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Trouble Beneath the Surface: ***Detecting and Treating*** ***Hypersomnolence*** in Everyday Psychiatric Practice

MasterClass

Supported by an educational grant from Jazz Pharmaceuticals.



Faculty

David T. Plante, MD, PhD

*Associate Professor of Psychiatry
University of Wisconsin-Madison*

Chelsie Monroe, MSN, APN, PMHNP-BC

*Balanced Mental Wellness
Littleton, CO*

Virend K. Somers, MD, PhD

*Director of the Cardiovascular Facility
and the Sleep Facility, Center for
Clinical and Translational Science,
Mayo Clinic*

Kristi Quinten

Patient Advocate

Faculty Disclosures

- **David T. Plante, MD, PhD:** Advisory Board — Alkermes, Centessa, Harmony Biosciences, Jazz Pharmaceuticals, Takeda; Consultant — Aditum Bio LLC (Terminated), Alkermes, Apnimed, Centessa, Eisai, Harmony Biosciences, Jazz Pharmaceuticals, Lundbeck, Takeda, Teva Pharmaceuticals Australia (Terminated)
- **Virend K. Somers, MD, PhD:** Consultant - Jazz Pharmaceuticals, Lilly, GEMSleep, ApniMed
- **Chelsie Monroe, MSN, APN, PMHNP-BC:** Advisory Board - AbbVie Inc, Alkermes, Axsome Therapeutics, Bristol Myers Squibb, Neurocrine Biosciences, Otsuka Pharmaceutical Development & Commercialization Inc, Teva Pharmaceuticals; Speaker's Bureau - AbbVie Inc, Alkermes, Axsome Therapeutics, Bristol Myers Squibb, Neurocrine Biosciences, Otsuka Pharmaceutical Development & Commercialization Inc, Teva Pharmaceuticals
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Learning Objectives

- Describe the prevalence, burden, and common clinical presentations of hypersomnolence in patients with mental illness, including the impact on quality of life and the role of psychiatry clinicians in early identification
- Assess evidence-based strategies to identify hypersomnolence in patients with mental illness, including differentiation from fatigue, use of validated screening and monitoring tools, interpretation of diagnostic testing, and appropriate referral to sleep specialists
- Differentiate among sleep-wake disorders underlying hypersomnolence, including obstructive sleep apnea (OSA), narcolepsy type 1 and type 2 (NT1, NT2), and IH, with consideration of psychiatric, cardiometabolic, and renal comorbidities
- Evaluate the safety, efficacy, and cardiovascular implications of traditional and off-label therapies compared with newer and emerging treatments for narcolepsy and IH, including considerations related to sodium burden, dosing, and titration

The State of Hypersomnolence

Most Psychiatric Disorders Are Associated With Sleep Disturbance

Diagnostic criteria:

- MDD
- Bipolar Disorder
- GAD
- PTSD

Common clinically:

- Schizophrenia
- Panic disorder
- OCD
- Borderline Personality Disorder
- Dementias
- ADHD
- Substance Use Disorders

Sleep Disturbance Is The Rule During A Major Depressive Episode

- **The majority of patients** will have a sleep complaint as part of a depressive episode
- The majority of research has been on insomnia in depression, **with little attention to hypersomnolence**

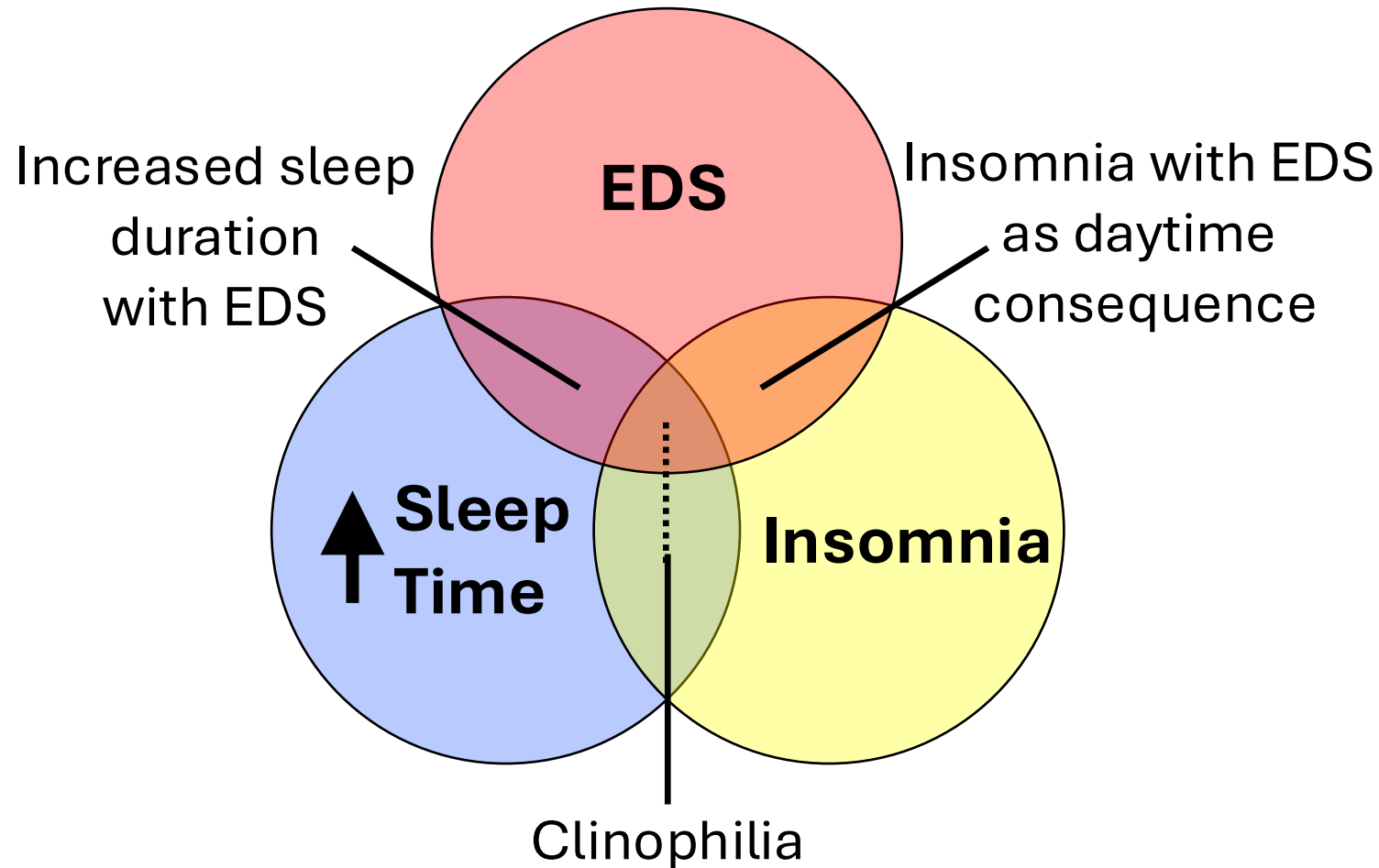
$\geq 80\%$

of patients report insomnia

~20-30%

report hypersomnolence

Key Conceptual Framework for Sleep Disturbance in Psychiatric Conditions



EDS = Excessive Daytime Sleepiness

Plante DT, et al. *J Sleep Res.* 2017;26(4):497-504.

Important Vocabulary

Hypersomnolence

- Excessive daytime sleepiness, often with excessive total sleep duration

Hypersomnia

- Excessive total sleep duration
[hyper- too much +
L. *somnus*, sleep]

Sleep inertia

- Temporary state of grogginess, disorientation, and reduced mental performance after awakening
- Excessive sleep inertia often observed in persons with hypersomnolence

Unfortunately, these terms are often used interchangeably

Hypersomnolence Disorder Prevalence

27.8%

Report of Excessive Sleepiness (ES)



15.6%

Presence of at least one of the following:

- Recurrent periods of irrepressible need to sleep or to nap within the same day (13.2%)
- Recurrent naps within the same day (1.9%)
- Nonrestorative (unrefreshing) prolonged main sleep episode $\geq 9\text{h/day}$
- Sleep drunkenness (4.4%)



4.7%

ES occurs ≥ 3 times/wk, for ≥ 3 mo despite main sleep period $\geq 7\text{h}$



2.6%

Significant distress or impairment in cognitive, social, occupational, or other areas of functioning



1.5%

Not better accounted for or exclusively during the course of another sleep disorder

Hypersomnolence and Mental Illness

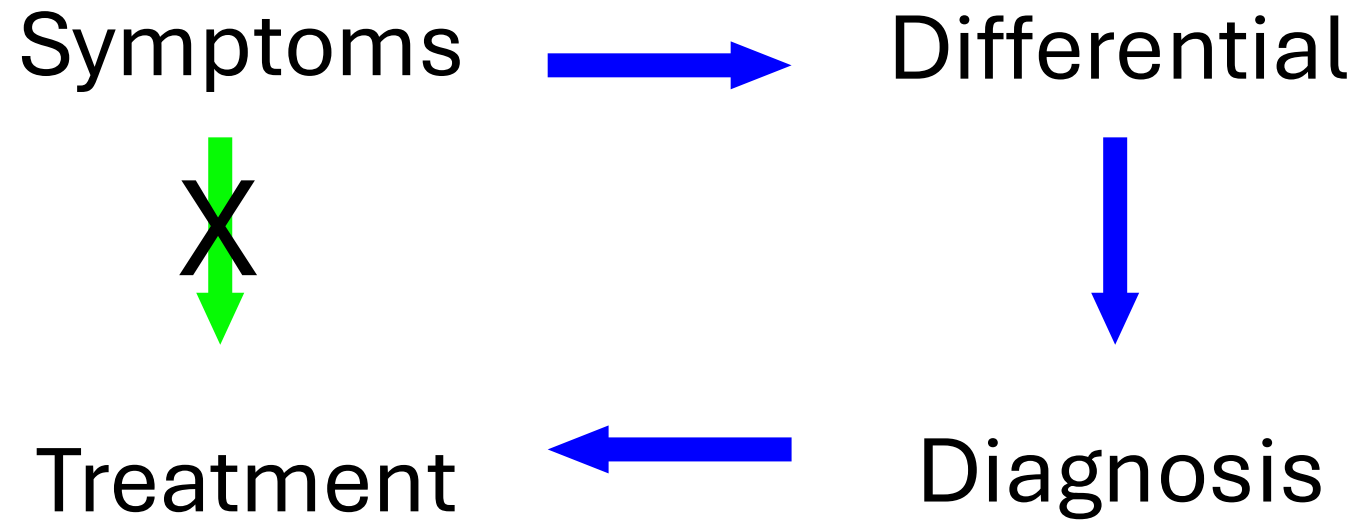
Condition	Adjusted OR (95%CI)
Major Depressive Disorder	4.8 (3.6-6.5)
Dysthymic Disorder	5.4 (3.1-9.3)
Bipolar Disorder	5.3 (3.2-8.7)
Generalized Anxiety Disorder	2.5 (1.7-3.8)
Posttraumatic Stress Disorder	2.5 (1.7-3.8)
Obsessive-Compulsive Disorder	5.9 (3.3-10.7)

Impacts of Hypersomnolence



Breslau N, et al. *Biol Psychiatry*. 1996;39(6):411-418; Roberts RE, et al. *Am J Psychiatry*. 2000;157(1):81-88; Worthington J, et al. *Psychopharmacol Bull*. 1995;31(2):223-226; Zimmerman M, et al. *J Clin Psychiatry*. 2005;66(9):1134-1138; Kaplan KA, Harvey AG. *Sleep Med Rev*. 2009;13(4):275-285; Kaplan KA, et al. *J Affect Disord*. 2011;132(3):438-444; Goldstein TR, et al. *J Consult Clin Psychol*. 2008;76(1):84-91; Fitzgerald CT, et al. *J Clin Sleep Med*. 2011;7(4):351-356

Sleepiness in Psychiatric Disorders Requires a Careful Evaluation



Please do not jump directly from symptom to treatment!

Common Comorbid Sleep Disorders That May Contribute to Hypersomnolence in Psychiatric Patients

Behavioral Insufficient Sleep

Circadian Rhythm Disorders

Obstructive Sleep Apnea

Restless Legs Syndrome

Narcolepsy/Idiopathic Hypersomnia

Key Learning Points



- Hypersomnolence is a significant problem in persons with mental illness
 - **About 20-30% of patients with depressive episodes report hypersomnolence**
- It can impact the 24-hour day and have severe impacts on functioning and the course of mental illness
- Building a differential diagnosis is a critical step in optimizing treatment

Identifying Hypersomnolence in Patients with Mental Illness

Sleep-Wake Disorders in DSM-5-TR

DSM-5 Sleep-Wake-Circadian Disorders/Groups

Insomnia Disorder

Hypersomnolence Disorder

Narcolepsy

Breathing-Related Sleep Disorder (eg, OSA)

Circadian Rhythm Sleep-Wake Disorders

Non-REM Sleep Arousal Disorders

Nightmare Disorder

REM Sleep Behavior Disorder

} Parasomnias

Restless Legs Syndrome

Substance/Medication-Induced Sleep Disorder

Complaints are of dissatisfaction regarding the quality, timing, and amount of sleep.

