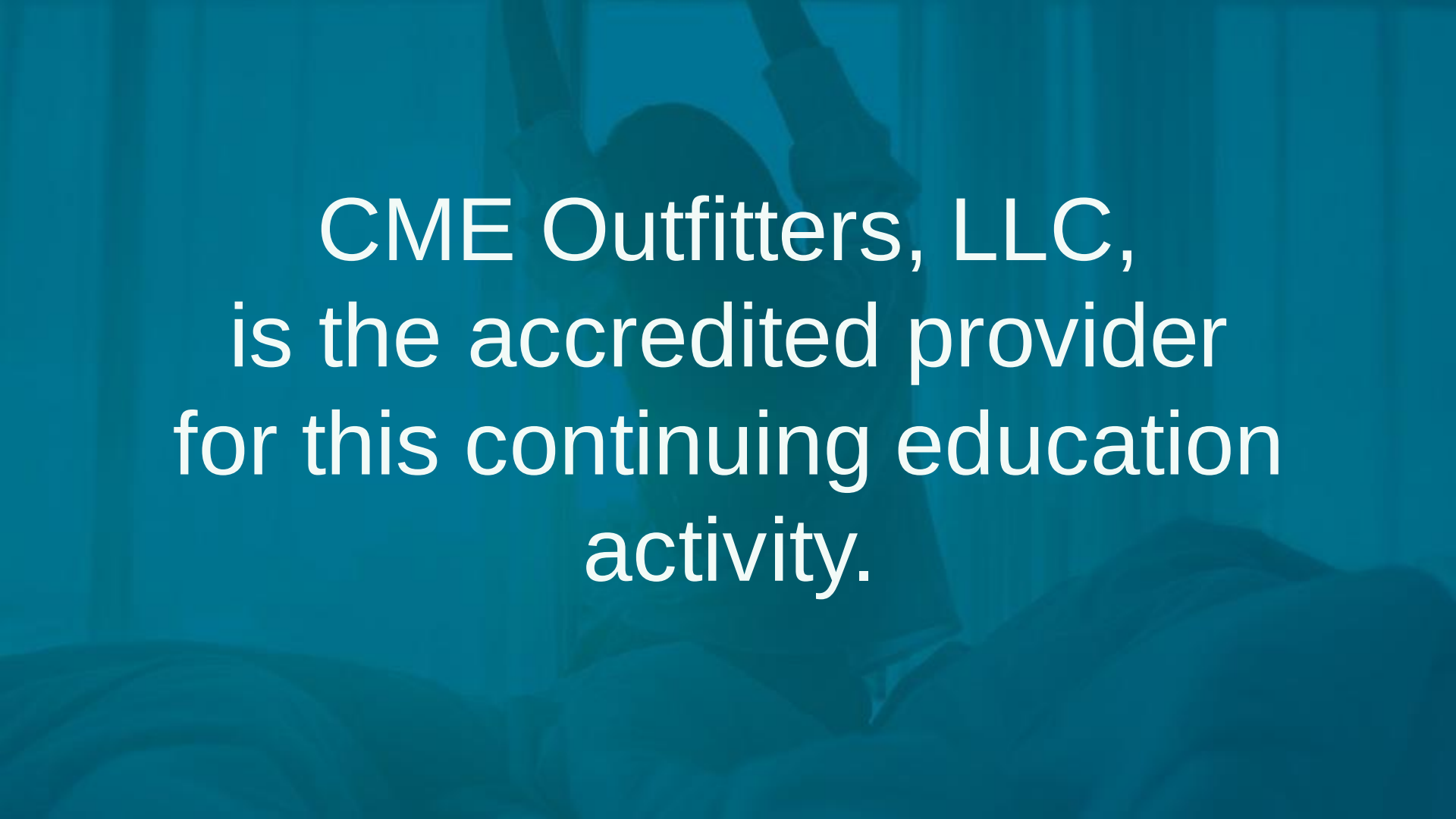


Achieving Optimal Outcomes in Patients with Narcolepsy:

Aligning Treatment Goals with Patients

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**Author, *Wide Awake and Dreaming:
A Memoir of Narcolepsy***

Los Angeles, CA



Explain the patient's journey with narcolepsy, including the extensive impact of work, psychosocial, and daily functioning to overall health.

