=Porassium

Wang YJ, et al. *Nutrients*. 2020;12(10):2934. Va P, et al., MMWR Morb Mortal Wkly Rep. 2018;67(7):225-229. https://www.cdc.gov/salt/reduce-sodium-intake/index.html. Accessed 8-20-25. https://www.fda.gov/food/nutrition-facts-label/how-understand-and-use-nutrition-facts-label? Accessed 8-20-25.

Limitations of Traditional Treatments for Narcolepsy and IH

Craig Chepke, MD, DFAPA

American Academy of Sleep Medicine Guideline-Recommended Medications for Narcolepsy

Intervention	Strength of Recommendation	Critical Outcomes Showing Clinically Significant Improvement			
		EDS	Cataplexy	Disease Severity	QoL
Modafinil	Strong	X		X	X
Pitolisant	Strong	X	X	X	
Sodium oxybate	Strong	X	X	X	
Solriamfetol	Strong	X		X	X
Armodafinil	Conditional	X		X	
Dextroamphetamine	Conditional	X	X		
Methylphenidate	Conditional			X	

Challenges in Use of Stimulants for Narcolepsy

- Stimulant shortages, Schedule II
- Common Adverse Effects (≥5%): headache, nausea, dizziness, and insomnia
- May cause or worsen aggression, irritability, hostility, anxiety, mood swings
- Increases cardiovascular risk

Amphetamine & Methylphenidate Products with a Labeled Narcolepsy Indication

Mixed amphetamine salts
Mixed amphetamine salts tablets (Adderall)

Amphetamine sulfate (single salt)
Amphetamine sulfate tablets (Evekeo)

Dextroamphetamine sulfate
Dextroamphetamine IR tablets (Zenzedi)
Dextroamphetamine ER Spansules
Dextroamphetamine oral solution (ProCentra)

Methylphenidate hydrochloride
Methylphenidate IR tablets (Ritalin)
Methylphenidate SR tablets (Ritalin-SR)
Methylphenidate ER tablets (Metadate ER)
Methylphenidate chewable tablets (Methylin)
Methylphenidate oral solution (Methylin)

EDS=Excessive Daytime Sleepiness; QoL, Quality of Life. IR=Immediate-Release; ER= Extended-Release; SR= Sustained-Release

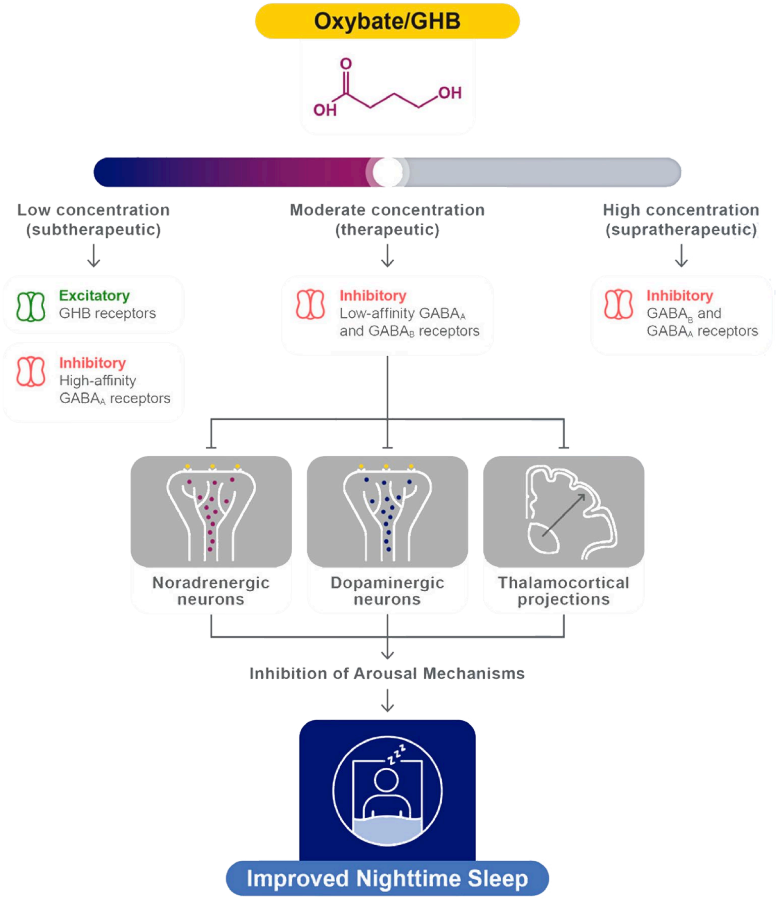
Maski K, et al. "Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline." Journal of Clinical Sleep Medicine 17.9 (2021): 1881-1893. Prescribing Ianformation. Drugs@FDA: Accessed 8.20.25. www.accessdata.fda.gov/scripts/cder/daf/.

Sodium Oxybate Robustly Treats the EDS and Cataplexy of Narcolepsy

Sodium Oxybate is a salt of gamma-hydroxybutyrate, an endogenous compound that is a metabolite of GABA

Its therapeutic effects may be mediated through $GABA_B$ actions during sleep at NE, DA, and thalamocortical neurons

The net effects are consolidation of nocturnal sleep and improved sleep architecture, which reduces daytime sleepiness



Changes in Alerting Agents in 180 Days Following Oxybate Initiation in the Oxybate Naïve (n=283)

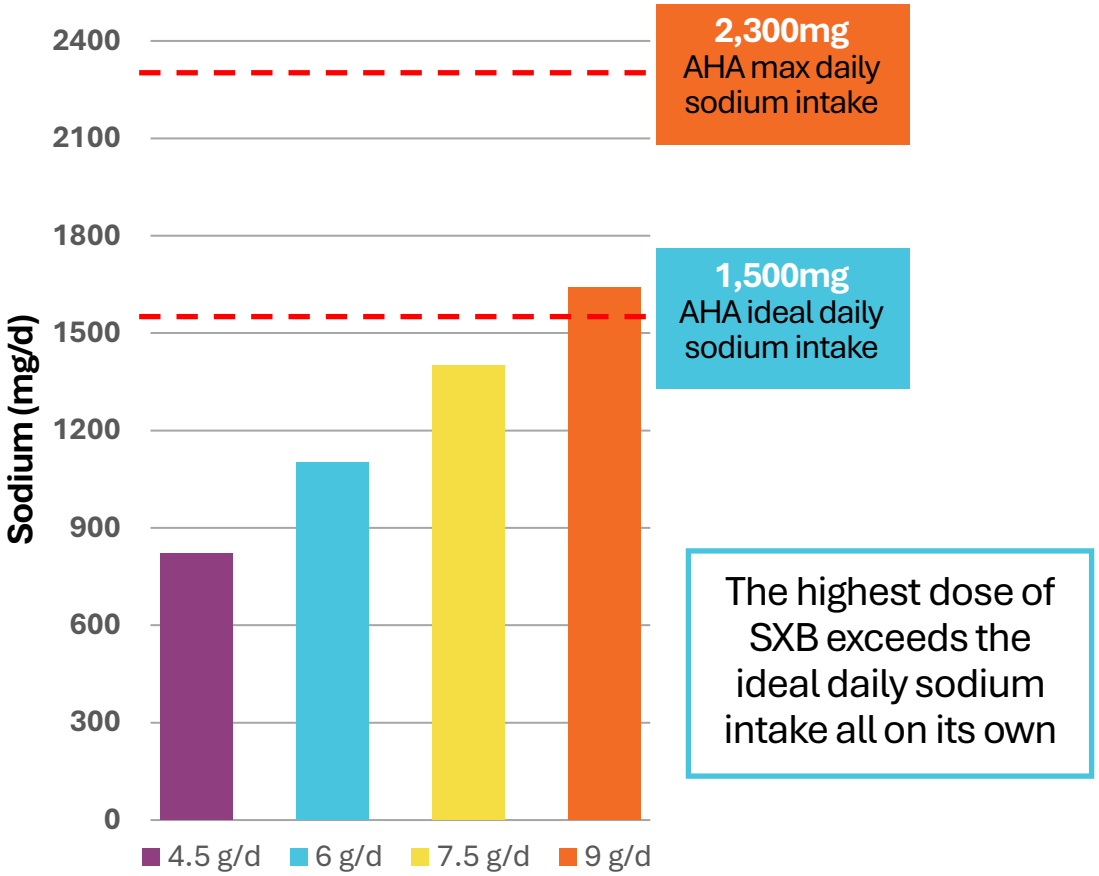
Reduction	87 (30.7%)
Discontinuation	58 (20.5%)
Switch	25 (8.8%)
No Change	60 (21.2%)

from a real-world retrospective EHR and claims analysis study

GABA=Gamma-Aminobutyric Acid; NE=Norepinephrine, DA=Dopamine, EDS=Excessive Daytime Sleepiness

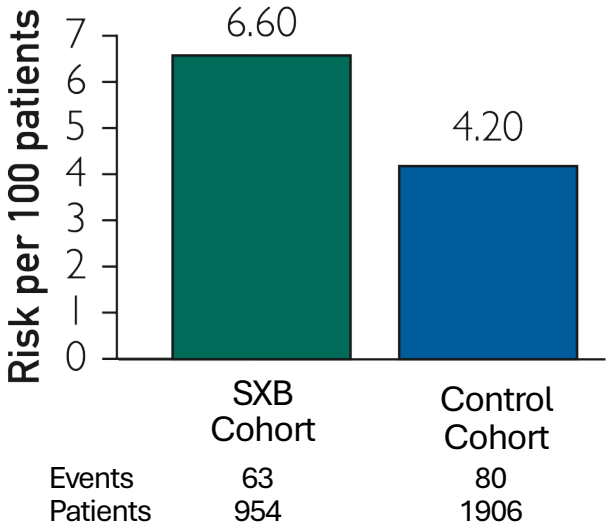
Prescribing Information. Drugs@FDA: Accessed 8.20.25. www.accessdata.fda.gov/scripts/cder/daf/. Schneider LD, et al. Journal of Clinical Sleep Medicine (2025): jcsm-11566. Lavender M, et al. CNS drugs (2025): 1-13. Markt, et al. 2025. Poster Presented at SLEEP 2025, the 39th Annual Meeting of the Associated Professional Sleep Societies, LLC (APSS); June 8–11, 2025; Seattle, WA.

Unfortunately, Sodium Oxybate Has a *Very High* Sodium Content



The highest dose of SXB exceeds the ideal daily sodium intake all on its own

New-onset hypertension diagnosis or antihypertensive medication initiation



Starting SXB increased the odds of a new HTN diagnosis or added antihypertensives by **61%** over controls

in a real-world claims-analysis study

Sodium oxybate has been a gold standard in treating narcolepsy for decades, but it massively increases sodium intake, which could increase CV risk

SXB=Sodium Oxybate; HTN=Hypertension; CV=Cardiovascular

Prescribing Information. Drugs@FDA: Accessed 8.20.25. www.accessdata.fda.gov/scripts/cder/daf/. Ben-Joseph RH, et al. Mayo Clinic Proceedings. Vol. 99. No. 11. Elsevier, 2024.