However, resulting **daytime distress and impairment** are core features shared by all sleep-wake disorders.

Sleep disorders are often accompanied by **depression, anxiety, and cognitive changes** that must be addressed in treatment planning and management.

Furthermore, persistent sleep disturbances (both insomnia and excessive sleepiness) are established **risk factors** for the subsequent development of mental illnesses and substance use disorders.

They may also represent a **prodromal expression** of an episode of mental illness, allowing the possibility of early intervention to preempt or attenuate a full-blown episode.

OSA=obstructive sleep apnea; REM=rapid eye movement.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition-Text Revision*. American Psychiatric Association Publishing; 2023.

What to Pay Attention to in a Clinical Interview

 **Feeling excessive sleepiness (despite treating their underlying psychiatric conditions)**

 **Episodes of inadvertently falling asleep**

 **Unrefreshing sleep**

 **Recurrent naps**

 **Sleep inertia**

 **Fatigue**

 **Cognitive impairment**



Photo: AI Generated (Gemini)

“I’m Tired.”

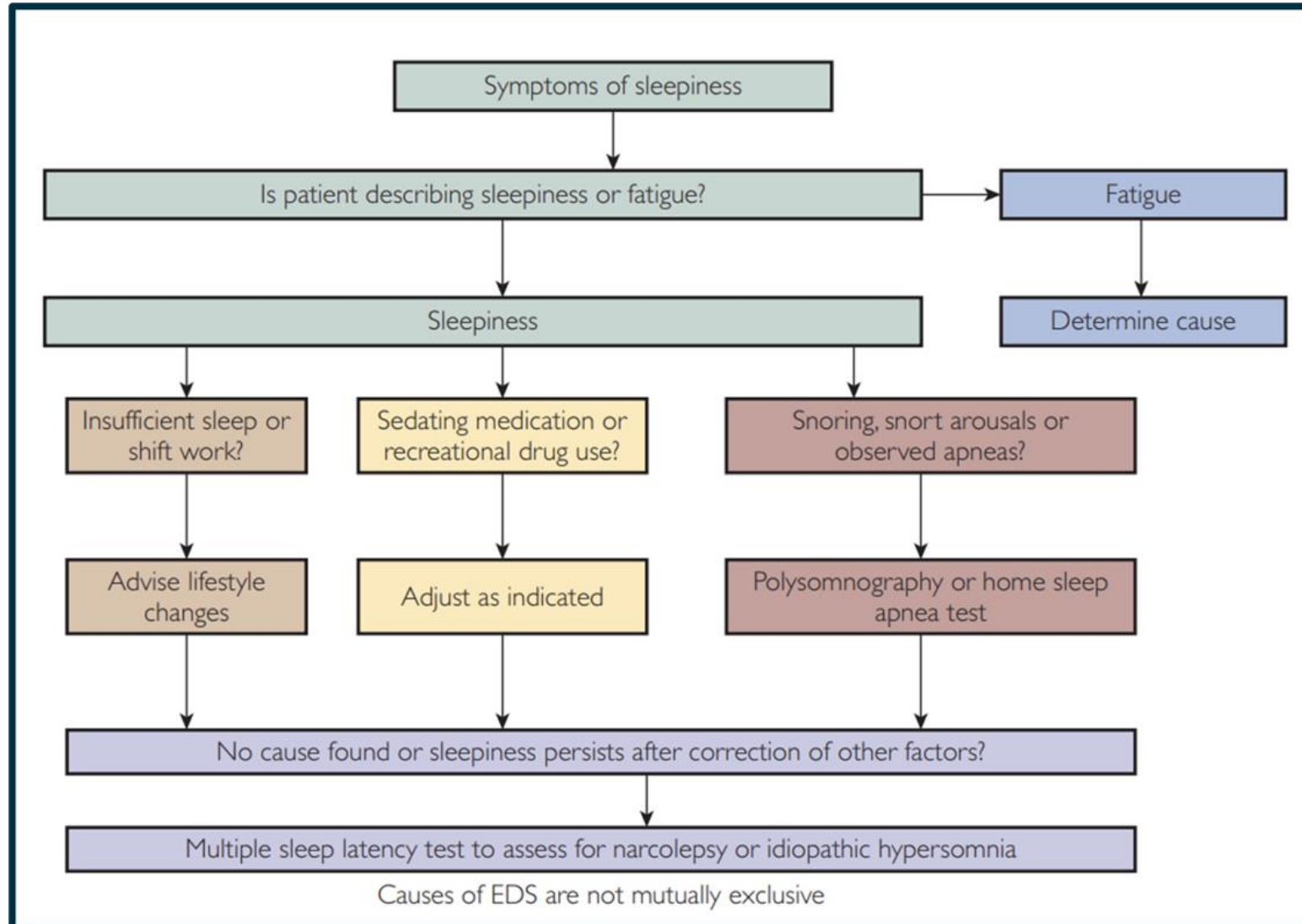
- How do we begin to assess hypersomnolence in our patient population?
- What does a patient mean when they report feeling “tired?”
- **Excessive daytime sleepiness (EDS)** could affect 50-80% of patients in a typical psychiatric practice.
- **Fatigue** could affect as many as 47% of stable psychiatric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

Distinguishing Between EDS and Fatigue

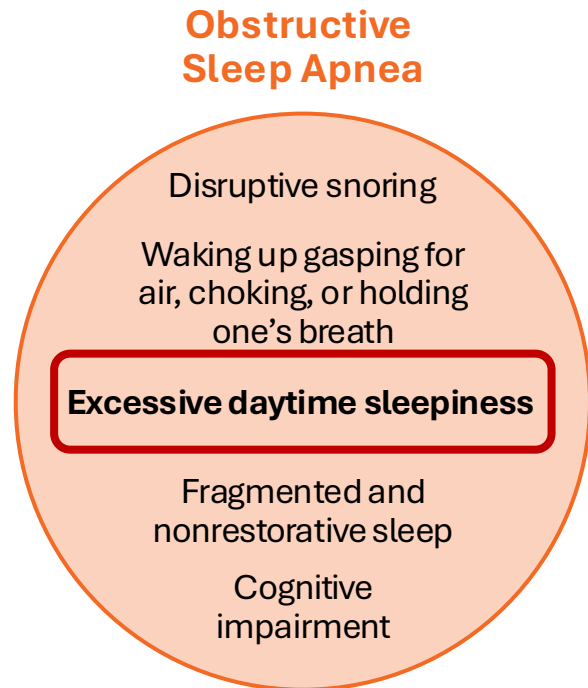


- Distinguishing between EDS and fatigue can be difficult. ***Definitions are blurred.***
- Fatigue is generally characterized by:
 - Lack of energy
 - Reduced ability to perform physical activities
 - Poor concentration and memory
 - Chronic medical, neurological, or psychiatric conditions, or in isolation as in chronic fatigue syndrome.
- Fatigue is ***not*** generally associated with inappropriate episodes of sleep during the day.

Evaluation of Excessive Daytime Sleepiness



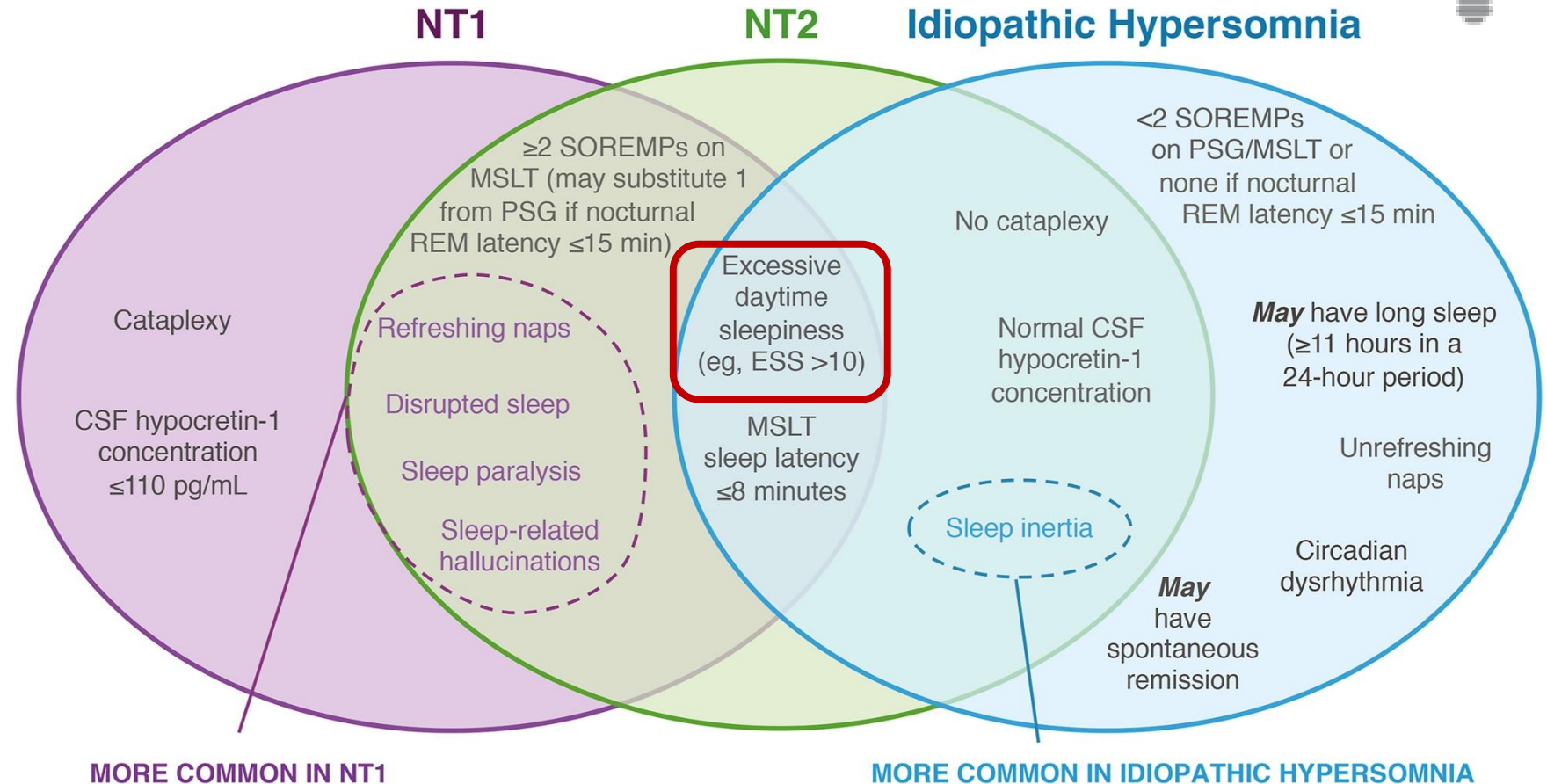
Differential Diagnosis of Hypersomnolence



Medication-Induced Sleep Disorder

Circadian Rhythm Disorder

Kleine-Levin Syndrome



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

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-cafeination
- Habitual total sleep $\geq 10-11$ h (**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 Depressive 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

There Are Many Assessment Options

The Epworth Sleepiness Scale

The Epworth Sleepiness Scale is widely used as the best of sleep medicine as a subjective measure of a patient's sleepiness. The scale is a list of eight situations in which you rate your tendency to become sleepy or asleep if, on the basis of sleeping, it is a high chance of falling asleep, either you have the test, and up the value of your responses. Your responses are added on a scale of 0 to 24. The scale estimates whether you are experiencing excessive sleepiness that requires medical attention.

How Sleepy Are You?

How likely are you to fall asleep or fall asleep in the following situations? (You should rate your tendency of dozing off, not just falling asleep. Even if you have not done some of these things recently or to determine how likely you would have affected you. For each situation, decide whether or not you would have done it.)

- No chance of dozing
- Slight chance of dozing
- Moderate chance of dozing
- High chance of dozing

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

Situation	Chance of Dozing
Sitting and reading	
Sitting and watching TV	
Sitting in a public place (e.g., restaurant or a meeting)	
As a passenger in a car for an hour without a driver	
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 = _____

Interpretation:

0-5: No chance of dozing. You are normally sleepy.

6-10: Slight chance of dozing. You are slightly sleepy.

11-15: Moderate chance of dozing. You are moderately sleepy depending on the situation. You may need to consider having medical attention.

16-24: High chance of dozing. You are excessively sleepy and should consider seeking medical attention.