LEARNING OBJECTIVE 1



Audience Response



How often do you discuss the challenges of living with narcolepsy with your patients?

- A. 0% of the time
- B. 1%-25% of the time
- C. 26%-50% of the time
- D. 51%-75% of the time
- E. 76%-100% of the time

Multifaceted Impact of Narcolepsy^{1,2}



**Worsened
HRQoL**



**Falling asleep
throughout the day**



**Impaired social life
and isolation**



**Increased risk of
accidents while driving**



**Strain on
relationships**



Memory problems



**Impaired
critical thinking**



**Employment: job loss,
frequent job changes,
absenteeism / presenteeism**



Brain fog



**Poor school
performance**

HRQoL = health-related quality of life

1. Waldman LT, et al. *Health Qual Life Outcomes*. 2020;18:128. 2. Morse AM. *Med Sci (Basel)*. 2019;7(12):106.

Comorbidities Associated with Narcolepsy^{1,2}



Disturbed Nocturnal Sleep by the Numbers

N = 57 with NT1¹



Sleep Apnea

43% loud snoring
21% experience apneas
20% awakening with dyspnea during the night



Waking Up

50% felt unrefreshed
17 ± 28 minutes to get up in the morning
24% experienced sleep drunkenness

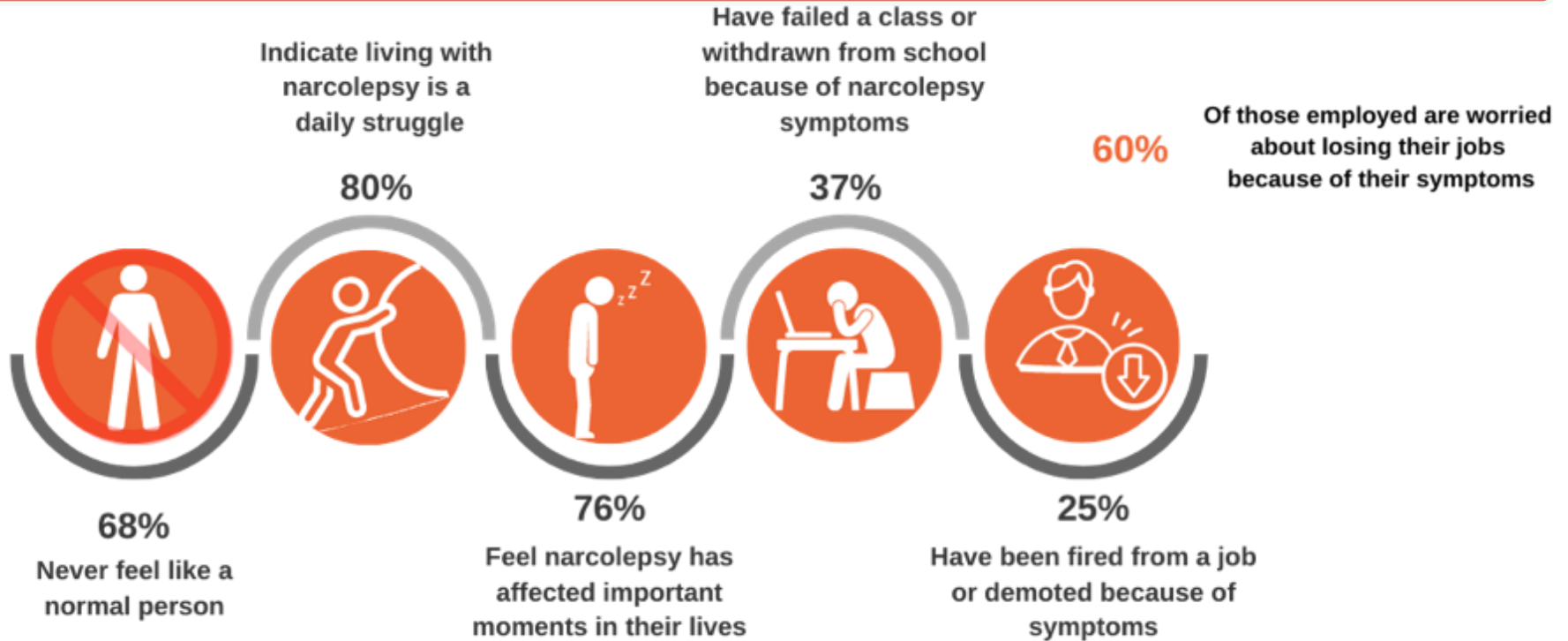
Sleep 71% unable to sleep without awakening
31% got up at night to eat