Key Learning Points

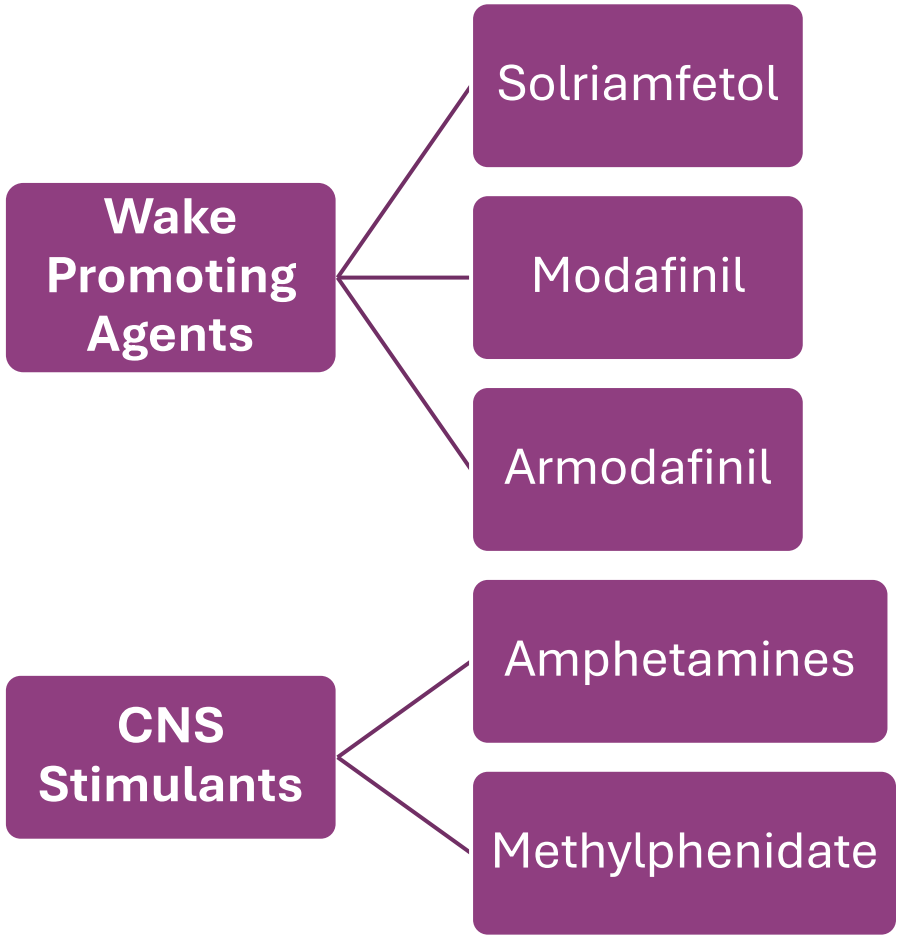
- Individuals with hypersomnolence disorders—just like those with psychiatric conditions—are at greater risk for cardiovascular comorbidities and earlier death from cardiovascular disease
- Sodium intake is a key risk factor in cardiovascular disease and one that psychiatric clinicians are very capable of helping patients to modify
- Sodium oxybate is one of the foundational treatments of narcolepsy, but it has an extremely high sodium content

Newer and Emerging Treatments for Narcolepsy and IH

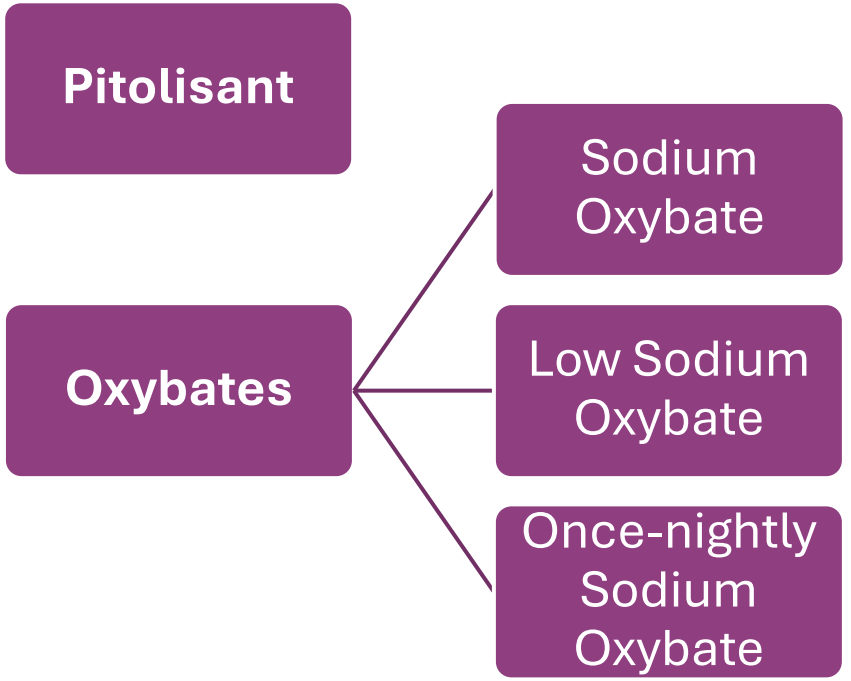
W. Christopher Winter, MD, DABSM, DABPN, FAASM

Pharmacotherapy Overview

Daytime Alerting Agents



Sleep-Wake Stabilizing Agents



Oxybate

Photo: Gemini AI generate image

Sodium [illegible]te

Xyrem (sodium oxybate) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2020.

Oxybate Side Effects

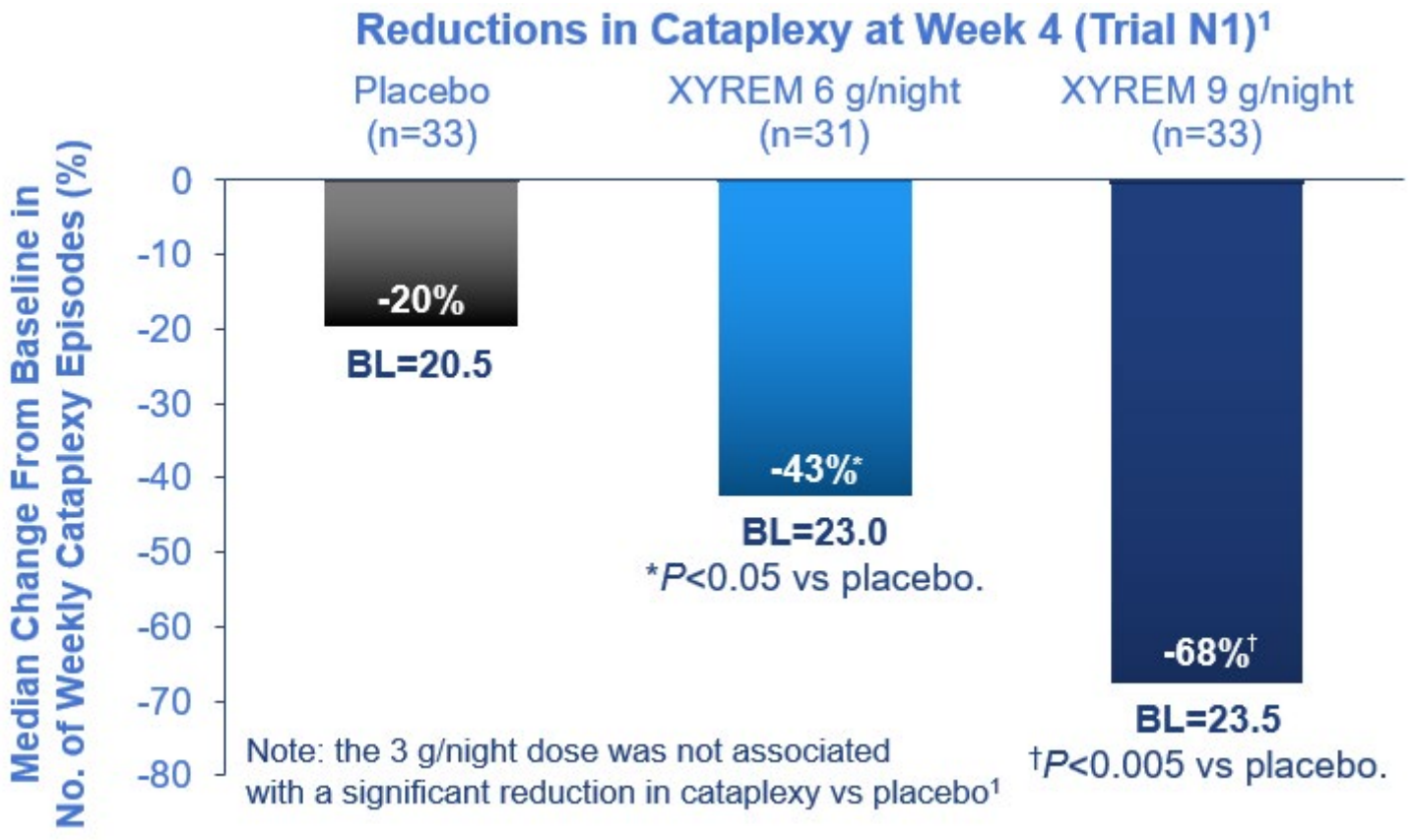
Side Effects/Risks

- Side effects are often dose-dependent
- Side effects include nausea, dizziness, headache, weight loss, urinary incontinence, mood swings, worsening of depression, sleepwalking, and psychosis
- Household safety should be discussed (ability to respond to emergencies, care for children, etc). Over-dosage can result in respiratory depression, coma, and death
- Coadministration with alcohol and CNS depressants increases the risk for impaired consciousness and respiratory depression
- Risk Evaluation and Mitigation Strategies (REMS) programs

Bogan RK, et al. *Sleep.* 2021;44(3):zsaa206.