Reference scores with a normal test measuring daytime sleepiness: The Epworth Sleepiness Scale sleep score ranges from 0 to 24.

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? 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.

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.

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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

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SLEEP COUNTS

IDIOPATHIC HYPERSOMNIA SEVERITY SCALE (IHSS)

Name: _____ Date: _____

The Idiopathic Hypersomnia Severity Scale (IHSS) was developed and validated by sleep experts with feedback from patients. The scale is a 10-item questionnaire that is used to measure the severity of symptoms and provide a measure that might be useful for patient identification, follow-up visits, and management. The scale assesses various aspects of symptoms and signs of hypersomnia and the sleep-related to each, as well as required daytime functioning for the hypersomnia. Symptoms frequency, intensity, and consequences are rated using a 0 to 4 scale, with higher scores indicating more severe and longer symptoms.

Considering your symptoms during the past month:

1. What for you is the total duration of night sleep on the weekend or on holiday, for example?

0: 10 hours or more
1: 9 hours and 30 minutes
2: 9 hours
3: 8 hours and 30 minutes
4: 8 hours or less

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?

0: Often
1: Sometimes
2: Often
3: Often
4: Often

3. Is it unusually difficult for you, or even impossible, to wake up in the morning without several alarm clocks in the beds of common use?

0: Often
1: Sometimes
2: Often
3: Often
4: Often

4. After a night's sleep, how long does it take you to feel like you are functioning properly after you get up?

0: 2 hours or more
1: 2 hours and 30 minutes
2: 2 hours
3: 1 hour and 30 minutes
4: 1 hour or less

5. In the weeks after waking up, do you ever do limited things under say traditional things, and are you still doing for example, trying to break things or trying things?

0: Often
1: Sometimes
2: Often
3: Often
4: Often

6. During the day, when circumstances allow, do you ever take a nap?

0: Often (more than 3 times a week)
1: Sometimes (2 to 3 times a week)
2: Often
3: Often
4: Often

7. What for you is the total length of your naps for the weekend or on holiday, for example?

0: 1 hour or more
1: 1 hour and 30 minutes
2: 1 hour
3: 30 minutes
4: 30 minutes or less

Submit

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 my 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. Reading 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 produces 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

Knight, L. B., LaRocca, N. G., Mori-Niemi, J., & Steinberg, A. D. (1980). *Fatigue Severity Scale (FSS)*. (Database record, APA Paper Tests. <https://doi.org/10.1037/0898-9180.100>)

<https://www.copyright.com/>

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

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

1. Rate your level of fatigue on the day you felt most fatigued during the past week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

2. Rate your level of fatigue on the day you felt least fatigued during the past week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

3. Rate your level of fatigue on the average on the last week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

4. Rate your level of fatigue right now.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

5. Rate how much, in the past week, fatigue interfered with your general level of activity.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

6. Rate how much, in the past week, fatigue interfered with your ability to bathe and dress yourself.

No interference 1 2 3 4 5 6 7 8 9 10 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).

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

8. Rate how much, in the past week, fatigue interfered with your ability to concentrate.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

9. Rate how much, in the past week, fatigue interfered with your social life.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

10. Rate how much, in the past week, fatigue interfered with your enjoyment of life.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

11. Rate how much, in the past week, fatigue interfered with your mood.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

12. Indicate how many days, in the past week, you felt fatigued for any part of the day.

Days 0 1 2 3 4 5 6 7

13. Rate how much of the day, on average you felt fatigued in the past week.

Days 0 1 2 3 4 5 6 7 8 9 10

14. Indicate how many days, in the past week, you felt fatigued for any part of the day.

Days 0 1 2 3 4 5 6 7 8 9 10

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 item applies to you.

1. Rate your level of fatigue on the day you felt most fatigued during the past week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

2. Rate your level of fatigue on the day you felt least fatigued during the past week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

3. Rate your level of fatigue on the average on the last week.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

4. Rate your level of fatigue right now.

Not at all fatigued 1 2 3 4 5 6 7 8 9 10 As fatigued as I could be

5. Rate how much, in the past week, fatigue interfered with your general level of activity.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

6. Rate how much, in the past week, fatigue interfered with your ability to bathe and dress yourself.

No interference 1 2 3 4 5 6 7 8 9 10 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).

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

8. Rate how much, in the past week, fatigue interfered with your ability to concentrate.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

9. Rate how much, in the past week, fatigue interfered with your social life.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

10. Rate how much, in the past week, fatigue interfered with your enjoyment of life.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

11. Rate how much, in the past week, fatigue interfered with your mood.

No interference 1 2 3 4 5 6 7 8 9 10 Extreme interference

12. Indicate how many days, in the past week, you felt fatigued for any part of the day.

Days 0 1 2 3 4 5 6 7

13. Rate how much of the day, on average you felt fatigued in the past week.

Days 0 1 2 3 4 5 6 7 8 9 10

14. Indicate how many days, in the past week, you felt fatigued for any part of the day.

Days 0 1 2 3 4 5 6 7 8 9 10

With kind permission from Springer Science+Business media: Hans 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.
- 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.

EDS=Excessive Daytime Sleepiness

Johns MW. Sleep (1991).

Sleep History/Sleep Log

[illegible]

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)

Sleep History/Sleep Log

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 (l) 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.

TWO WEEK SLEEP DIARY

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
sample	Mon.	Work		E					A													C				
5/12	Mon	work						E		M												M			C	
5/13	Tues	work						E		M											M				C	
5/14	Wed	work						E		M												M			C	
5/15	Thur	work								M												M			C	
5/16	Fri	Day off (endoscopy) *								M													M		C	
5/17	Sat	Day off						A		M															C	
5/18	Sun	Day off	E	A						M				A								M			C	
5/19	Mon	Day off						E		M												M			C	
5/20	Tues	Day off								M												M			C	
5/21	Wed	work						E		M												M			C	
5/22	Thurs	Sick leave	C							M												M			C	
5/23	Fri	work							E	M												M			C	
5/24	Sat	Day off	C						E	M												M			C	
5/25	Sun	Day off						E		M												M			C	

- 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

* put out w/ anesthesia for EGD

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.

Causes of EDS: Quantity vs. Quality

Poor Sleep Quality



Poor Sleep Quantity

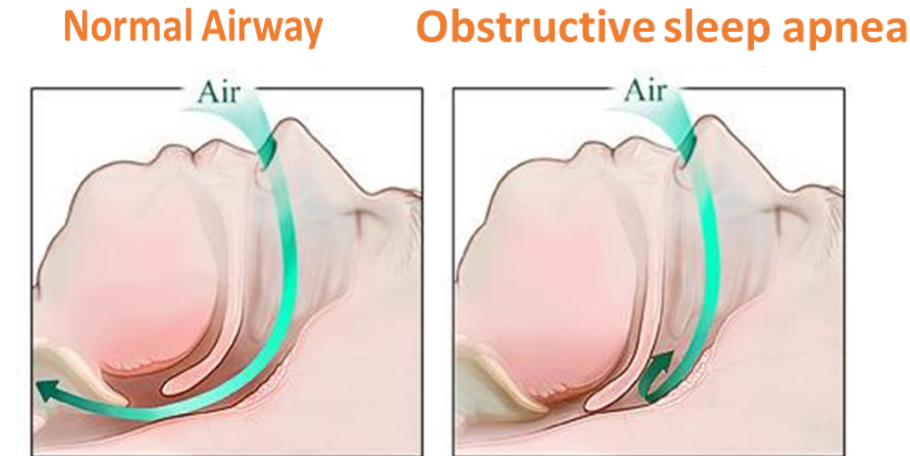


- A high EDS typically indicates one of both are present.
- Generally, it is most practical to begin with assessing for inadequate sleep quantity:
 - Sleep history
 - Sleep diary/log
 - Sleep tracker

Poor Sleep Quality

Obstructive Sleep Apnea (OSA)

- OSA is the most common type of sleep disordered breathing and is prevalent in **up to 20% of MDD patients**
- Restless sleep, insomnia, EDS, fatigue, snoring
- Intermittent hypoxia, which chronically cause neuronal damages and white matter changes
- Increasing age and BMI
- 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: # respiratory events (accurate), total sleep time (overestimate)



~50% with OSA may have residual EDS despite any amount of PAP use

Sleep Apnea Assessment: STOP-BANG

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		
-------------	--	--

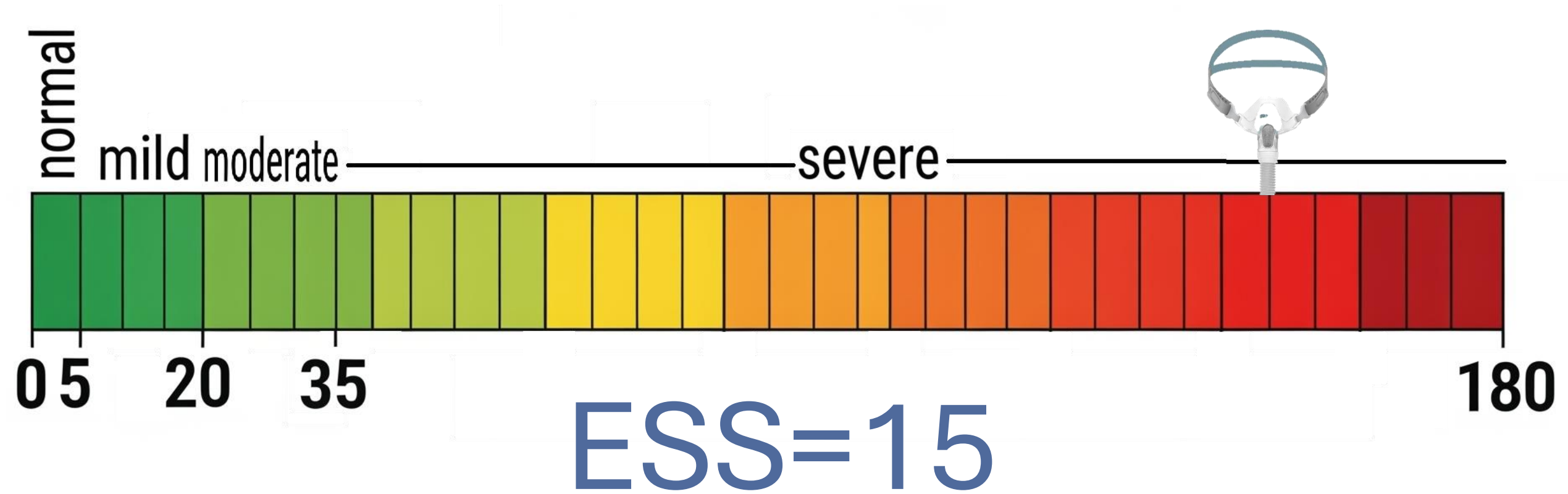
High risk of OSA: Yes 5 - 8

Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

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

Sleep Apnea Assessment



“What’s Really Going On?”

Hypersomnias

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

American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed, text rev. 2023.

Hypersomnolence Disorder in DSM-5-TR

Idiopathic Hypersomnia

- Excessive sleepiness despite adequate sleep time – Idiopathic Hypersomnia
- At least one of the following:
 - Recurrent period of sleep during the day
 - Prolonged main sleep period (9 hours +)
 - Difficulty waking up
- At least 3 times/week for at least 3 months
- Clinically significant distress or impairment

**Long sleep time +
nonrestorative sleep is a clue**

*Individuals can sleep 10–12 hours
and still feel exhausted*

**Rule out medical and
medication causes first**

*OSA, hypothyroidism, anemia, and
sedating psychotropics are far more
common than primary hypersomnolence*

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 month²:

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

☐

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

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://reprovidemapi-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;93(15):e1764-e1765. 2. Dauvilliers Y. Idiopathic hypersomnia severity scale. 2018. Accessed October 3, 2022. <http://rftbts.com/IDH/IDHSSA>. 3. Rattu 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.

IHSS © Yves Dauvilliers, 2018



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- 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

Identifying Sleep Inertia: Sleep Inertia Questionnaire

On a typical morning in the past week, after you wake up, to what extent do you....

	not at all 0	a little 1	somewhat 2	often 3	all the time 4
1. Have problems getting out of bed?					
2. Need an alarm to wake up?					
3. Hit the snooze button on the alarm?					
4. Bump into and drop things?					
5. Notice that you move more slowly?					
6. Notice that you feel sleepy?					
7. Notice that your eyes feel heavy, sore, or itchy?					
8. Notice that your arms and/or legs feel tired or heavy?					
9. Notice that your mind feels groggy, fuzzy or hazy?					
10. Notice that you get winded more easily?					