In a sample of 248 patients with NT1, disturbed nocturnal sleep severity was associated with higher scores on the Narcolepsy Severity Scale, higher sleepiness, anxiety/depressive symptoms, autonomic dysfunction, and worse quality of life.²

Living with Narcolepsy: The Patient Perspective

In a survey of 200 individuals living with narcolepsy:



Living with Narcolepsy: Patient and Clinician Perspectives

In a survey of 200 patients
and 251 physicians:



**Alter lives to
accommodate symptoms**

40% of patients avoid
social situations

20% of patients avoid
strong emotions

93.6% of clinicians say patients
unknowingly do this



**Symptoms are mostly or
completely under control**

12.0% of patients agree

27.5% of clinicians agree



**EDS is a major
disruptive symptom**

87.5% of patients agree

92.0% of clinicians agree

EDS = excessive daytime sleepiness

Thorpy MJ, et al. *Sleep*. 2019;42(Suppl 1):A236.

Audience Response



Now, how often will you discuss the challenges of living with narcolepsy with your patients?

- A. 0% of the time
- B. 1%-25% of the time
- C. 26%-50% of the time
- D. 51%-75% of the time
- E. 76%-100% of the time

A Patient's Journey: Addressing the Unmet Needs of Patients Living with Narcolepsy



Analyze the practice implications of using evidence-based screening tools and diagnostic criteria to accelerate the early, accurate diagnosis of narcolepsy.

**LEARNING
OBJECTIVE**

2



Audience Response



What percentage of your patients with narcolepsy were initially misdiagnosed?

- A. 0% of patients
- B. 1%-25% of patients
- C. 26%-50% of patients
- D. 51%-75% of patients
- E. 76%-100% of patients

Audience Response



How familiar are you with best practices to implement diagnostic criteria and evidence-based screening tools into routine practice to detect and diagnose narcolepsy?

- A. Not familiar at all
- B. Somewhat familiar
- C. Familiar
- D. Extremely familiar

Predictors of Diagnostic Delays



Children¹

- ▶ Strongest predictor → pediatric onset of symptoms
- ▶ Manifestation in children and adolescents



Adults and Children²

- ▶ Comorbid sleep disorders
- ▶ Comorbid psychiatric disorders
- ▶ Presence of sleep-related hallucinations
- ▶ Media portrayal and presentation
- ▶ Gap in physician knowledge
- ▶ Absence of cataplexy



ICSD-3 Diagnostic Criteria for NT1 and NT2

Criteria in **red** must be met for NT1 and NT2

Narcolepsy Type 1

- ▶ Narcolepsy with cataplexy
- ▶ EDS for at least 3 months (with validated questionnaires such as ESS)
- ▶ At least one of the following:
 - ▶ Cataplexy and a positive MSLT*
 - ▶ Low mean sleep latency < 8 mins
 - ▶ ≥ 2 SOREMPs on MSLT-PSG
 - ▶ Low CSF hypocretin-1 concentrations ($\leq 110\text{pg/ml}$ or $< 1/3$ of normal)

*Positive MSLT: mean sleep latency of < 8 minutes and ≥ 2 SOREMPs

CSF = cerebrospinal fluid; EDS = excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; MSLT = Multiple Sleep Latency Test; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSAS = obstructive sleep apnea syndrome; PSG = polysomnogram; SOREMPs = sleep onset REM periods

Sateia MJ. *Chest*. 2014;146(5):1387-1394.