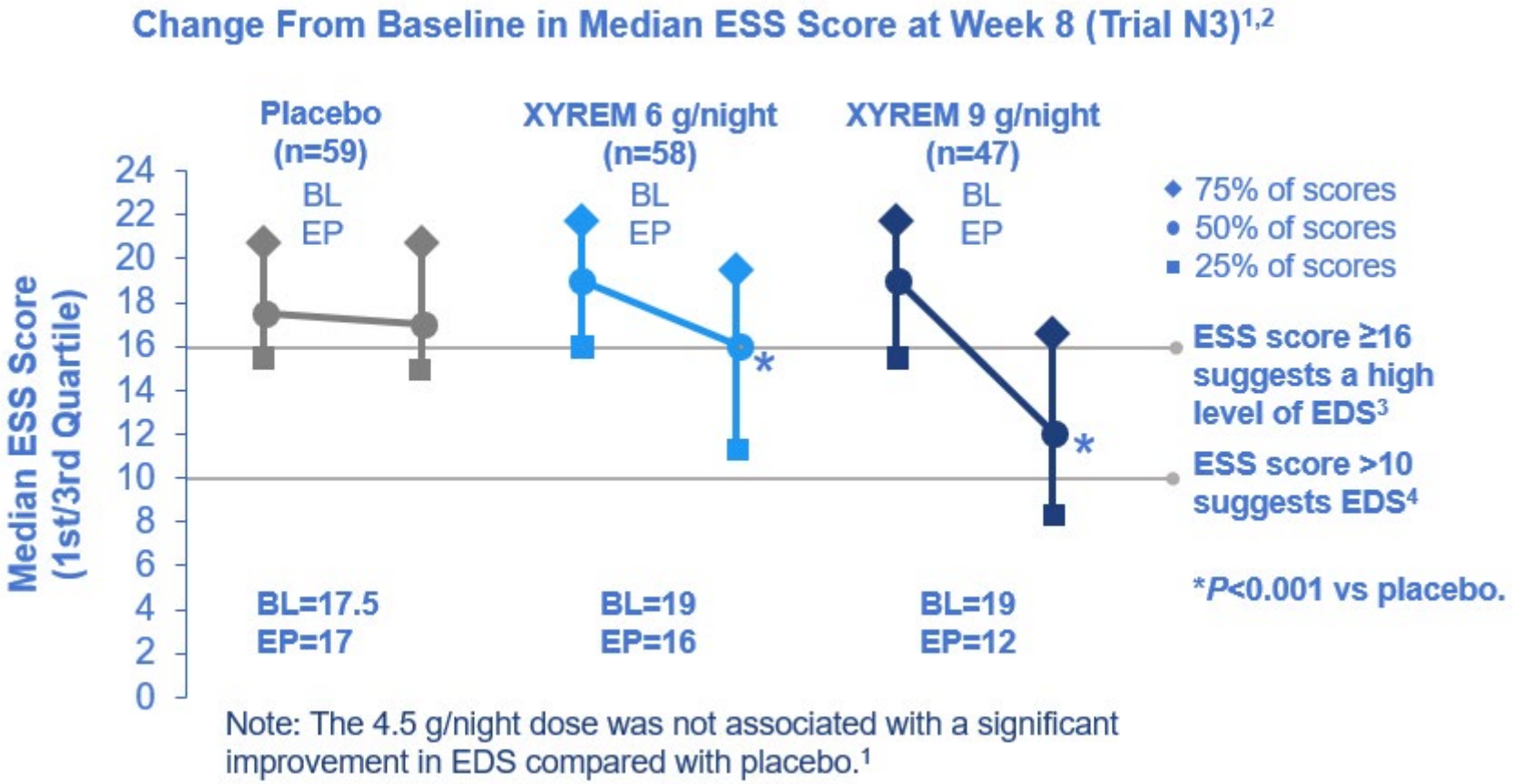
Twice Nightly
Sodium Oxybate

Twice Nightly Sodium Oxybate Efficacy Cataplexy



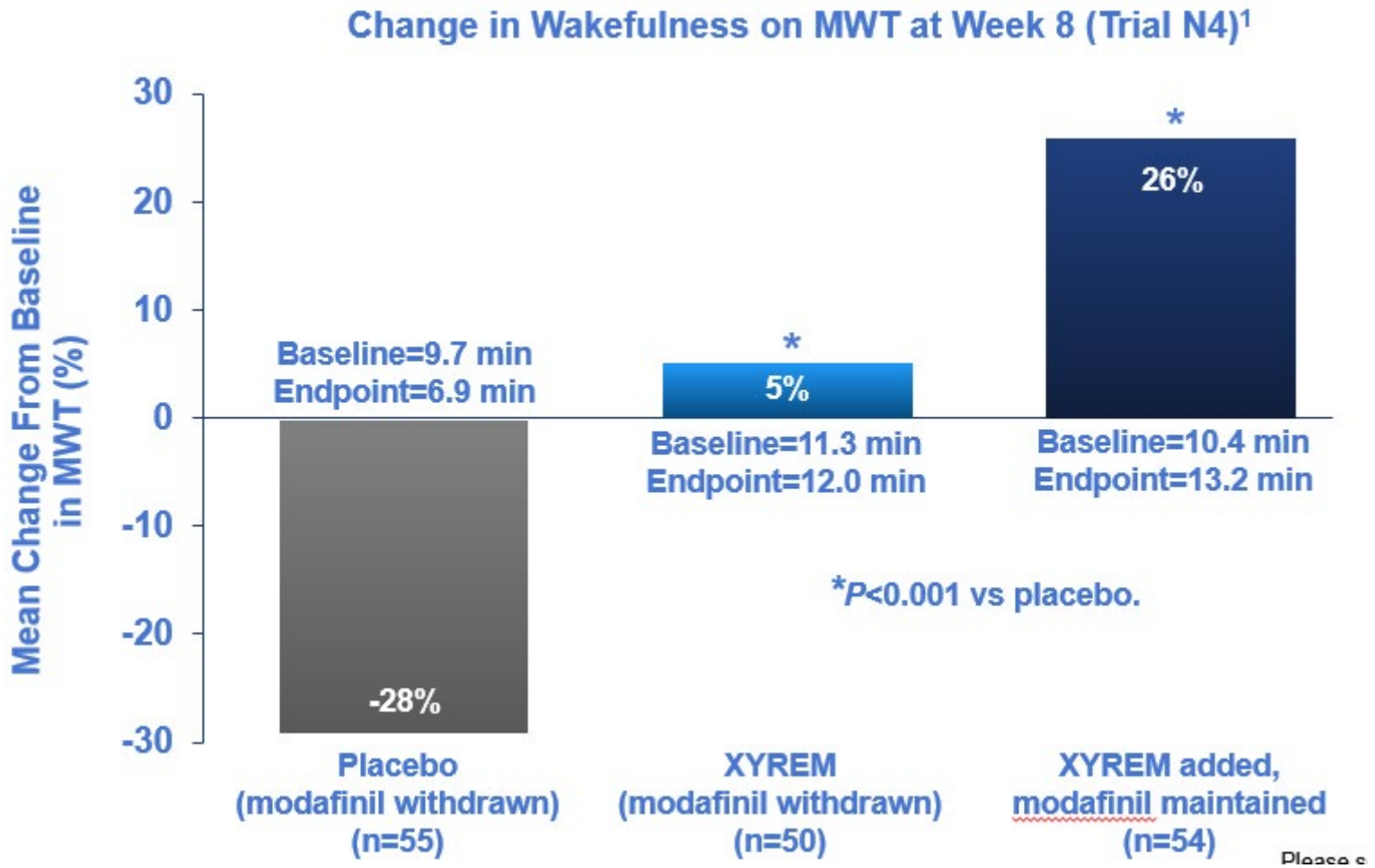
Xyrem [prescribing information] Palo Alto, CA; Jazz Pharmaceuticals, Inc., 2018

Twice Nightly Sodium Oxybate Efficacy
EDS (ESS)



Xyrem [prescribing information] Palo Alto, CA; Jazz Pharmaceuticals, Inc., 2018

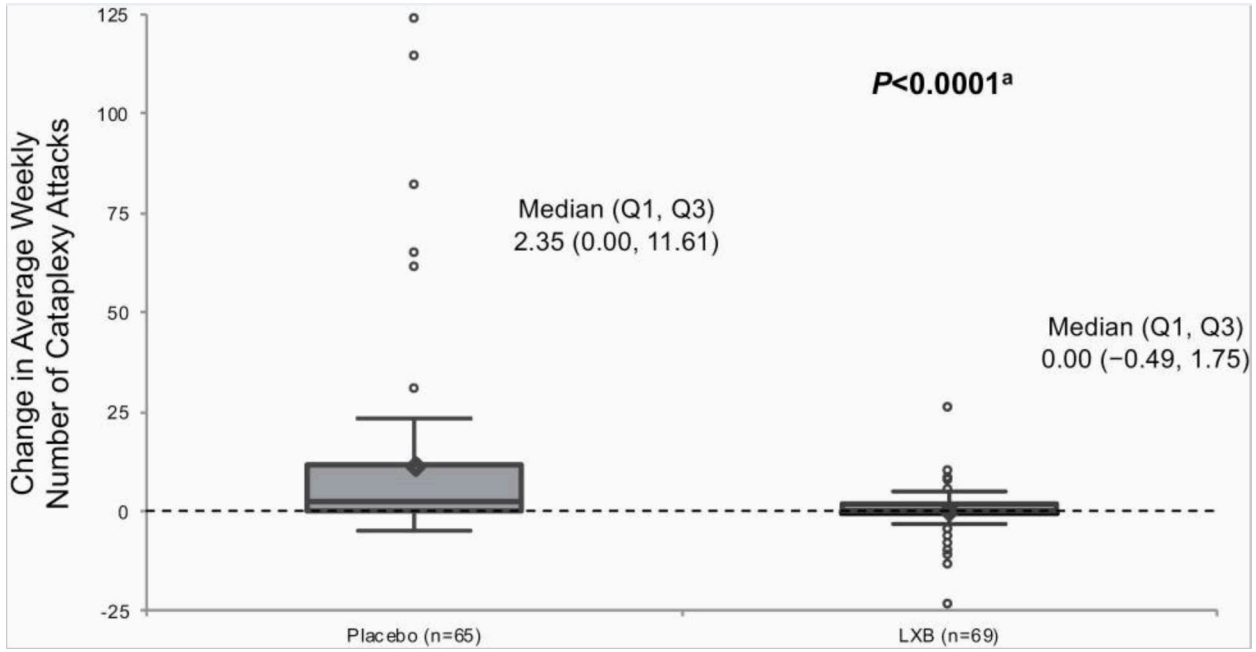
Twice Nightly Sodium Oxybate Efficacy EDS (MWT)