SIQ Continued

	not at all 0	a little 1	somewhat 2	often 3	all the time 4
11. Notice that it is difficult to keep your balance?					
12. Notice that you feel tense?					
13. Feel anxious about the upcoming day?					
14. Dread starting your day?					
15. Wish you could sleep more?					
16. Have difficulty concentrating?					
17. Find that you think more slowly?					
18. Find that you react more slowly?					
19. Find that you make more mistakes/errors?					
20. Can't imagine being able to wake up?					
21. Have difficulty getting your thoughts together?					

Differentiation of IH from Narcolepsy

- **Idiopathic Hypersomnia**
 - Does not involve cataplexy
 - No sleep-onset REM periods
 - No hypocretin/orexin deficiency
 - IH patients take long, unrefreshing naps; NT1 patients find short naps refreshing
 - MSLT findings: <2 SOREMPs

Clinical Pearl: Ask directly about cataplexy

“Knees buckling with laughter” is highly suggestive and often not volunteered

Testing For Idiopathic Hypersomnia and Narcolepsy

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.

Be Careful with This Approach

Circadian
Rhythm
Disorders

Hypersomnias

Insomnia

Sleep-Related
Movement
Disorders/RLS/
PLMD

Parasomnias

Other

Sleep Related Breathing

Putting It All Together With Psychiatric Patients

Case For Further Workup

- MZ, 38 yo female seen for the last 7 years for MDD and GAD
- Treated with IV ketamine and dextromethrophan/bupropion.
- Experienced post-partum depression with 2 pregnancies but now in remission.
- Still feels "tired" and experiencing concern after trying to raise her two young children ages 3 and 18 months with difficulty in energy.

ESS = 17

IHHS = 20

HST = negative for OSA

Red Flags that Caused Suspicion upon Further Questioning

Reports chronic need for sleep, historically 10-14 hours unrefreshed prior to children

Before children, napped 2+ hours, unrefreshed upon waking

Sleeps better now that depression and anxiety are well-controlled, but still feeling excessive daytime sleepiness, with inertia in the mornings

Feels tiredness and low energy are now most bothersome symptoms



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 may masquerade as other psychiatric conditions and cloud the clinical picture, so always keep hypersomnolence disorders on your differential diagnosis
- Separate sleepiness and fatigue. Avoid “tired”
 - **Recurrent, inappropriate episodes of falling asleep** are a feature that helps distinguish excessive daytime sleepiness from fatigue
- In patients with chronic excessive daytime sleepiness, a mean sleep latency of ≤ 8 minutes and ≥ 2 sleep-onset REM periods supports narcolepsy; the absence of cataplexy distinguishes narcolepsy type 2 from narcolepsy type 1.

An Expert Perspective on The Role of Sodium in Cardiovascular and Renal Health

Cardiometabolic Risk in Hypersomnolence - Emerging Evidence and Implications of Salt Consumption

Virend K Somers, MD, PhD
Alice Sheets Marriott Professor
Department of Cardiovascular Medicine
Mayo Clinic
Rochester, MN

Sleep as a Determinant of CV Health

AHA PRESIDENTIAL ADVISORY

Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory from the American Heart Association



- **Healthy diet**
- Participation in physical activity
- Glucose control
- Weight management
- Lipid control
- **Blood pressure control**
- Smoking avoidance
- **Healthy sleep**

Hypersomnolence & Cardiovascular Considerations



**CV Risk
Factors**



**Prevalent
CVD**



**Incident
CVD**



**Implications
of Salt Intake**

Hypersomnolence & Cardiovascular Considerations



**CV Risk
Factors**



**Prevalent
CVD**

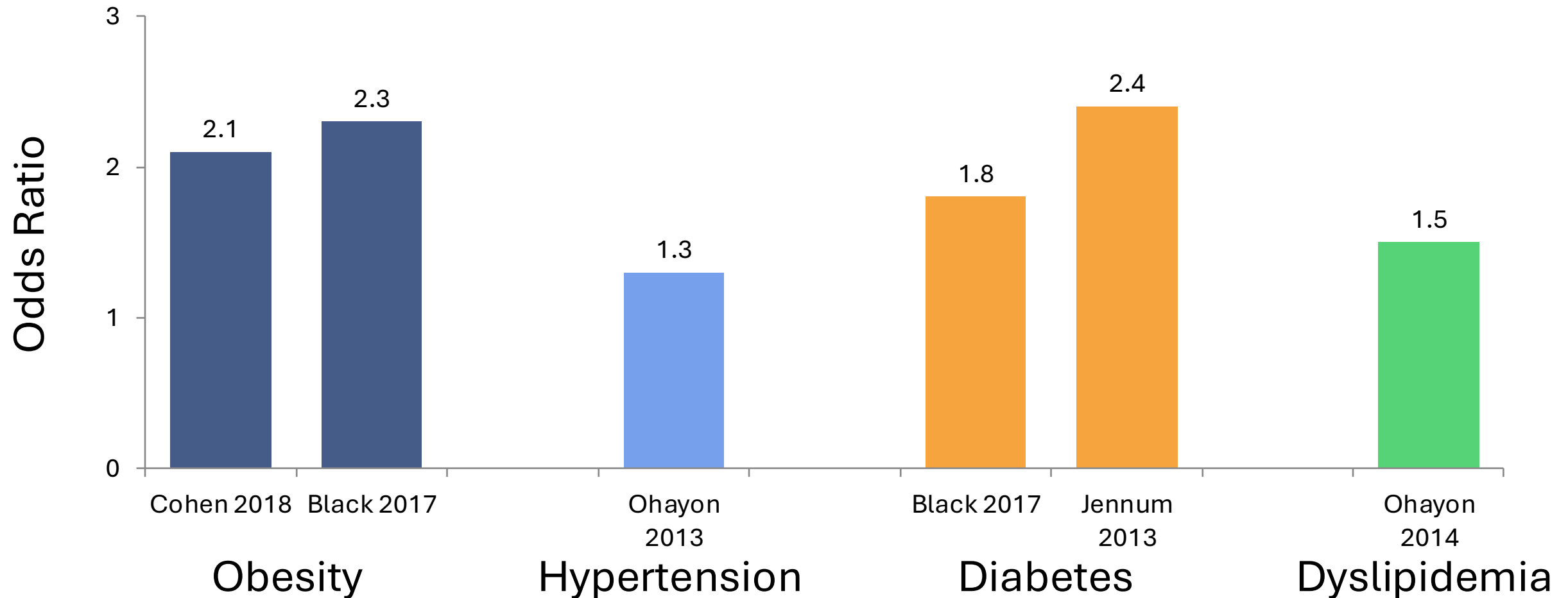


**Incident
CVD**



**Implications
of Salt Intake**

Cardiovascular and Cardiometabolic Risk Associated With Narcolepsy

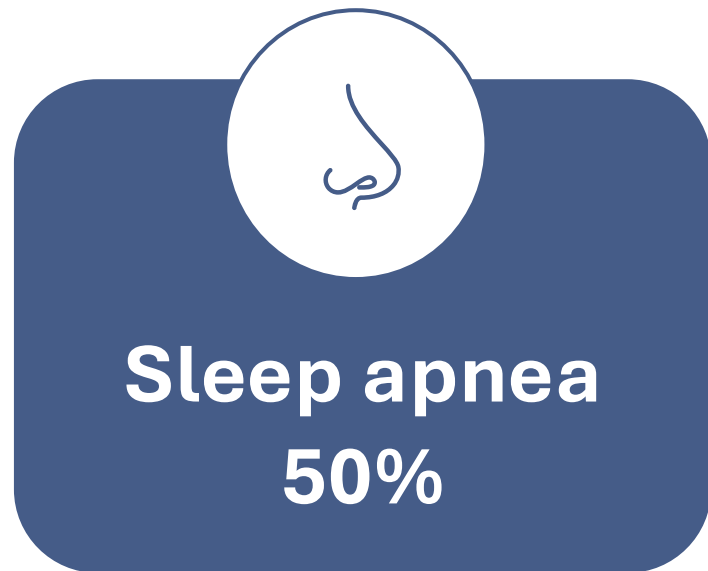
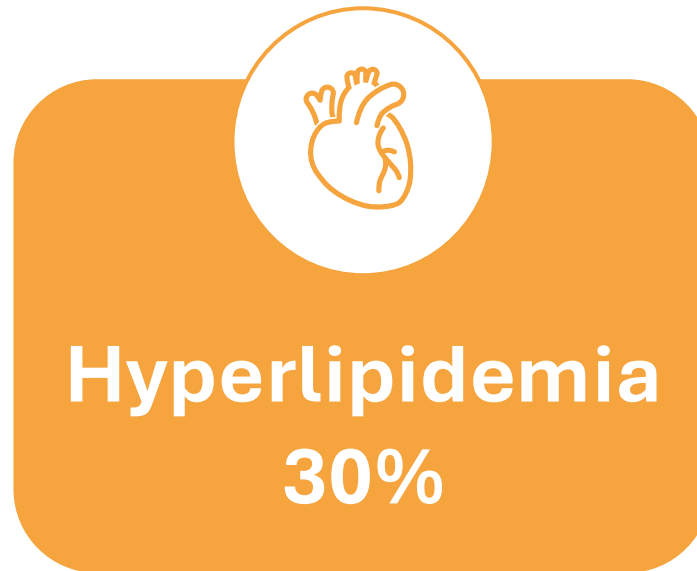


Cohen A, et al. *Sleep Med.* 2018;43:14-18. Black J, Reaven NL, Funk SE, et al. *Sleep Med.* 2017;33:13-18. Ohayon MM. *Sleep Med.* 2013;14(6):488-492. Jennum P, et al. *Sleep.* 2013;36(6):835-840.

CV Risk Factors in IH

- MarketScan database
- 4980 individuals with a diagnosis of IH – Age 43; two thirds female