ICSD-3 Diagnostic Criteria for NT1 and NT2

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 - ▶ Low CSF hypocretin-1 concentrations ($\leq 110\text{pg/ml}$ or $< 1/3$ of normal)

Narcolepsy Type 2

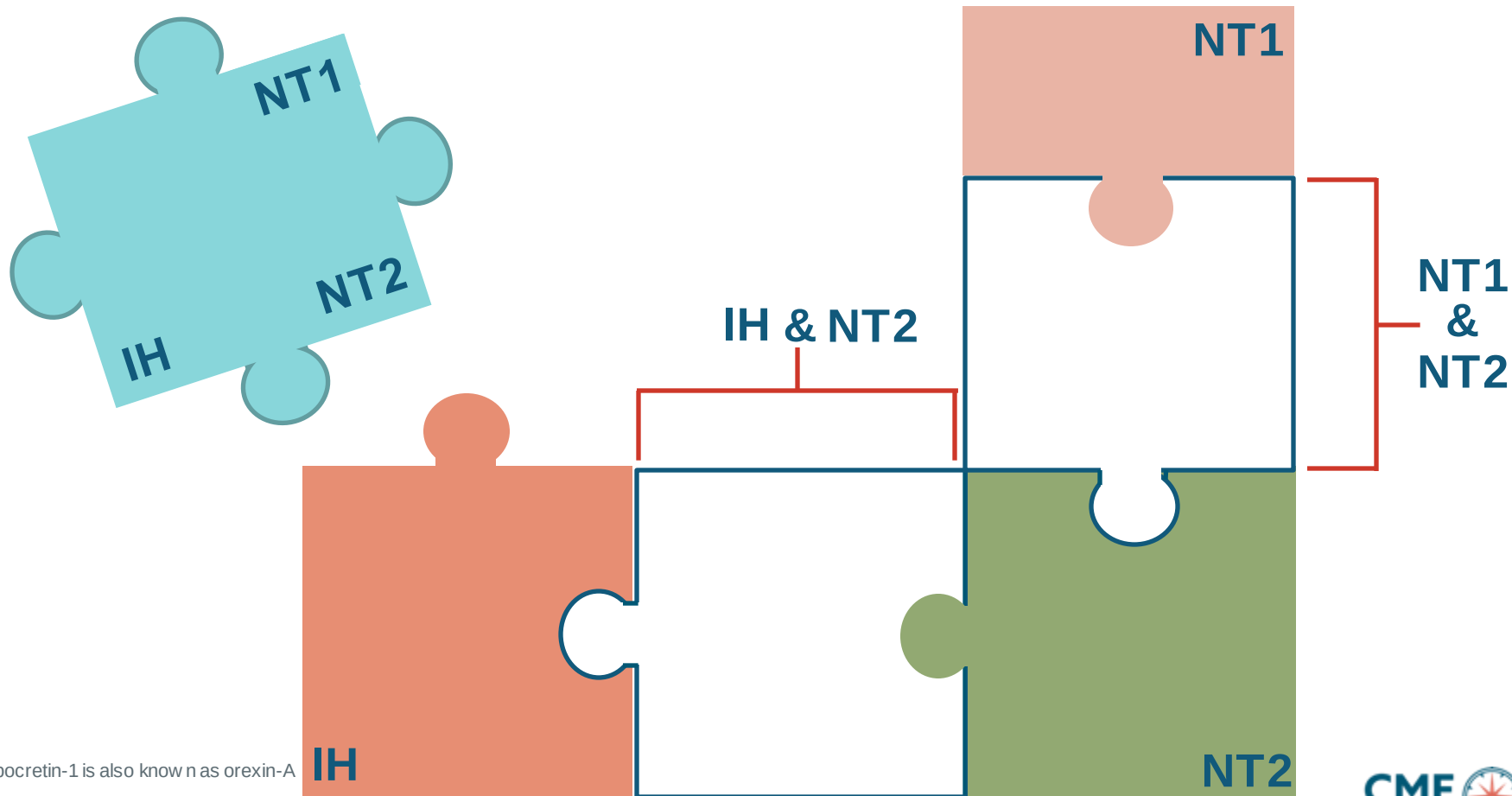
- ▶ Narcolepsy without cataplexy
- ▶ **EDS for at least 3 months**
- ▶ **Positive MSLT***
 - ▶ **Low mean sleep latency < 8 mins**
 - ▶ **≥ 2 SOREMPs on MSLT-PSG**
- ▶ CSF hypocretin-1 concentrations
 - ▶ $> 110\text{pg/ml}$ if measured
- ▶ Hypersomnolence and MSLT findings not better explained by other causes:
 - ▶ Insufficient sleep, OSAS, delayed sleep phase, drug intake/withdrawal