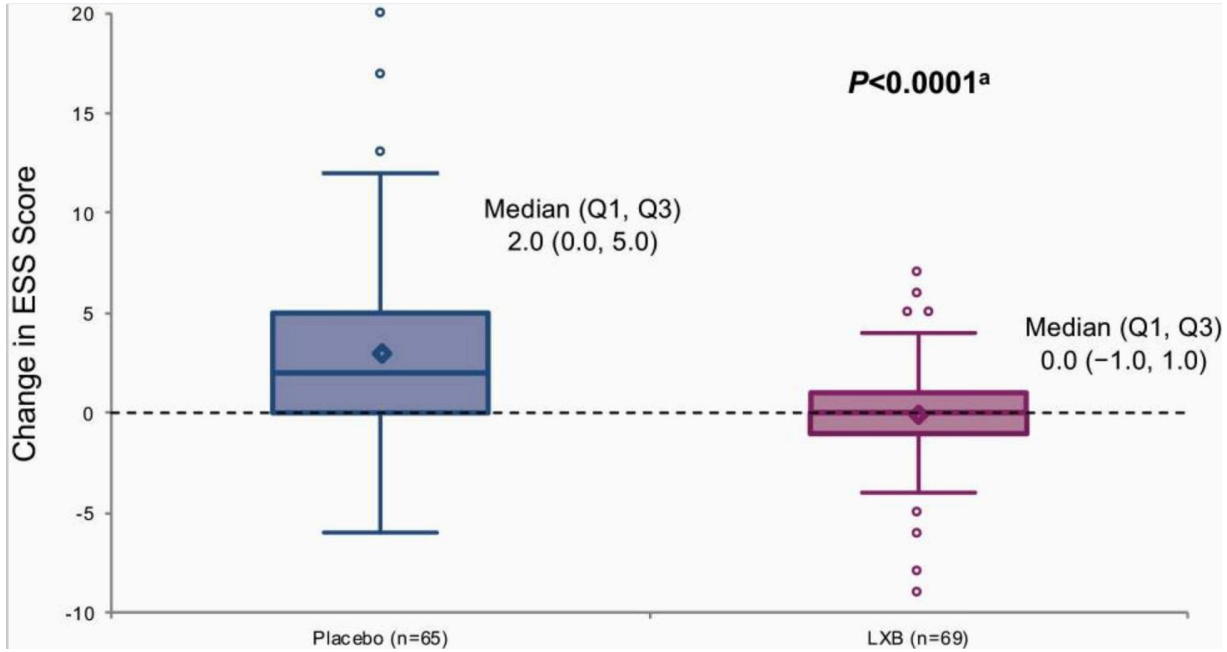


Xyrem [prescribing information] Palo Alto, CA; Jazz Pharmaceuticals, Inc., 2018

Twice Nightly
Low Sodium Oxybate

Twice Nightly Low Sodium Oxybate Efficacy Cataplexy/EDS

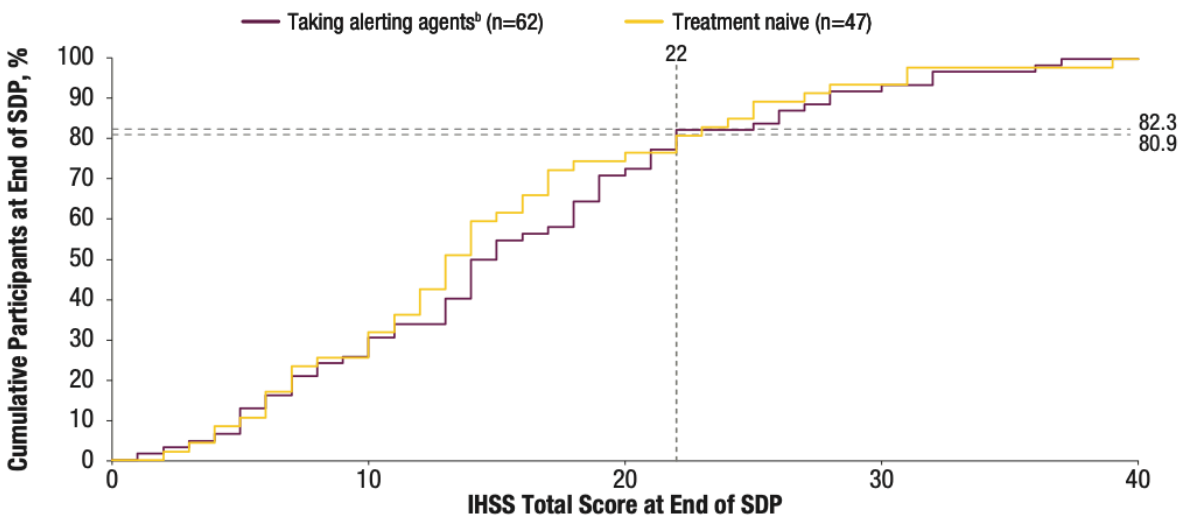




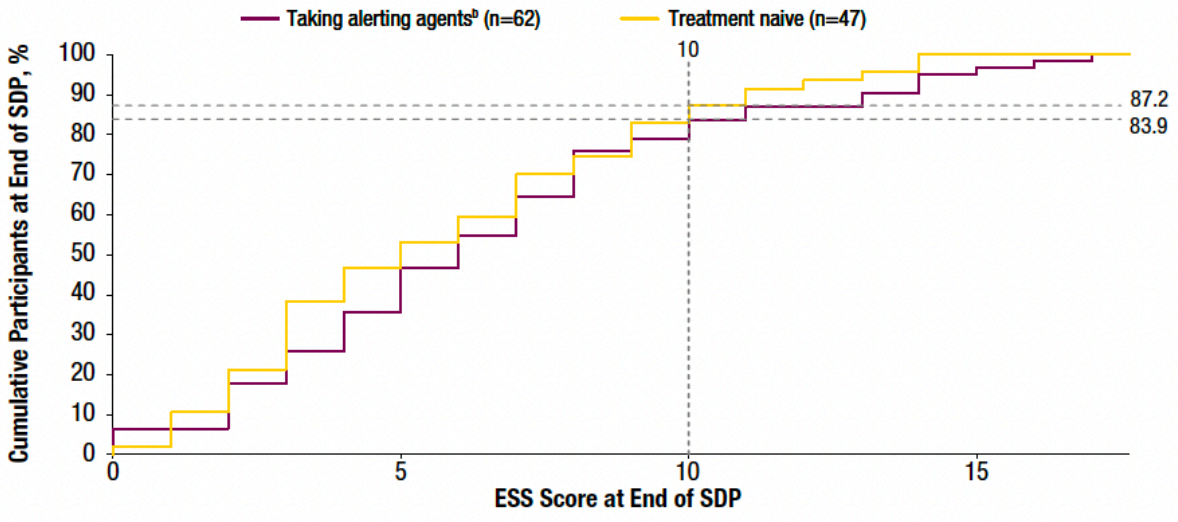
Bogan RK, et al. *Sleep.* 2021;44(3):zsaa206.

Twice Nightly Low Sodium Oxybate Efficacy Idiopathic Hypersomnia

Over 80% of Participants Achieved IHSS Total Score of ≤22 Points (Remission) by End of SDP



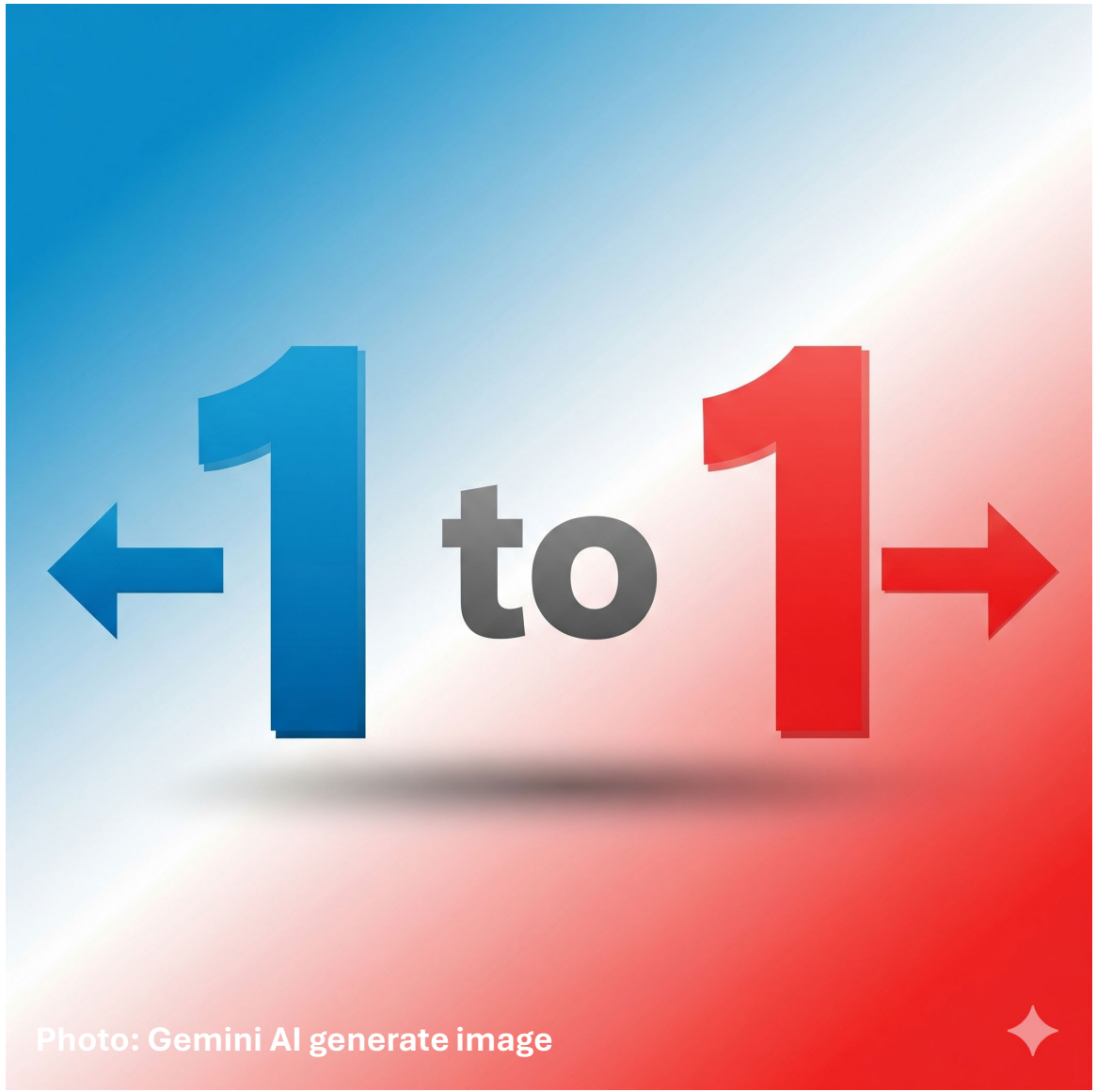
Over 80% of Participants Achieved ESS Score of ≤10 Points (Remission) by End of SDP



IHSS = Idiopathic Hypersomnia Severity Scale; SDP = stable-dose period.

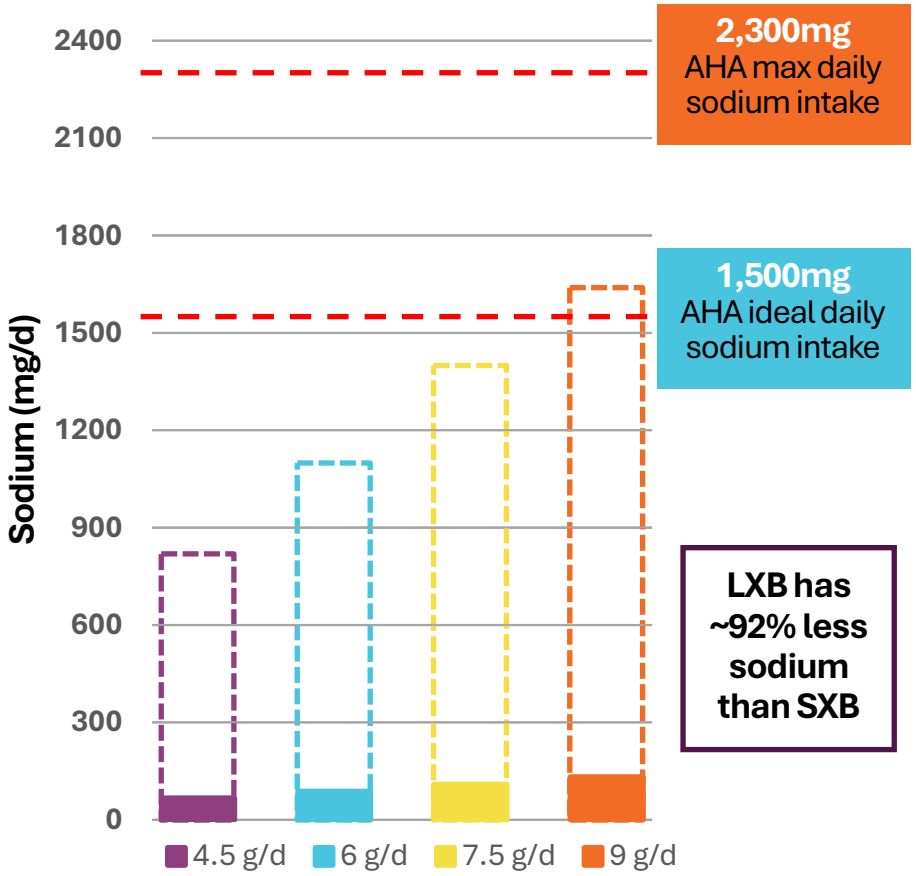
Dauvillers Y, et al. Efficacy of lower-sodium oxybate in the treatment of idiopathic hypersomnia: evaluation of response based on the idiopathic hypersomnia severity scale score. Presented at: Psych Congress, 2022; New Orleans, LA. Poster 138.
Rosenberg R, et al. Efficacy of lower-sodium oxybate in the treatment of idiopathic hypersomnia: evaluation of the response based on the Epworth Sleepiness Scale score. Presented at: Psych Congress, 2022; New Orleans, LA. Poster 137.

Switching Patients from Sodium Oxybate to Low Sodium Oxybate



- Switching patients from high to low sodium oxybate is simple and requires simply putting patients on the equivalent dose of low sodium oxybate
- In the event that switching back is necessary, the same applies.
- There may be a need to slightly adjust a patient's dose of low sodium oxybate as data indicates for some, efficacy might differ between the dose forms.

Differences in CV Risk with Low Sodium Oxybate vs Sodium Oxybate

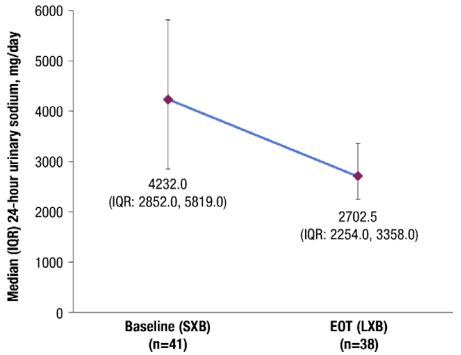


2,300mg
AHA max daily sodium intake

1,500mg
AHA ideal daily sodium intake

LXB has ~92% less sodium than SXB

Reductions in 24-hr Urinary Sodium
in an Open-Label, Single-Arm Switch Study



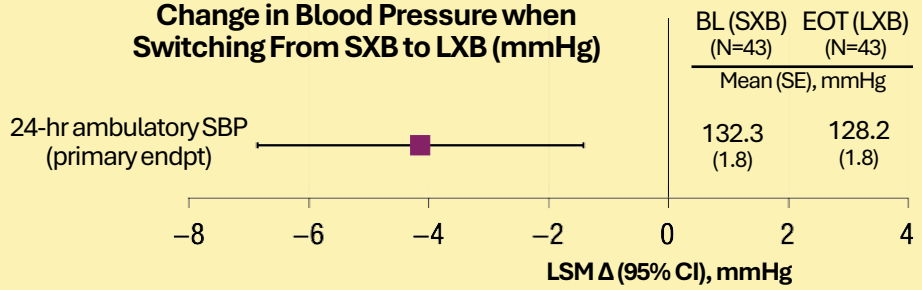
Reductions in 24-hr urinary sodium paralleled reduced sodium intake when switching **from SXB** to **LXB**

(Completer Population)