Comorbidity Prevalence



Hypersomnolence & Cardiovascular Considerations



**CV Risk
Factors**



**Prevalent
CVD**

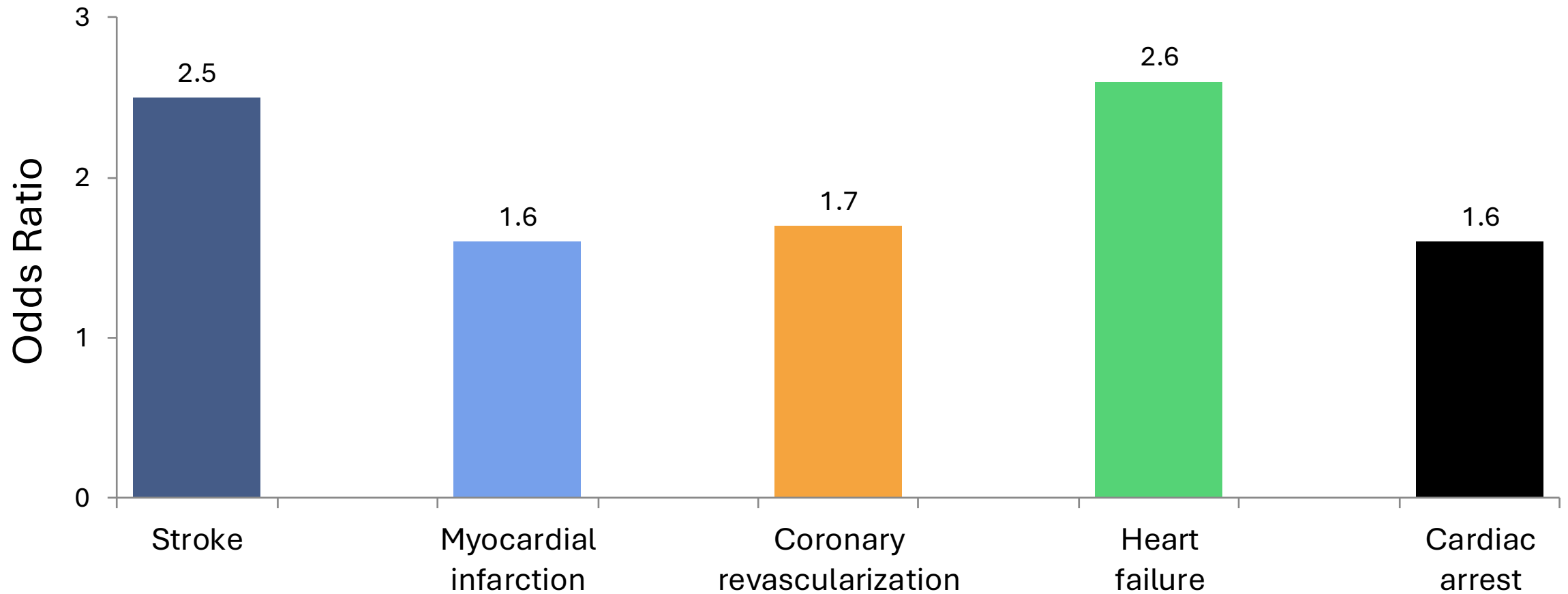


**Incident
CVD**



**Implications
of Salt Intake**

Narcolepsy and Cardiovascular Disease



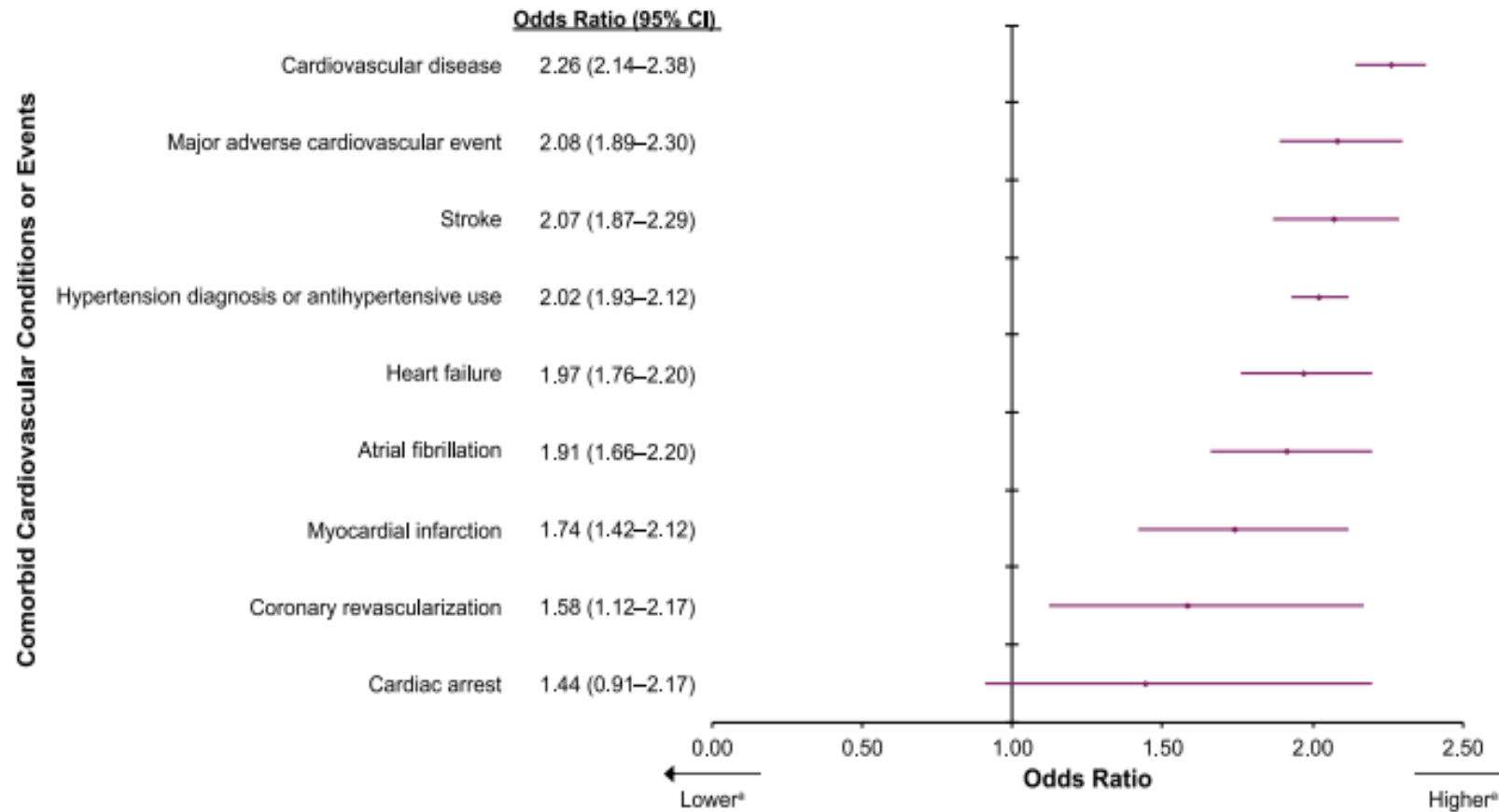
Cardiovascular Comorbidities Associated With IH

- Study of 11,428 patients with IH versus 57,138 controls
- 65% female, Mean age 45 years

CVD, Stroke and MACE increased – Odds ratios of >2.2

Hypertension and Heart Failure increased – Odds ratio of 2.0

Cardiovascular Burden of Patients with IH



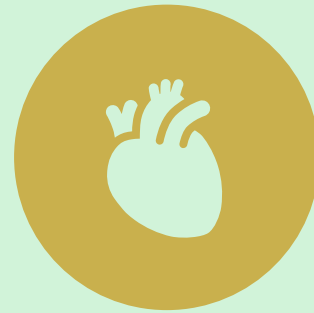
Hypersomnolence & Cardiovascular Considerations



**CV Risk
Factors**



**Prevalent
CVD**



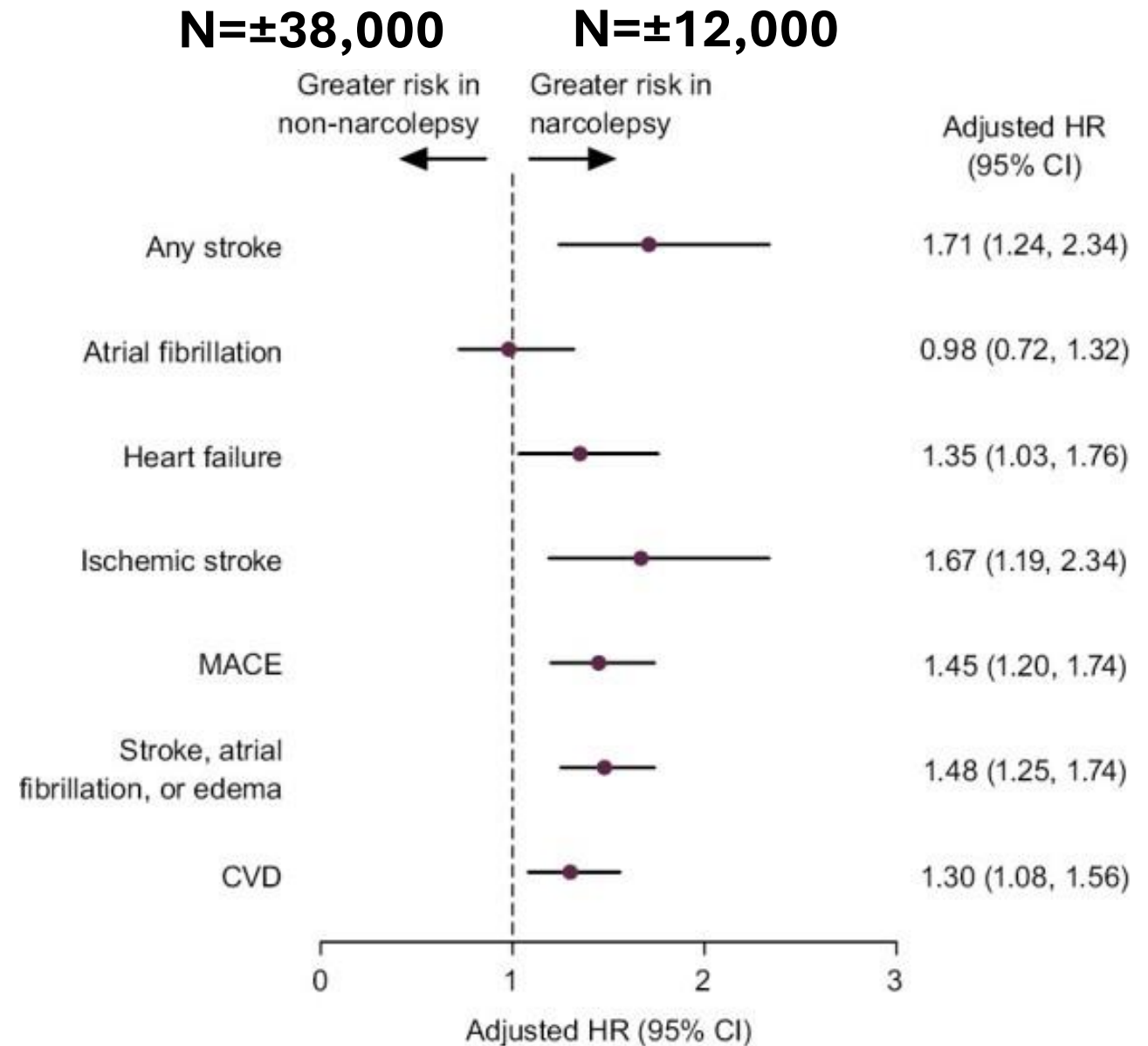
**Incident
CVD**



**Implications
of Salt Intake**

CV Bond Study

Adjusted Hazard Ratios
for Incidence of
Newly-Diagnosed
Cardiovascular/Renal
Conditions in Patients
with Narcolepsy and
Matched Non-
Narcolepsy Controls



Incident CVD in Narcolepsy



Sleep
Research
Society®

SLEEPJ, 2025, 00, 1–10

[doi:10.1093/sleep/zsaf197](https://doi.org/10.1093/sleep/zsaf197)

Advance Access publication 14 July 2025

Original Article

Original Article

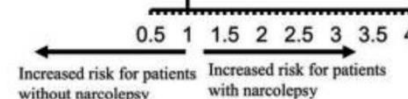
Narcolepsy and risk of cardiovascular outcomes beyond stimulant use

Munaza Riaz¹, Rakesh Bhattacharjee², Weihsuan Lo-Ciganic ^{3,4}, Debbie Wilson¹, Emerson M. Wickwire⁵, Atul Malhotra⁶,
Christopher N. Kaufmann^{7,*} and Haesuk Park ^{1,*}

Riaz M, et al. *Sleep*. 2025;48(12)

Increased Risk of MACE in Narcolepsy

Subgroups	No. of Events/No. of Patients		Incidence per 100 person-years		Adjusted Hazard Ratio (95% CI)	
	Narcolepsy	Without narcolepsy	Narcolepsy	Without narcolepsy		
Main Analysis	1,431/34,562	2,275/100,405	1.50	0.85	1.89 (1.71 – 2.09)	
Age group, years						
≤25	47/8,627	52/21,119	0.22	0.10	1.76 (1.04 – 2.97)	
26-44	239/12,652	215/34,144	0.67	0.23	3.14 (2.34 – 5.00)	
45-65	729/11,102	839/28,910	2.23	1.00	2.22 (1.89 – 2.59)	
>65	399/1,723	611/4,846	9.64	5.92	1.50 (1.23 – 1.82)	
Sex						
Male	615/13,001	956/37,596	1.69	0.92	2.13 (1.83 – 2.47)	
Female	814/21,470	1,129/58,145	0.92	0.47	2.18 (1.90 – 2.51)	
Sleep apnea						
With sleep apnea	579/12,893	870/30,305	1.70	1.05	2.07 (1.77 – 2.43)	
Without sleep apnea	845/21,302	1,075/61,643	1.40	0.67	2.17 (1.88 – 2.49)	
Hyperlipidemia						
With hyperlipidemia	604/7,436	789/20,572	2.95	1.30	2.43 (2.01 – 2.87)	
Without hyperlipidemia	826/27,035	1,221/72,320	1.11	0.67	1.91 (1.67 – 2.19)	
Diabetes						
With diabetes	356/3,206	526/8,755	4.46	2.21	1.95 (1.59 – 2.40)	
Without diabetes	1,072/31,252	1,490/86,080	1.23	0.66	2.26 (2.01 – 2.55)	
Hypertension						
With hypertension	711/6,960	1,011/19,207	3.79	1.87	2.10 (1.82 – 2.43)	
Without hypertension	717/27,502	1,013/73,997	0.94	0.53	2.13 (1.84 – 2.47)	
Type of narcolepsy						
Narcolepsy type 1	191/5,563	251/16,625	1.29	0.58	2.10 (1.58 – 2.79)	
Narcolepsy type 2	1,237/28,943	1,756/83,627	1.54	0.80	2.08 (1.86 – 2.32)	



- N = 134,967
- Propensity matched
- Ratio of 1:3
- Age 40
- 60% female
- 89% increased CVD
- 95% increased MACE

Hypersomnolence & Cardiovascular Considerations



**CV Risk
Factors**



**Prevalent
CVD**



**Incident
CVD**



**Implications
of Salt Intake**

Salt Intake Recommendations



**Average Daily US
Sodium Intake**
3,400mg

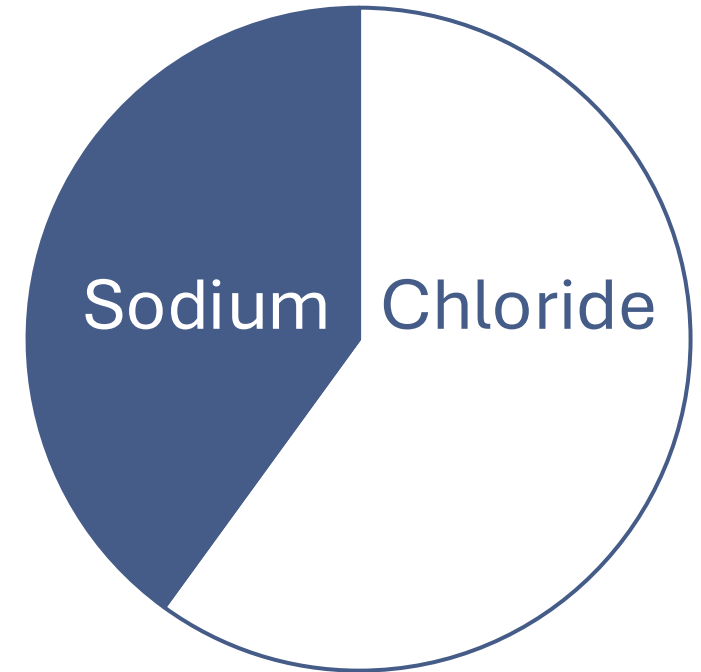


**AHA Recommended
Daily Sodium Intake**
2,300mg



**AHA Optimal Daily
Sodium Intake**
1,500mg

**~40% of table salt is sodium
The rest is chloride**



**10 grams of table salt =
4 grams of sodium**

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.