*Positive MSLT: mean sleep latency of < 8 minutes and ≥ 2 SOREMPs

CSF = cerebrospinal fluid; EDS = excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; MSLT = Multiple Sleep Latency Test; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSAS = obstructive sleep apnea syndrome; PSG = polysomnogram; SOREMPs = sleep onset REM periods

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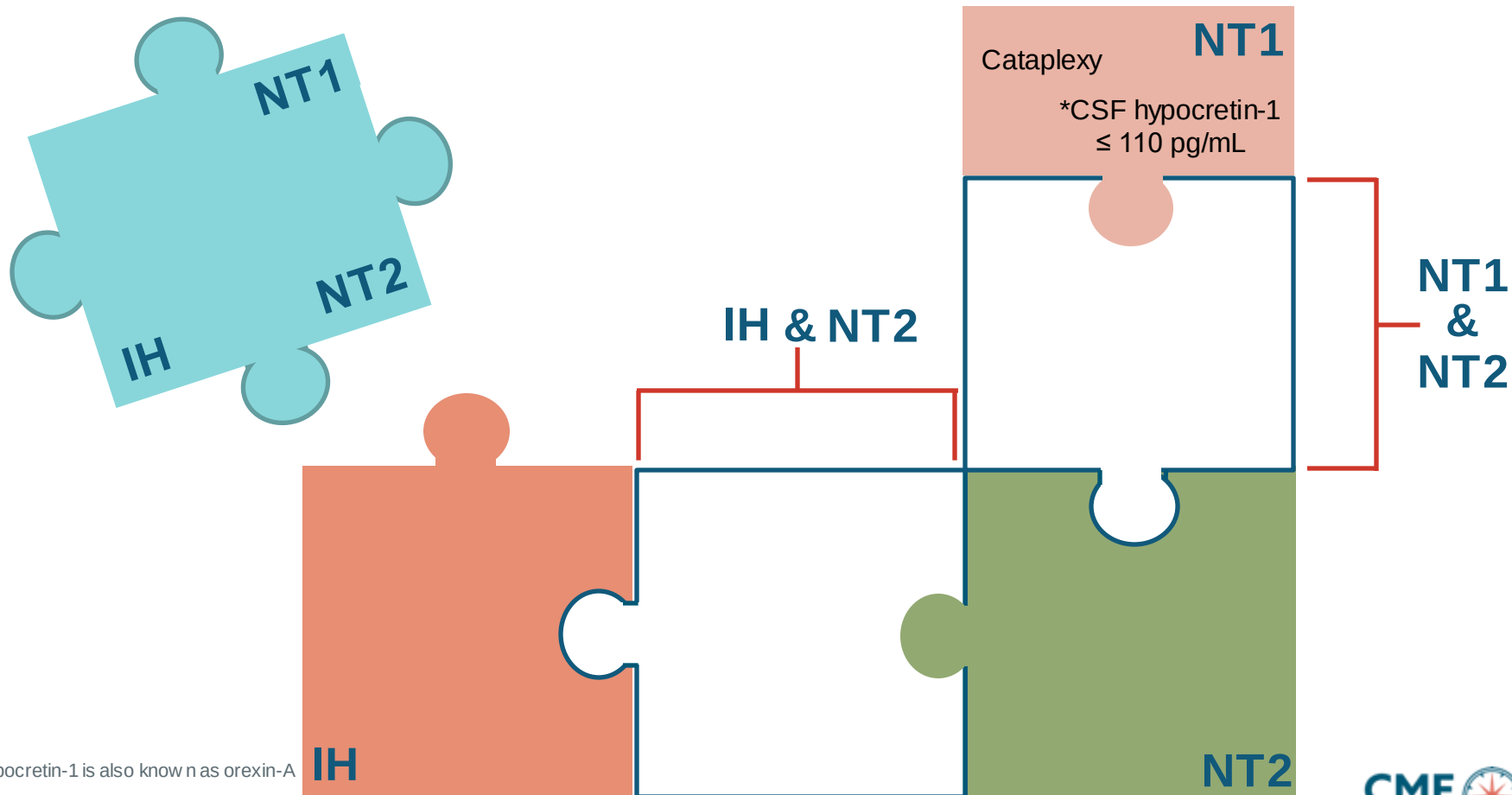
Differentiating Narcolepsy: Putting the Puzzle Together