Each increment of **1000 mg/d** in sodium excretion is associated with an **18% increase** in CV risk

in a meta-analysis of prospective cohort studies

Change in Blood Pressure when Switching From SXB to LXB (mmHg)



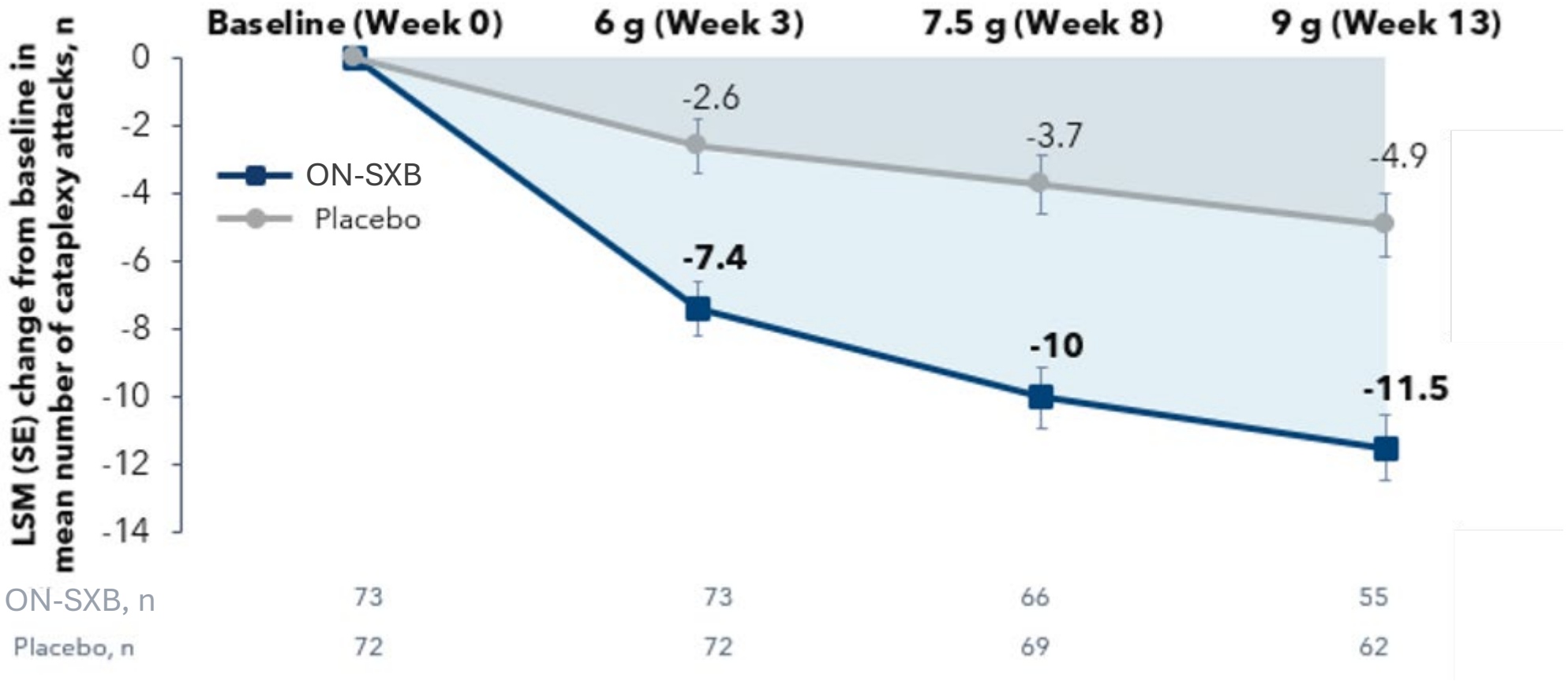
Reducing SBP by 5 mmHg reduces the risk of major CV events by about 10% (w/ or w/o previous CVD and at normal or high-normal BP) in large (n>300,000) meta-analyses

SXB=Sodium Oxybate; LXB=Low-Sodium Oxybate; BL=Baseline; EOT=End of Treatment; LSM=Least Squares Means; CV=Cardiovascular Disease

Prescribing Information. Drugs@FDA: Accessed 8.20.25. www.accessdata.fda.gov/scripts/cder/daf. Somers VK, et al. Impact of Switching From High- to Low-Sodium Oxybate on Ambulatory Blood Pressure in Patients With Narcolepsy. Presented at SLEEP 2025, the 39th Annual Meeting of the Associated Professional Sleep Societies (APSS); June 8–11, 2025; Seattle, WA, USA. Nazarzadeh M, et al. Lancet Diabetes Endocrinol. 10.9 (2022): 645-654.

Once Nightly Sodium Oxybate

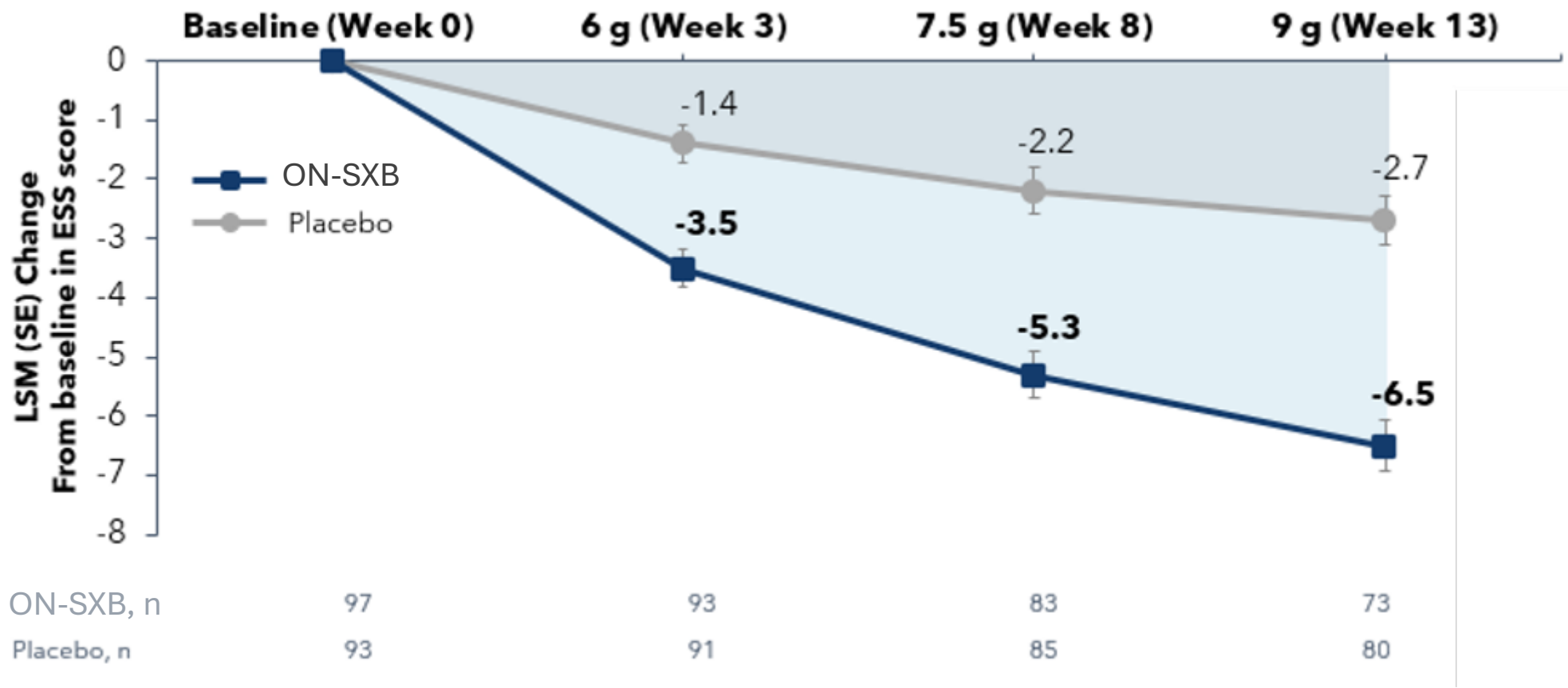
Once Nightly Sodium Oxybate Efficacy Cataplexy (REST-ON)



ON-SXB=Once Nightly Sodium Oxybate

1) Kushida CA et al Sleep. 2022, 2)Lumryz package insert, 3) Thorpy MJ, et al Sleep Medicine 2024.

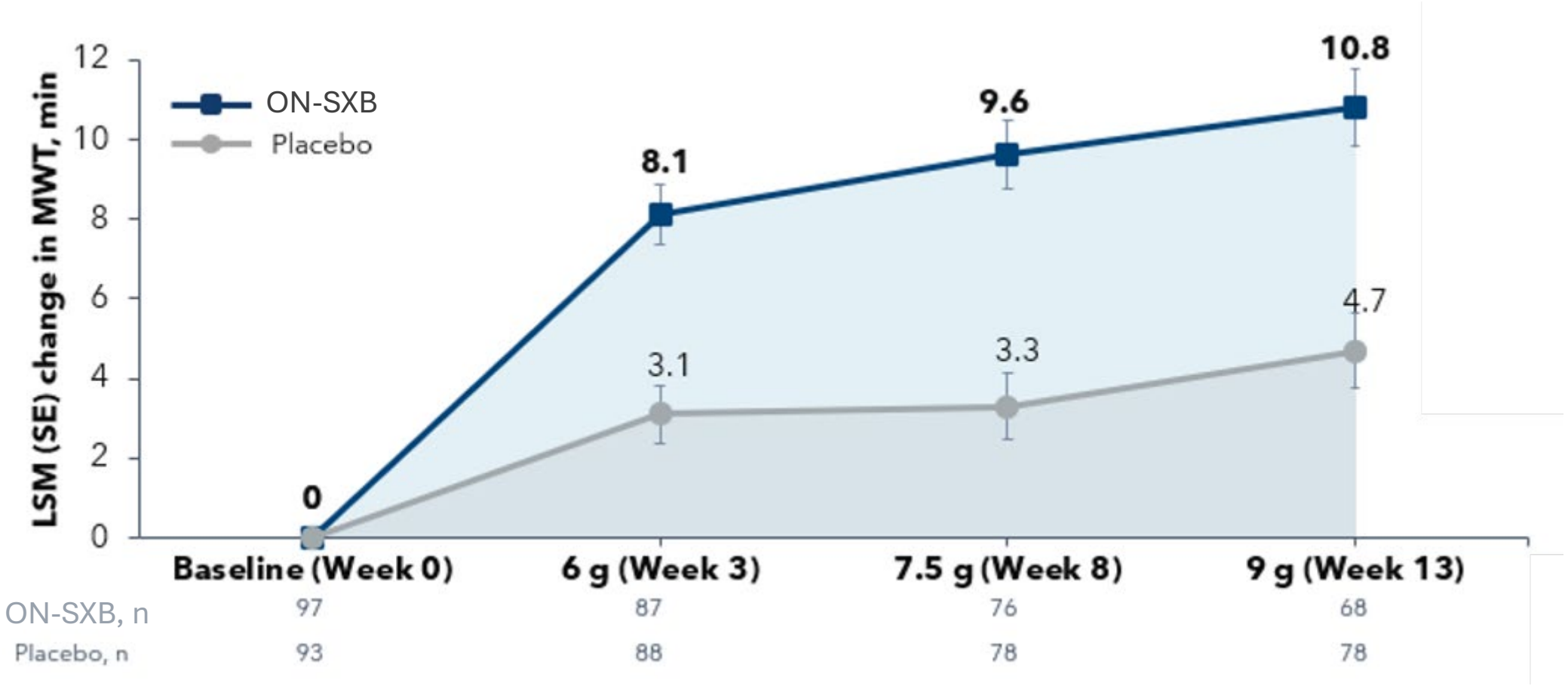
Once Nightly Sodium Oxybate Efficacy EDS (ESS) (REST-ON)



ON-SXB=Once Nightly Sodium Oxybate

1) Kushida CA et al Sleep. 2022, 2)Lumryz package insert, 3) Thorpy MJ, et al Sleep Medicine 2024.