Sodium Intake is a Critical Target for CV Health

High sodium intake is linked to:

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 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

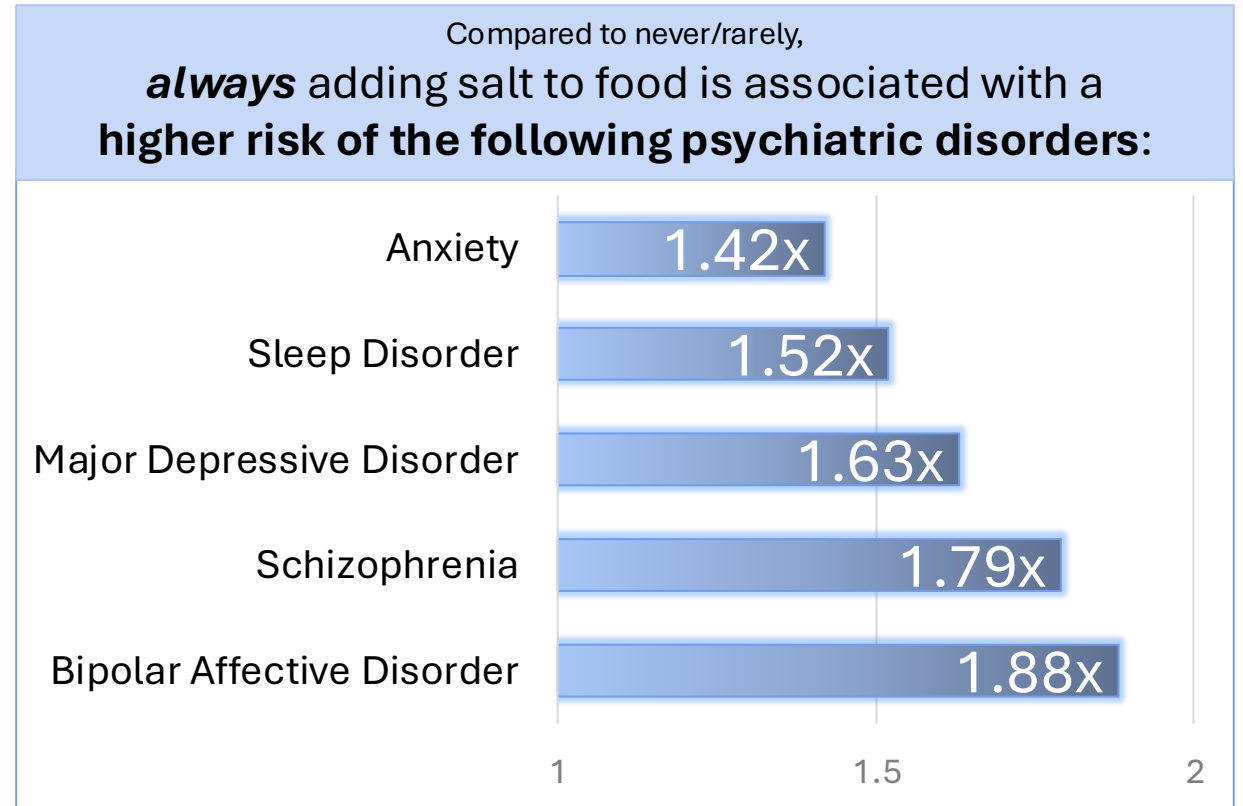
There is a **~6% increase in CVD risk** for every 1000mg of sodium consumed

Higher risk of stroke

Those who consume $\geq 5\text{g}$ of salt per day have **~20% higher risk of stroke**

Worse Mental Health Outcomes

...and Linked to Worse Mental Health



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

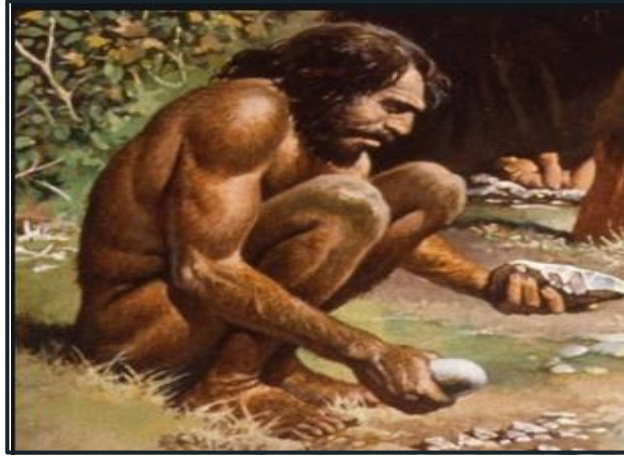
BMI=Body Mass Index.

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.

Current Dietary Intake of Sodium and K⁺



Mismatch between the modern diet introduced over the last 10,000 years, and the nutritional requirements encoded into the human genome, which developed over the several million years from the Stone age



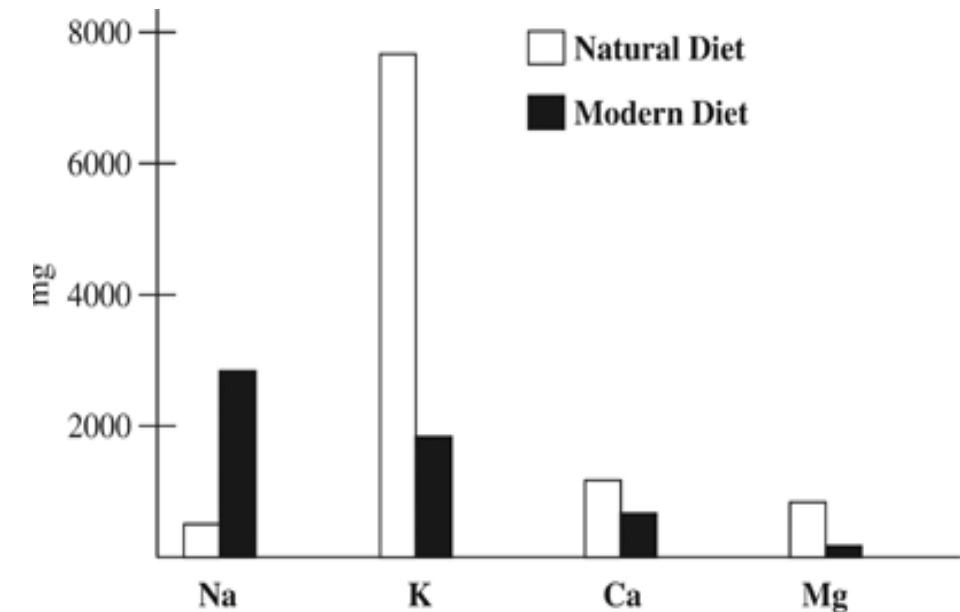
K⁺ intake of prehistoric man was estimated to be 15,000 mg/day²

Diet has shifted from:

HIGH K⁺ ➡ LOW Na

to

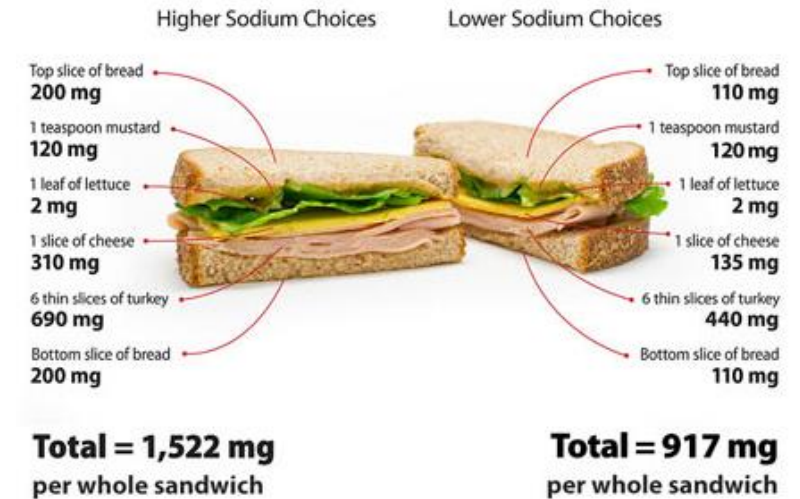
LOW K⁺ ➡ HIGH Na



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, $\geq 20\%$ 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; HTN=Hypertension; Na=Sodium, Cl=Chloride; K=Potassium

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.

Key Learning Points

- **Sleep is a core vital sign for cardiovascular health** — AHA's Life's Essential 8 formally added healthy sleep alongside diet, physical activity, glucose control, weight, lipids, blood pressure, and smoking avoidance
- **Hypersomnolence disorders carry markedly elevated cardiovascular risk** — narcolepsy and idiopathic hypersomnia show high comorbidity burden and, in narcolepsy, 2–3x greater odds of CVD, stroke, MACE, and heart failure across multiple large cohort studies
- **Excess dietary sodium is a major, modifiable CV (and mental health) risk factor** — average U.S. intake (~3,400mg/day) far exceeds AHA targets (2,300mg recommended, 1,500mg optimal); a simple salt-substitute intervention cut major CV events by 13%

Limitations of Traditional and Off-Label Treatments for Narcolepsy and IH

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 ($\geq 5\%$): 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

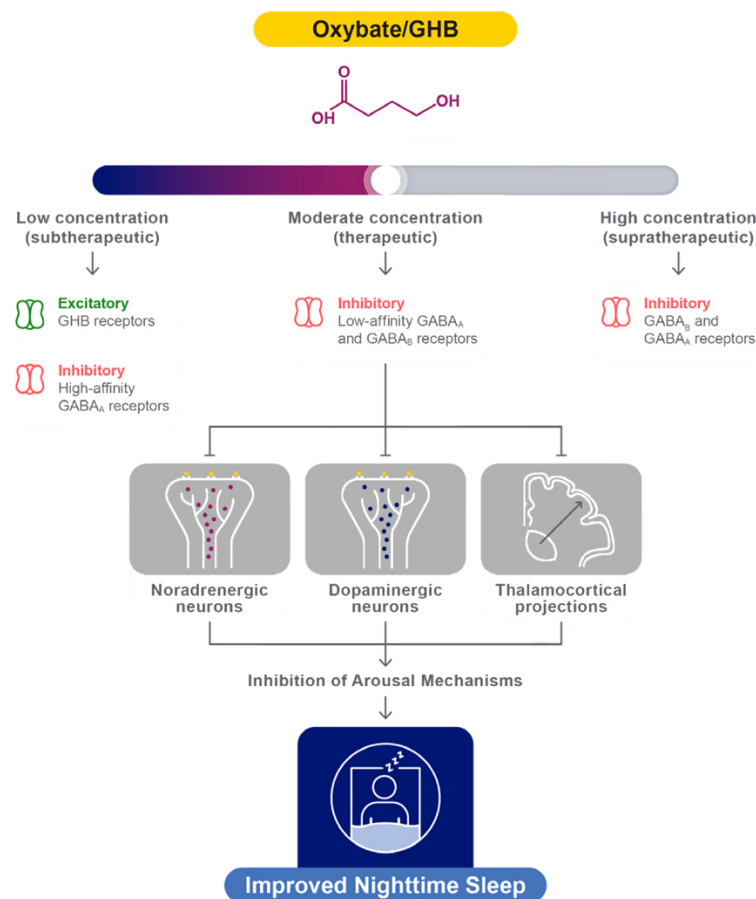
Maski K, et al. "Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline." *Journal of Clinical Sleep Medicine* 17.9 (2021): 1881-1893. Prescribing Information. Drugs@FDA: Accessed 8.20.26. www.accessdata.fda.gov/scripts/cder/daf/.