*CSF hypocretin-1 is also known as orexin-A

CSF = cerebrospinal fluid; ESS = Epworth Sleepiness Scale; IH = idiopathic hypersomnia; MSLT = Multiple Sleep Latency Test; PSG = polysomnogram; REM = rapid eye movement; SOREMPs = sleep onset REM periods

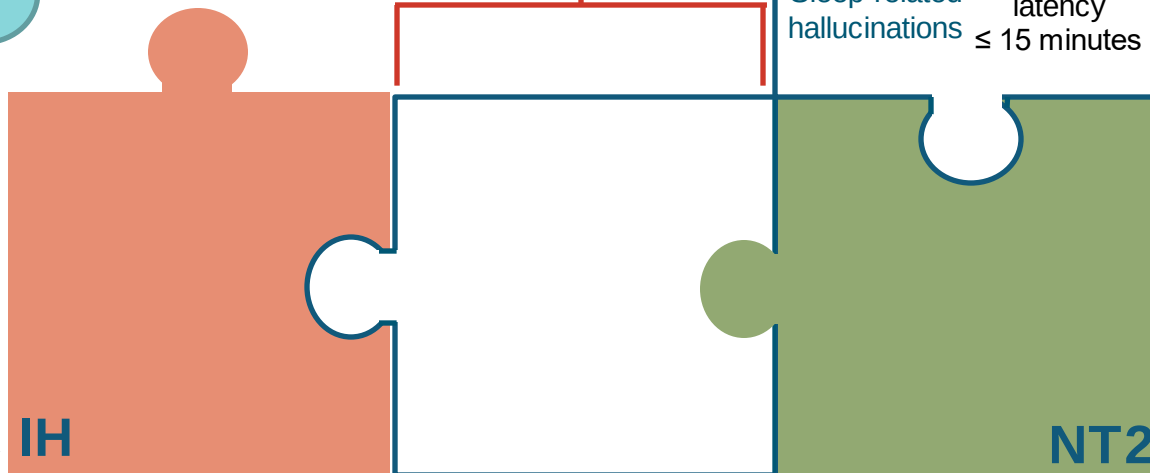