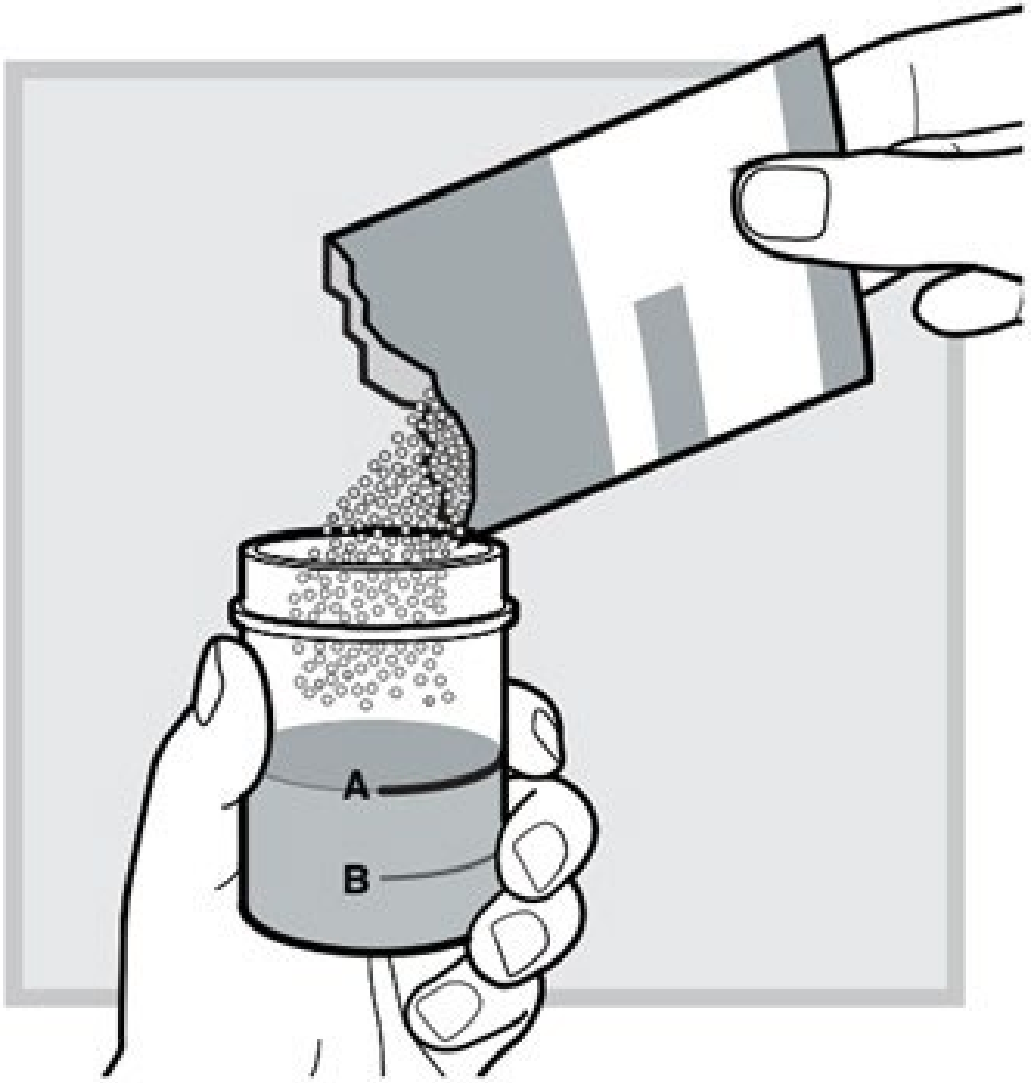
Once Nightly Sodium Oxybate Efficacy EDS (MWT) (REST-ON)



ON-SXB=Once Nightly Sodium Oxybate

1) Kushida CA et al Sleep. 2022, 2)Lumryz package insert, 3) Thorpy MJ, et al Sleep Medicine 2024.

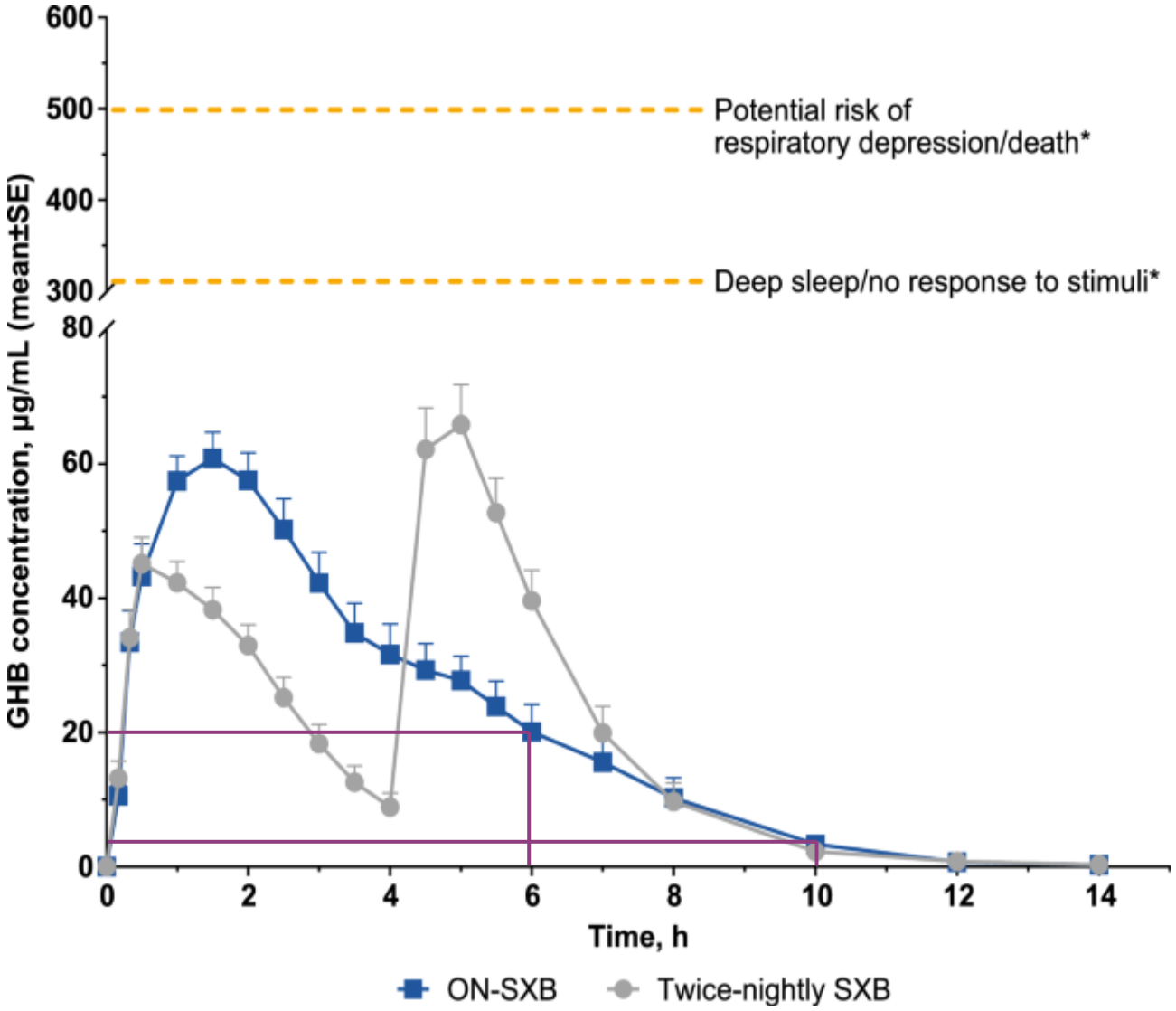
Once Nightly Sodium Oxybate



- Similar sodium content to twice nightly sodium oxybate
- Eliminates the need to awaken for second dose
- Less flexibility in dosing

Roth T, et al. 2022;36(4):377-387.

Once Nightly Sodium Oxybate



- While both share an identical black box warning
  - *"You should not drive, operate heavy machinery, or perform any activities requiring full alertness for at least six (6) hours after taking [the drug]—or until you know how the medication affects you."*
- While this is FDA-approved for children down to the age of 7, a child under 44 lbs would need to be started on a twice-nightly medication and transitioned.

Roth T. CNS Drugs. 2025;39(Suppl 1):37-51.

Safety and Efficacy of Low Sodium Oxybate

Adverse Reactions Occurring in ≥6% of Patients Treated With Xywav in the OTTp and SDp (Study 2)

Adverse Reaction	OL OTTp + SDp (%) (up to 16 weeks, N=154)
Nausea	21
Headache	16
Anxiety*	12
Dizziness	12
Insomnia†	8
Hyperhidrosis‡	8
Decreased appetite	8
Vomiting	7
Dry mouth	6

* Includes anxiety, nervousness, panic attack.

† Includes middle insomnia, initial insomnia, insomnia, and terminal insomnia.

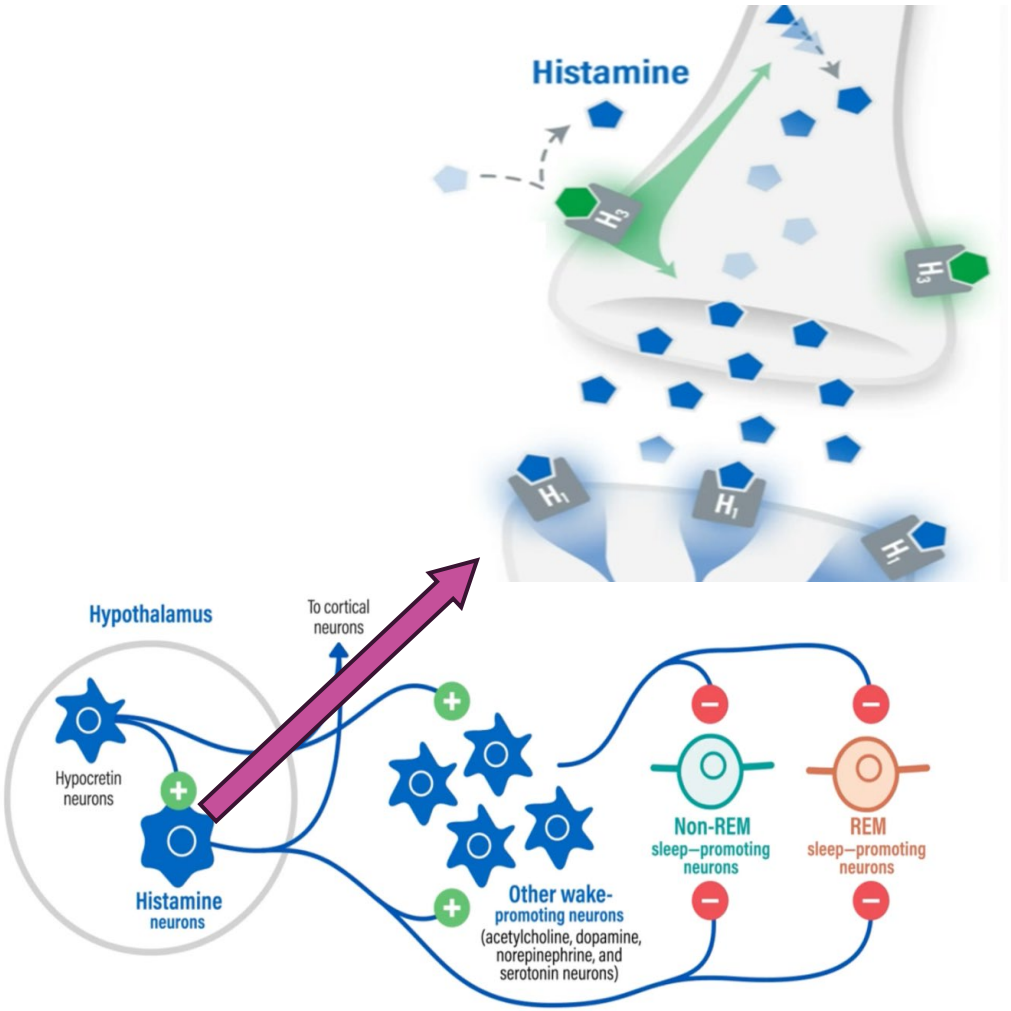
‡ Includes hyperhidrosis and night sweats.