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



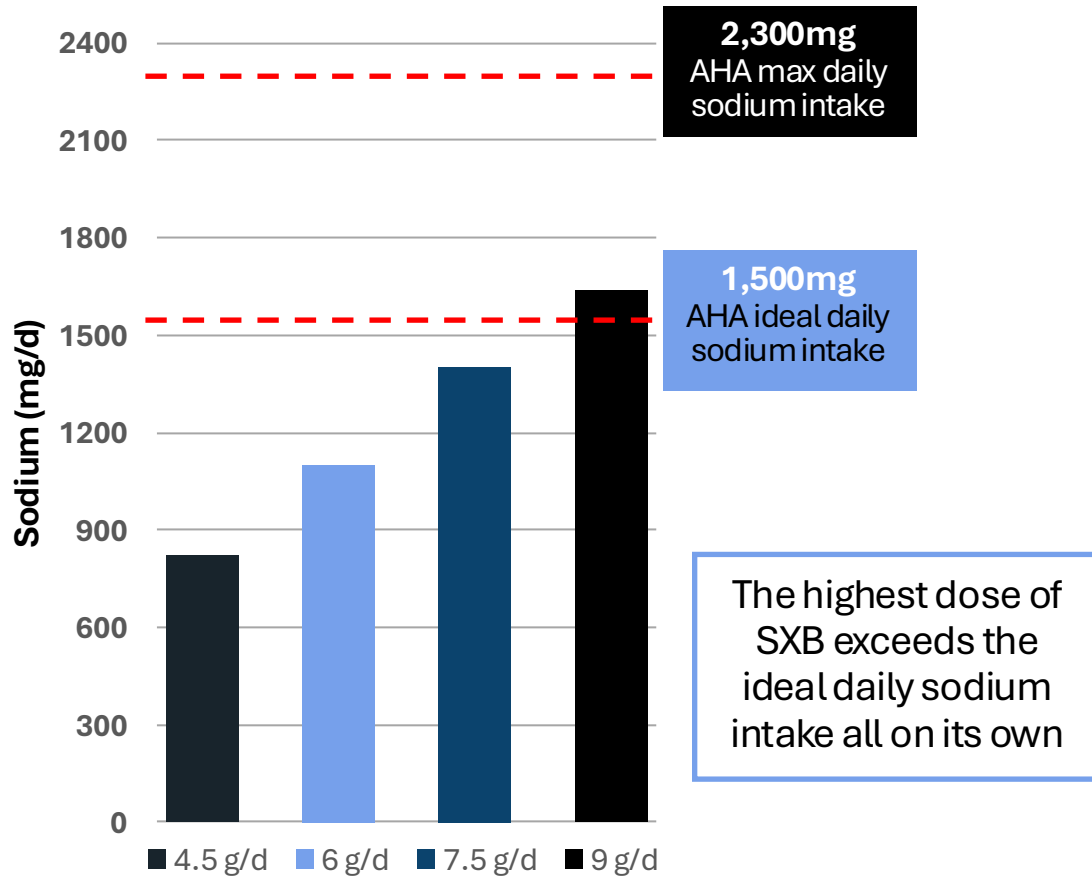
Changes in Alerting Agents in 180 Days Following Oxybate Initiation in the Oxybate Naïve (n=283)

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

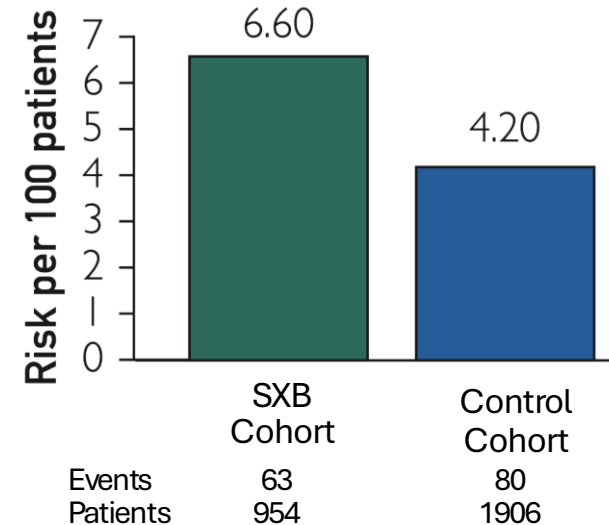
from a real-world retrospective EHR and claims analysis study

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): jcs-m-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



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

Key Learning Points



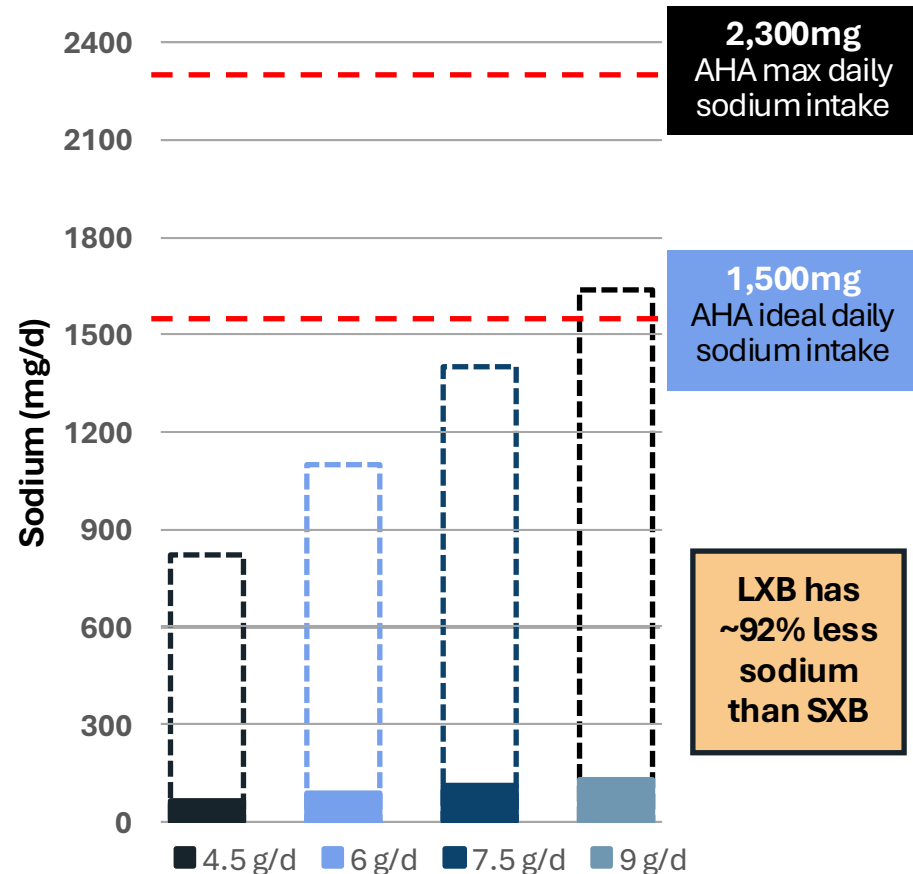
- As a psychiatric clinician, we shouldn't just focus on wakefulness. Sodium oxybate products are foundational for treating hypersomnolence disorders
- Individuals with hypersomnolence disorders, just like those with psychiatric conditions, are at greater risk for cardiovascular comorbidities and earlier 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

Lower Sodium Oxybate

Indication	Idiopathic Hypersomnia (IH) in adults Narcolepsy: EDS and cataplexy (ages 7 years and older)
Mechanism of action	Hypothesized GABA _B actions at noradrenergic and dopaminergic neurons
Typical doses	Narcolepsy: 4.5 g to 9.0 g nightly, divided into two doses at nighttime IH: may be prescribed once nightly, initially 3 g or less then up to 6 g
Warnings	Central nervous system depression; abuse and misuse Caution with hazardous activities, <u>depression</u> and <u>suicidality</u> , <u>confusion/anxiety</u> , parasomnias
Contraindications	In combination with sedative hypnotics or alcohol Succinic semialdehyde dehydrogenase deficiency
Adverse effects	In adults (≥ 5%): headache, nausea, dizziness, decreased appetite, parasomnia, diarrhea, hyperhidrosis, anxiety, and vomiting
Potential interactions	<u>Divalproex</u> – recommend initial sodium oxybate dose reduction
Special considerations	Risk Evaluation and Mitigation Strategy (REMS), central pharmacy Lower sodium content

Lower Sodium Oxybate

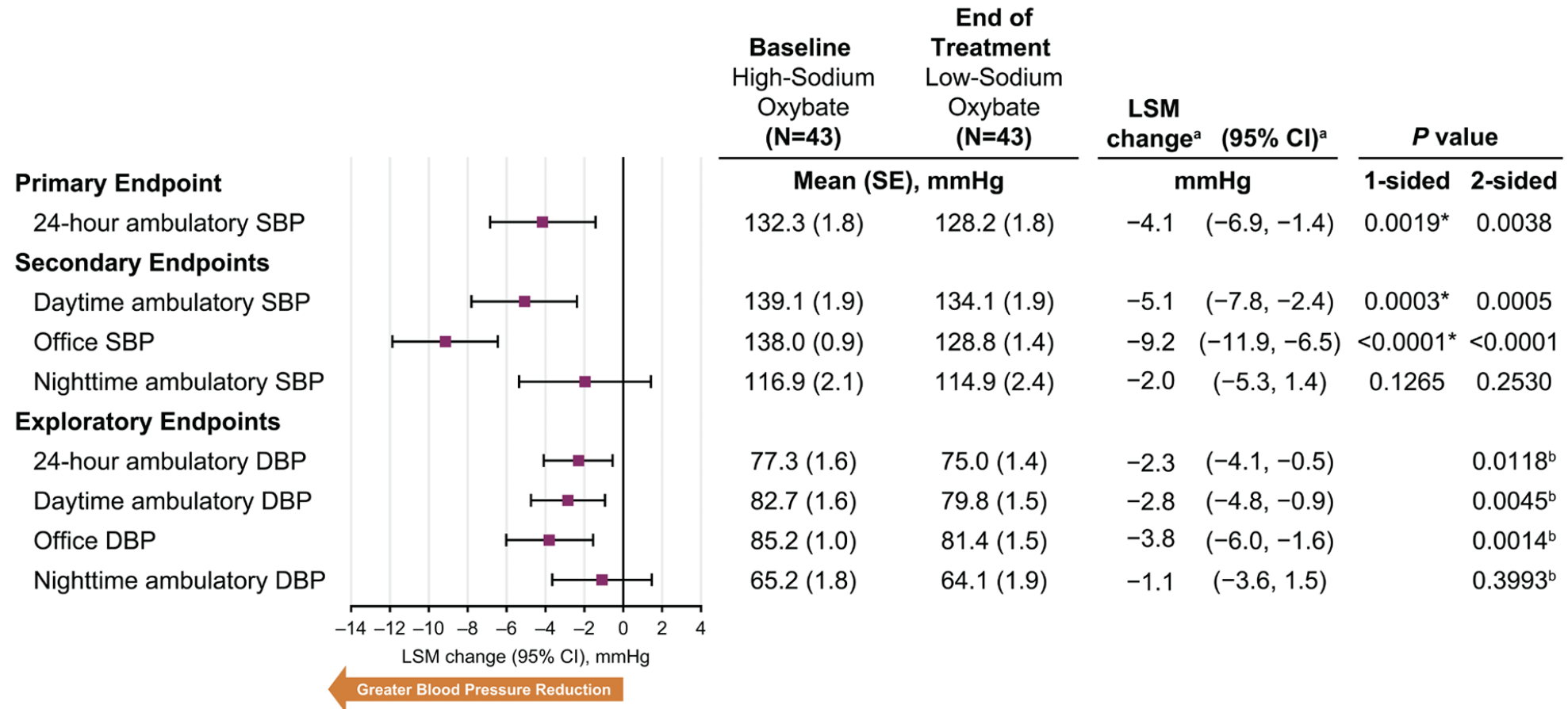


- At 6 mg to 9 mg/night, sodium oxybate contributes **1100 mg to 1640 mg** to daily sodium intake
 - **Yet...** The American Heart Association recommends total daily sodium intake of < 1500 mg as ideal and 2300 mg as the upper limit to maintain blood pressure and heart health