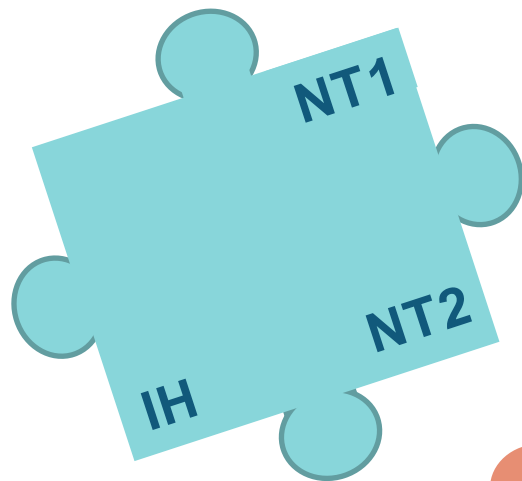
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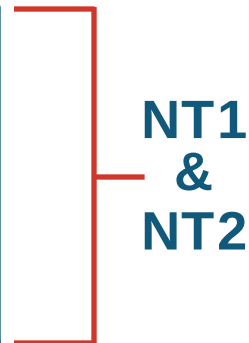
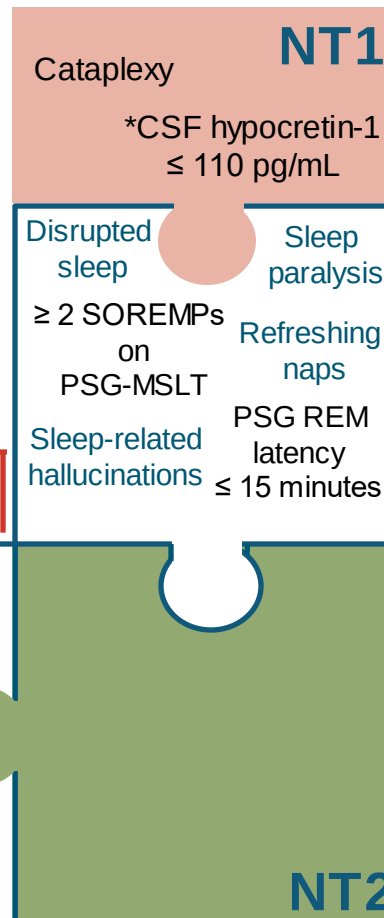
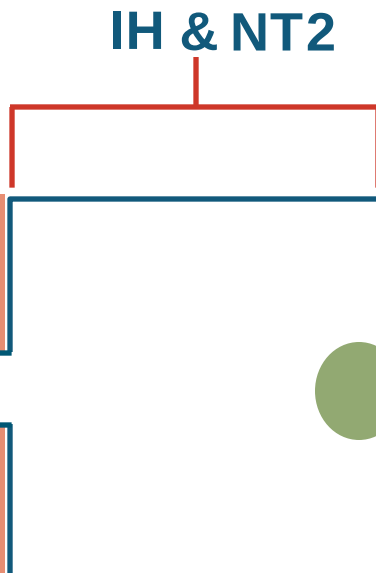
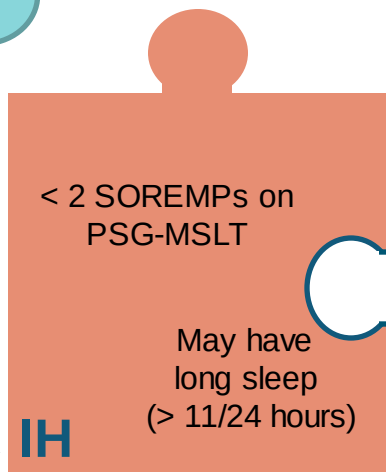
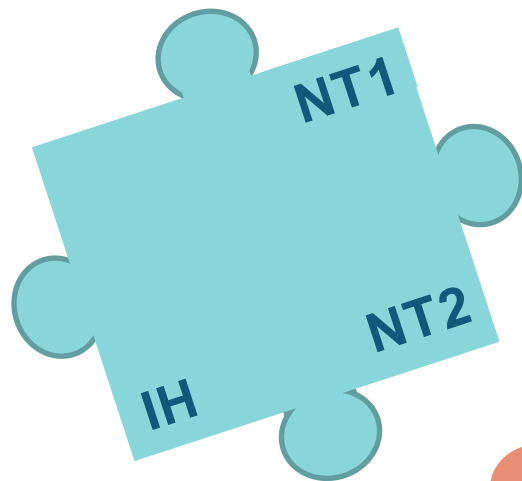