- The efficacy of low sodium oxybate is very similar to sodium oxybate with bother reducing cataplexy and EDS in clinically meaningful ways.
- Cataplexy Reduction: A pivotal double-blind trial found that sodium oxybate reduced weekly cataplexy attacks by 57% and 84% depending on dose, respectively 4.5–9 g/night, compared to placebo.
- At the highest dose (9 g/night), median cataplexy frequency decreased from 21 attacks/week to 3 attacks/week after 8 weeks.
- Long-term open-label studies confirm that efficacy is sustained for years with continued treatment.

Bogan RK,, et al. *Sleep*. 2021;44(3):zsaa206; Dauvilliers Y, et al. *Lancet Neurol*. 2022;21(1):53-65.

Pitolisant

Pitolisant



Mechanism of Action:

- Oral histamine H3 receptor inverse agonist
- MoA for hypersomnolence and cataplexy in narcolepsy is unclear
- May be mediated through antagonist/inverse agonist activity at H_3 receptors, **resulting in increased histamine levels in the CNS**
- Improves daytime sleepiness and reduces cataplexy in adults with narcolepsy
- Effects may take up to 6-8 weeks to be noticeable
- Not a scheduled drug
- Did not receive the indication for IH

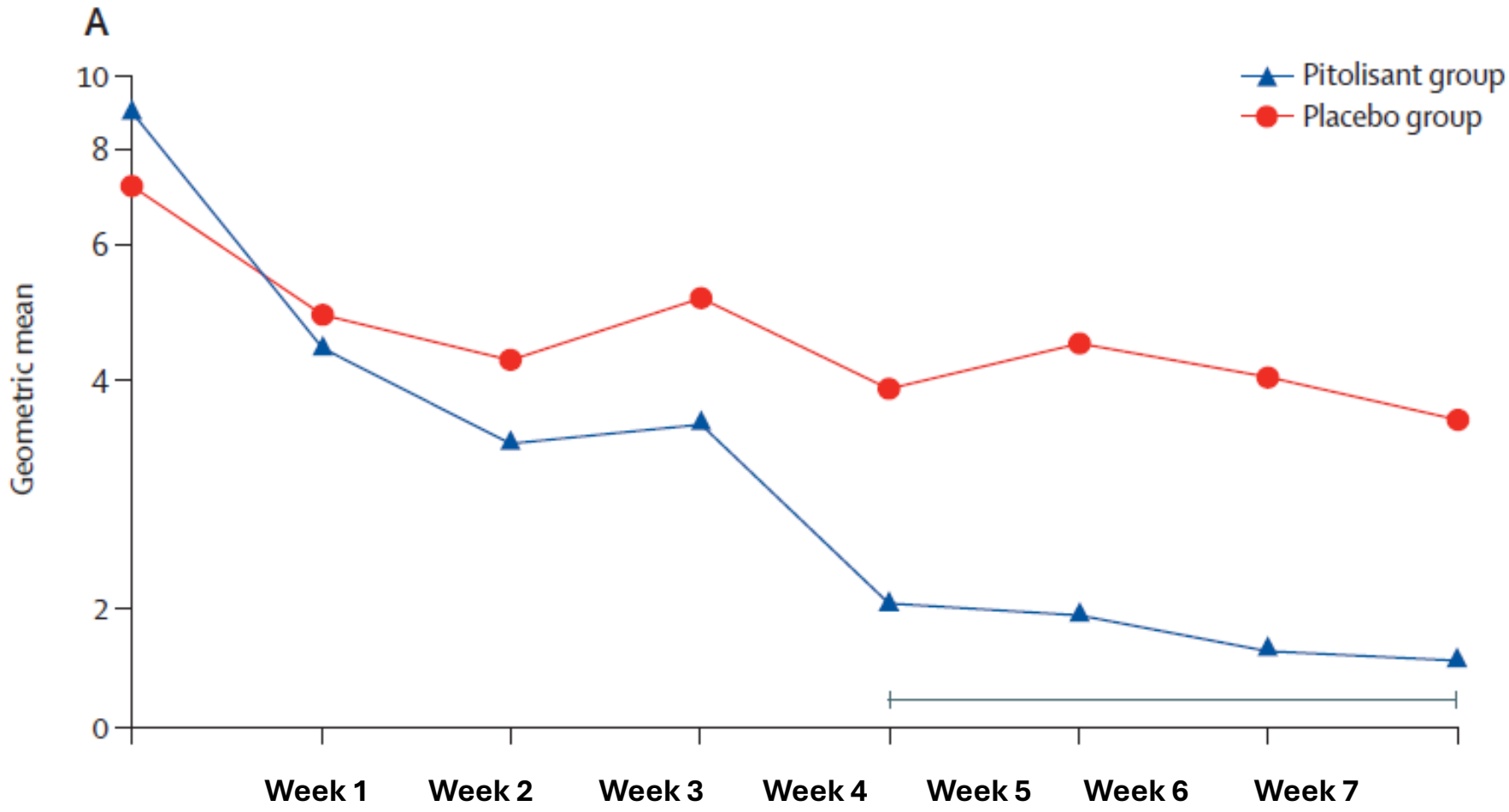
FDA. Drugs@FDA: FDA-Approved Drugs. Accessed March 20, 2024: https://www.accessdata.fda.gov/scripts/cder/daf/

Pitolisant

- Side Effects/Risks
  - Most common side effects are headache, insomnia, nausea, and anxiety
  - Dose-dependent prolongation of QT interval
  - May decrease the effectiveness of hormonal contraception via weak CYP3A4 induction
- Efficacy
  - Randomized trial of 95 patients with narcolepsy, pitolisant 8.9 to 35.6 mg reduced the Epworth Sleepiness Scale score by 5.8 points compared with a reduction of 3.4 points with placebo
  - MWT scores and frequency of hallucinations also improved compared with placebo
  - In a randomized trial of 106 adults with NT1, pitolisant (4.5 to 35.6 mg/day) was more effective than placebo at reducing weekly cataplexy rate (75 versus 35 percent relative reduction from baseline rates of seven to nine episodes per week)

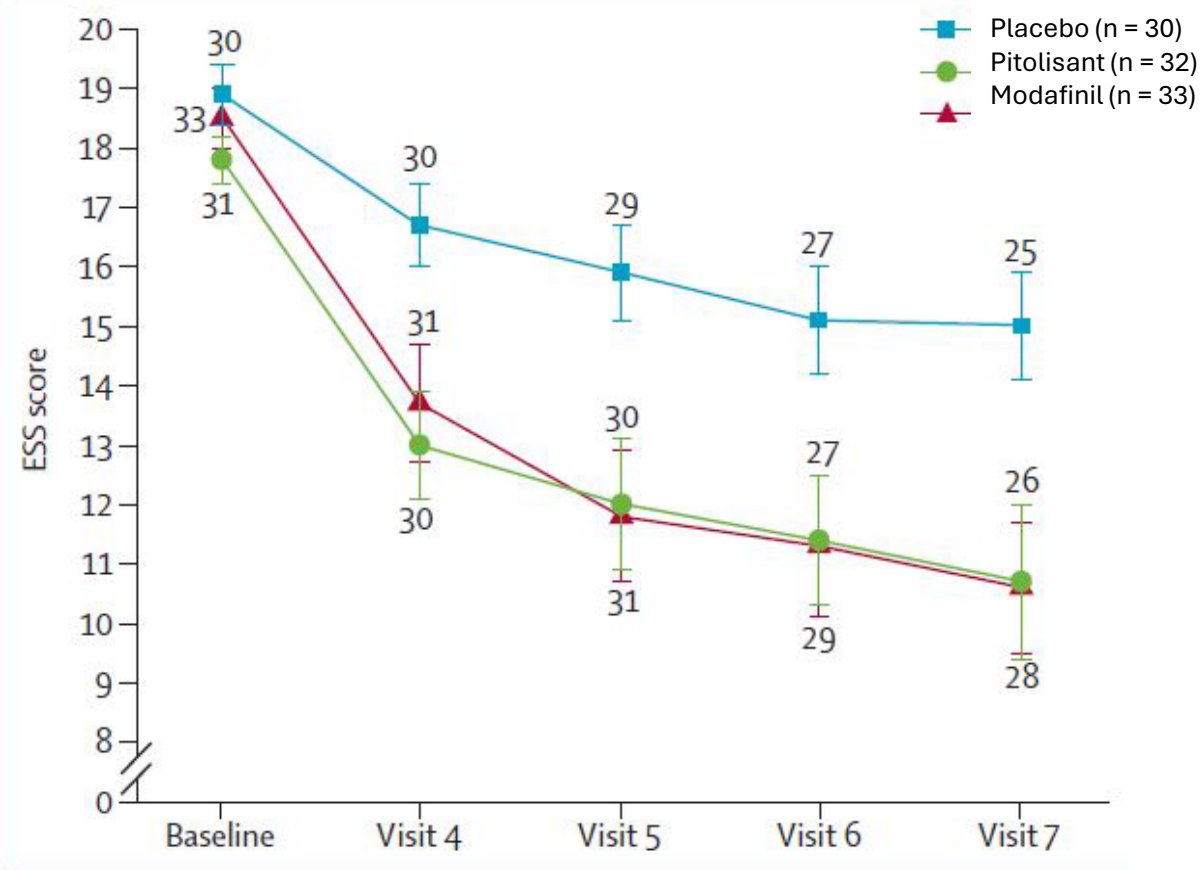
Szakacs Z. *The Lancet Neurology.* 2017;16(3):200-207. Dauvilliers Y, et al. *Lancet Neurol*. 2013;12:1068-1075.

Pitolisant, Efficacy Cataplexy



Szakacs Z. *The Lancet Neurology.* 2017;16(3):200-207. Dauvilliers Y, et al. *Lancet Neurol*. 2013;12:1068-1075.

Pitolisant, Efficacy EDS



- Between-group differences in mean ESS score at endpoint (adjusted for baseline value)
  - Pitolisant vs placebo:
    -3.0 (95% CI: -5.6, -0.4)
    P = .024
  - Pitolisant vs modafinil: 0.12 ((%% CI: -2.5, 2.7)
    P = .25

Dauvilliers Y, et al. *Lancet Neurol*. 2013;12:1068-1075.