Lower sodium oxybate (LXB) has 92% less sodium than sodium oxybate

Switching to Low-Sodium Oxybate

Significantly Reduced 24-Hour Blood Pressure



Once-Nightly Sodium Oxybate: Extended-Release Oral Suspension

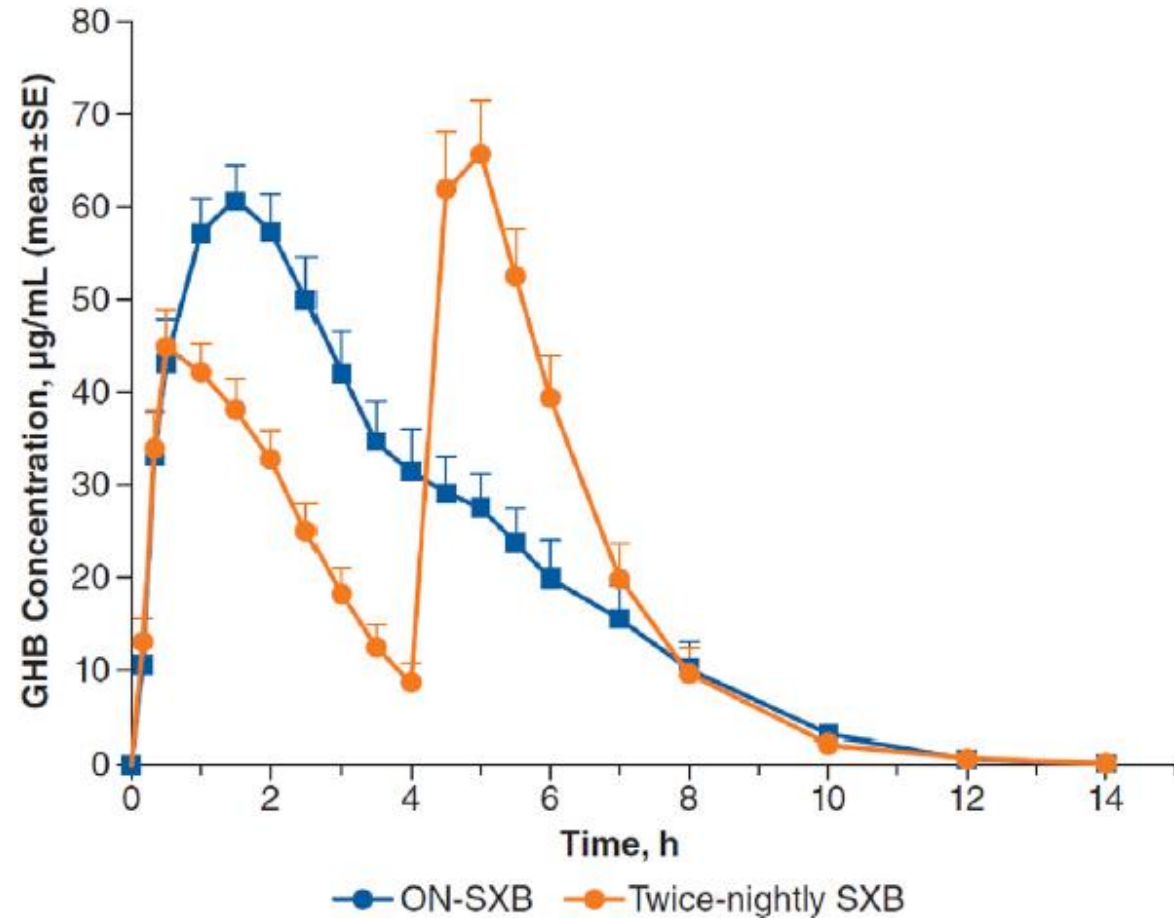
- GABA_B agonist
- DEA Schedule III
- Approved for cataplexy or EDS in adults with narcolepsy
- Dose
 - Initiate dosage at 4.5 gm/night orally, one dose
 - Titrate to effect in increments of up to 1.5 gm/night/week
 - Recommended dosage range: 6 grams to 9 grams once per night
- Contraindications: In combination with sedative hypnotics or alcohol, Succinic semialdehyde dehydrogenase deficiency
- AEs in adults ($\geq 5\%$): Nausea, dizziness, enuresis, headache, and vomiting

Mean Plasma Concentrations of GHB Following Oral Administration of ON-SXB or Twice-Nightly SXB

N=28 healthy volunteers

Main finding:

Once-nightly SXB provides sustained overnight exposure without the second concentration peak associated with middle-of-the-night redosing

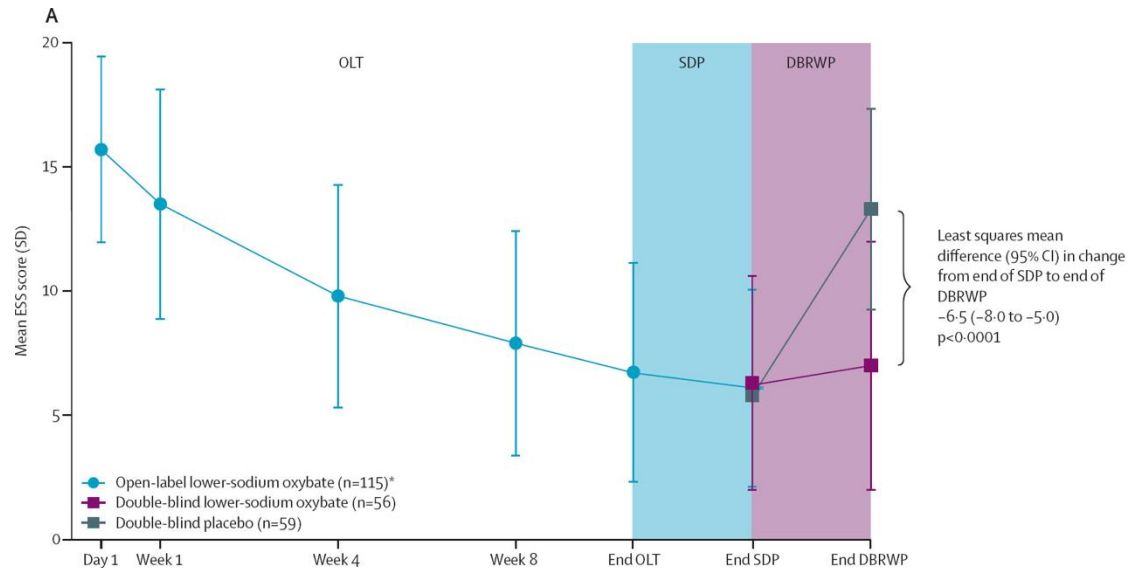
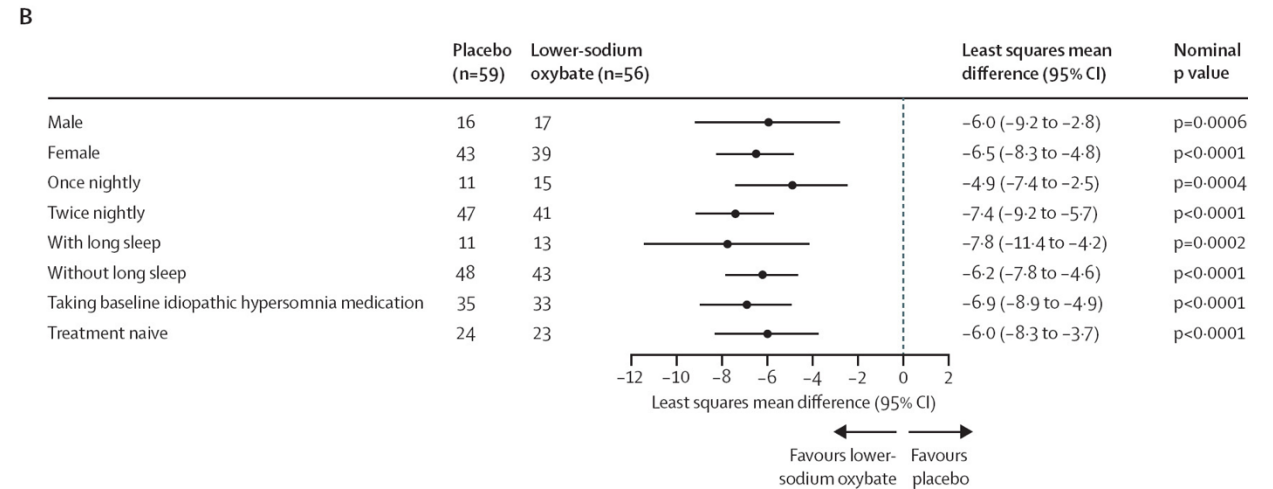


GHB=g-hydroxybutyrate; ON-SXB=once-nightly sodium oxybate; PK=pharmacokinetic; SXB=sodium oxybate

Error bars indicate standard error.

Bogan RK, et al. Sleep Med. 2022;100:442-447.

Once vs. Twice Nightly Low Sodium Oxybate in IH



- Efficacy in pivotal phase 3 trial observed in both once (23%) and twice nightly (77%) dosing
- Phase 4 DUET trial had 36.6% on once and 63.4% on twice nightly therapy
- Allowed investigator discretion/preference with maximum nightly dose of 9 grams (maximum once nightly dose of 6 grams)

Newer Oxybate Options: Summary

Lower Sodium Oxybate

- Substantially lower sodium load
- Flexible dosing
 - Once vs. twice nightly
 - Asymmetric
- Current indications for narcolepsy and IH

Once-nightly Sodium Oxybate

- Similar sodium load to standard sodium oxybate
- Regimented dosing
- Potential to avoid middle of the night awakenings
- Current indication for narcolepsy

Pitolisant

Indication	Narcolepsy: EDS or cataplexy in adults
Mechanism of action	Histamine H ₃ receptor antagonist/inverse agonist
Typical doses	17.8 to 35.6 mg daily (initial dose 8.9 mg) Dose reductions for hepatic and renal disease (not recommended for end-stage renal disease) and CYP2D6 poor metabolizers
Warnings	QT interval prolongation
Contraindications	Known hypersensitivity; severe hepatic impairment
Adverse effects	<u>Insomnia</u> , nausea, <u>anxiety</u>
Key potential interactions	<u>Strong CYP2D6 inhibitors</u> : 17.8 mg maximum recommended dose Strong CYP3A4 inducers: decreased pitolisant exposure Hormonal contraceptives and sensitive CYP3A4 substrate effectiveness may be reduced. Use alternate non-hormonal contraceptive method during pitolisant use and 3 weeks after use.
Special considerations	Central pharmacy

Pitolisant Phase 3 Trials

- Harmony 1 – Double blind RCT in narcolepsy
 - Pitolisant demonstrated significant improvements in ESS relative to placebo
 - Similar changes in ESS compared to modafinil
- Harmony CTP – Double blind RCT in narcolepsy with cataplexy
 - Pitolisant demonstrated significant reduction in weekly cataplexy rate
 - Also several other secondary endpoints
- INTUNE – Double blind randomized withdrawal trial in IH
 - Did not meet primary endpoint (ESS)

Orexin 2 Receptor Agonists: A New Treatment Class

Agent	Population studied	Current status*	Key clinical signal
Oveporexton (TAK-861)	NT1	FDA approved for adults with NT1 in August 2026	Phase 3: improved wakefulness, sleepiness, cataplexy, disease severity, and quality of life; median weekly cataplexy reductions of 79%-89%
Alixorexton (ALKS 2680)	NT1, NT2, IH	Phase 3: NT1 and NT2; Phase 2: IH	Phase 2 studies showed improved MWT and ESS outcomes in both NT1 and NT2; improvements also observed in fatigue and cognition
Cleminorexton (ORX750)	NT1, NT2, IH	Phase 2a	Early results showed improved objective and subjective wakefulness across NT1, NT2, and IH; NT1 cohort demonstrated an 87% relative reduction in weekly cataplexy versus placebo
TAK-360	NT1, NT2, IH	Phase 2	Being developed for hypersomnolence disorders with and without established orexin deficiency; efficacy results not yet available
Lu AH69593	Narcolepsy	Phase 1b; FDA Fast Track	Early clinical development assessing safety, pharmacokinetics, and pharmacodynamic effects; patient efficacy not yet established

*As of September 2026
Dauvilliers Y,, et al. *N Engl J Med*. Published online September 9, 2026. doi:10.1056/NEJMoa2601598; Plazzi G, et al. *Lancet Neurol*. Published online August 24, 2026; Alkermes. Accessed September 10, 2026; ClinicalTrials.gov. NCT06752668, NCT06812078; Lundbeck. July 23, 2026.



Key Learning Points

- Multiple oxybate preparations are commercially available that vary depending on cation(s) bound to the oxybate moiety (sodium vs. others), timing of administration, and current indications
 - Switching from high-sodium oxybate to low-sodium oxybate reduced 24-hour ambulatory blood pressure
- Pitolisant is a unique agent targeting histamine approved to treat daytime sleepiness and cataplexy in narcolepsy
- The first orexin receptor 2 agonist (ovexorexton) has recently been approved to treat type 1 narcolepsy, with other agents from this class under development

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

Best Practices for Counseling Patients on Sodium Intake

Building a Support Network with Sleep Specialists

Accessing Further Education/Consultation in Sleep Medicine



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Q&A