Pitolisant

Adverse Reactions That Occurred in ≥5% of WAKIX-Treated Patients and More Frequently Than in Placebo-Treated Patients*

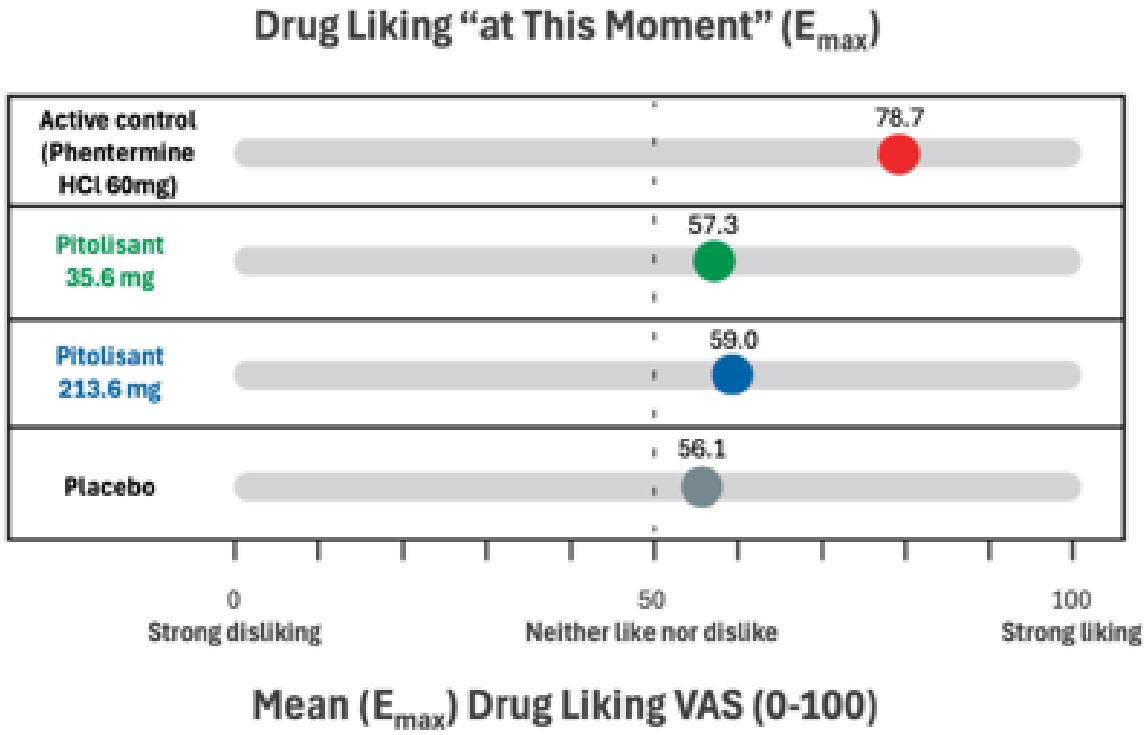
Adverse Reaction	WAKIX (n=152)	Placebo (n=114)
Headache†	18%	15%
Insomnia†	6%	2%
Nausea	6%	3%
Upper respiratory tract infection†	5%	3%
Musculoskeletal pain†	5%	3%
Anxiety†	5%	1%

- Low discontinuation rate
- Caution with oral birth control and certain drugs metabolized by the liver

3.9% Wakix discontinuation rate
3.5% placebo discontinuation rate

Harmony Biosciences, LLC. *Wakix* (pitolisant) [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences, LLC; Revised 2023.

Drug Linking Investigation



- In this study, WAKIX demonstrated an abuse potential profile similar to placebo
  - WAKIX was similar to placebo on drug liking
  - No signals from experimental measures suggestive of abuse

- Phentermine produced significantly higher drug liking vs both doses of pitolisant (therapeutic and supratherapeutic)
- Pitolisant (both doses) had drug liking Emax similar to placebo.
- Secondary measures (Overall Drug Liking, Willingness to Take the Drug Again) followed the same pattern: phentermine > pitolisant ≈ placebo.

Setnik, B., McDonnell, M., Mills, C., Scart-Grès, C., Robert, P., Dayno, J. M., et al. (2020). *Evaluation of the abuse potential of pitolisant, a selective H3-receptor antagonist/inverse agonist, for the treatment of adult patients with narcolepsy with or without cataplexy. Sleep*. PMID: **31626696**.

Solriamfetol

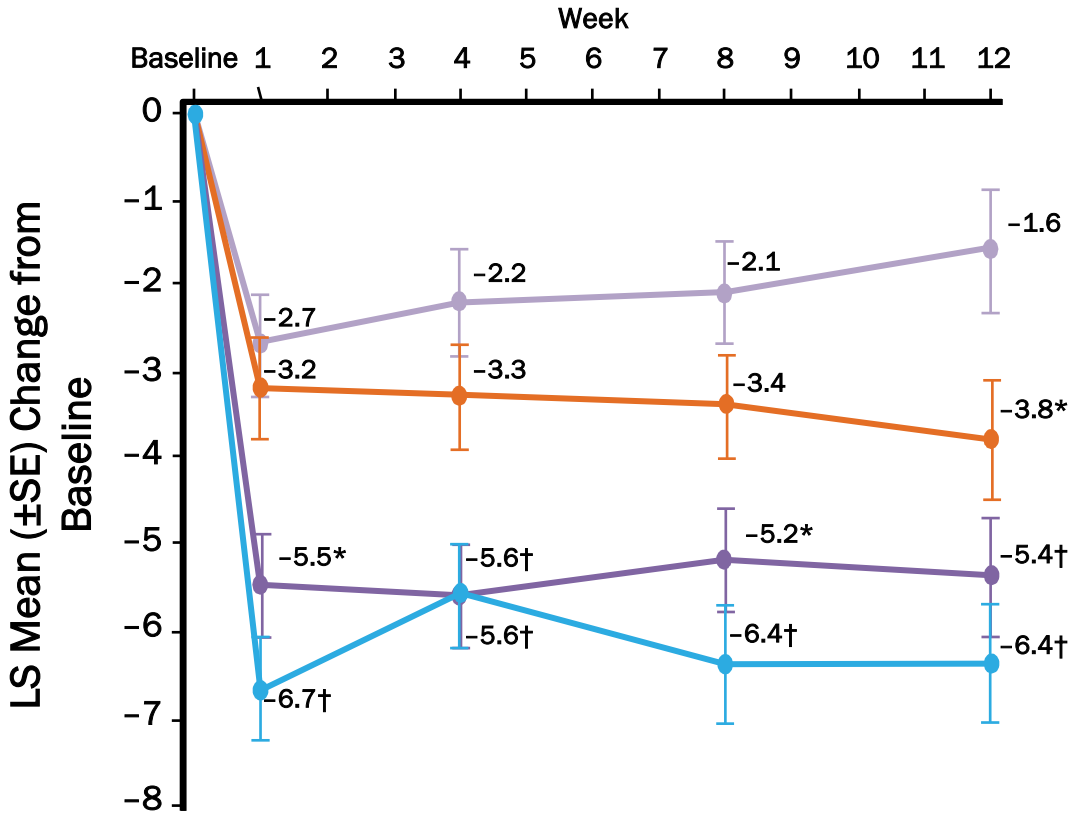
Solriamfetol

- Side Effects/Risks
  - Most common side effects are headache, nausea, decreased appetite, and anxiety
  - In the largest randomized trial, rates of discontinuation for adverse effects for solriamfetol 150 mg and placebo were 5.1 and 1.7 percent, respectively
  - Small, dose-dependent increases in mean blood pressure and heart rate were observed
- Efficacy
  - Randomized trial of 236 adults with narcolepsy who were randomly assigned to one of three doses of solriamfetol (75, 150, or 300 mg daily) or placebo
  - At 12 weeks, sleep latency on the MWT improved more in the 150 mg group than in the placebo group (mean change from baseline 9.8 vs 2.1 minutes)
  - Epworth Sleepiness Scale and global impression scores improved in both dose groups compared with placebo
  - Responses were maximal or near-maximal by one week and were sustained across the 12-week treatment period, as well as in an open-label follow-up for up to a year

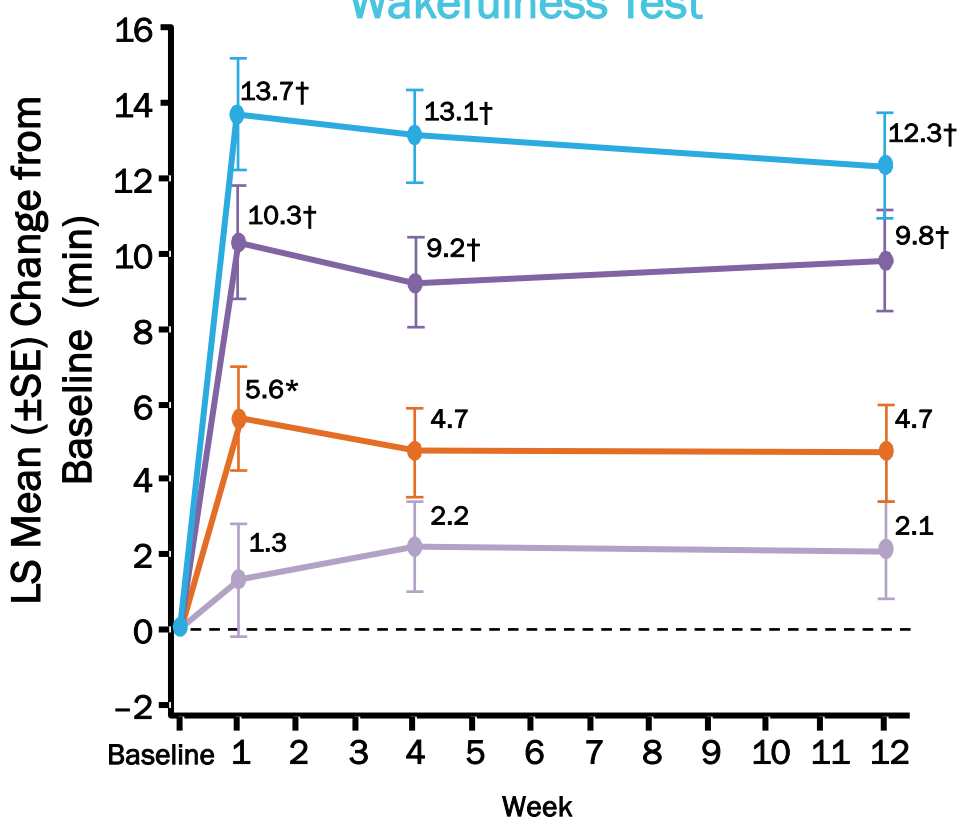
Thorpy MJ, et al. *Ann Neurol*. 2019;85(3):359-370.

Solriamfetol

Epworth Sleepiness Scale



Maintenance of Wakefulness Test



Placebo (n=58)
Solriamfetol 75 mg (n=56)
Solriamfetol 150 mg (n=55)
Solriamfetol 300 mg (n=59)

*P<.05, †P<.0001 vs placebo.

Thorpy MJ, et al. *Ann Neurol*. 2019;85(3):359-370.

Summary of Medications with FDA Indications in Narcolepsy or IH

Medication	EDS in Narcolepsy	Cataplexy in Narcolepsy	EDS in IH
Low sodium oxybate	X	X	X
Once-nightly sodium oxybate	X	X	
Sodium oxybate	X	X	
Pitolisant	X	X	
Modafinil/armodafinil	X		
Solriamfetol	X		
Methylphenidate	X		
Amphetamines	X		

EDS=Excessive Daytime Sleepiness; IH=Idiopathic Hypersomnia

US Food and Drug Administration. Drugs@FDA: FDA Approved Drugs. Accessed March 10, 2024. www.accessdata.fda.gov/scripts/cder/daf/.

Key Learning Points

- **Lower sodium oxybate** contains **92% less sodium** than the original sodium oxybate formulation (SXB) to mitigate cardiovascular risks associated with high sodium intake.
  - A recent open-label study found that switching patients from SXB to LXB was associated with a **-4.1mmHg mean reduction** in 24-hour ambulatory systolic blood pressure (SBP).

- **Pitolisant reduced ESS by 5.8 points** (compared to 3.4 points) in placebo and showed meaningful cataplexy changes.
  - It remains the **only unscheduled drug** for narcolepsy and is now approved in children ages 6 and older.

- Patients with narcolepsy showed **5.4 point reduction in ESS score** on 150mg of **solriamfetol** (vs. 1.6 on placebo), a 22% reduction in EDS.

- These drugs tend to not interfere with one another which makes it easier to use multiple medications for therapy. **Following patient symptoms over time is the key to optimal medication management.**

Faculty & Patient Advocate Panel Discussion

Patient Advocate Experience with Diagnosis and Treatment of Hypersomnolence

Role of Psychiatry Clinicians in the Care of Patients with Hypersomnolence

Building a Support Network with Sleep Specialists

Reaching Out for Further Education/Consultation

American Academy of Sleep Medicine

Sleep Research Society

Practical Take-Aways

- While narcolepsy and IH are considered rare disorders, there are high rates of psychiatric comorbidities, and therefore, these individuals may concentrate in our clinics and masquerade as other psychiatric conditions
- Patients may use many different terms to describe symptoms that may actually describe excessive daytime sleepiness, so we must differentiate and confirm what they are experiencing
- Low Sodium Oxybate provides a potentially “heart-healthier” option for people living with narcolepsy and the first and only approved option for those with Idiopathic Hypersomnia

Q&A