Cataplexy		NT1
*CSF hypocretin-1 ≤ 110 pg/mL		
Disrupted sleep	Sleep paralysis	NT1 & NT2
≥ 2 SOREMPs on PSG-MSLT	Refreshing naps	
Sleep-related hallucinations	PSG REM latency ≤ 15 minutes	

*CSF hypocretin-1 is also known as orexin-A

CSF = cerebrospinal fluid; ESS = Epworth Sleepiness Scale; IH = idiopathic hypersomnia; MSLT = Multiple Sleep Latency Test; PSG = polysomnogram; REM = rapid eye movement; SOREMPs = sleep onset REM periods

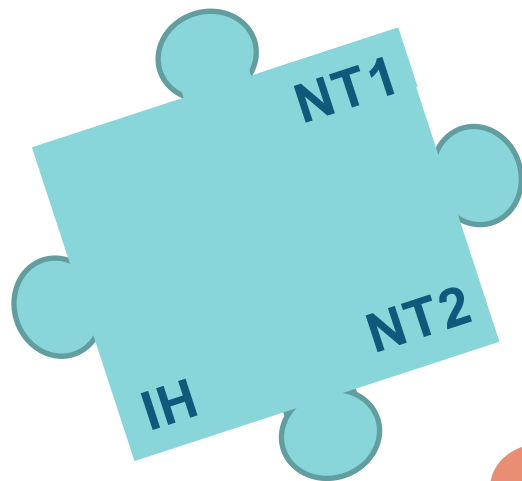
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Differentiating Narcolepsy: Putting the Puzzle Together



IH

< 2 SOREMPs on PSG-MSLT

May have long sleep (> 11/24 hours)

IH & NT2

No cataplexy

Unrefreshing naps

*Normal CSF hypocretin-1

Sleep inertia

May have spontaneous remission

NT1

Cataplexy

*CSF hypocretin-1 ≤ 110 pg/mL

Disrupted sleep

≥ 2 SOREMPs on PSG-MSLT

Sleep-related hallucinations

Sleep paralysis

Refreshing naps

PSG REM latency ≤ 15 minutes

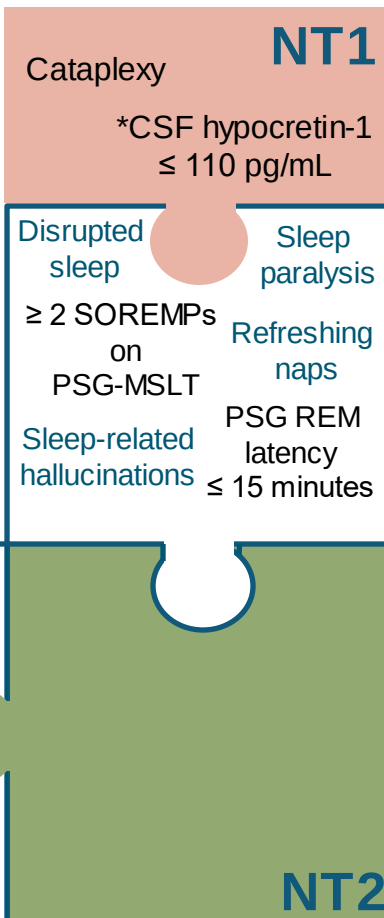
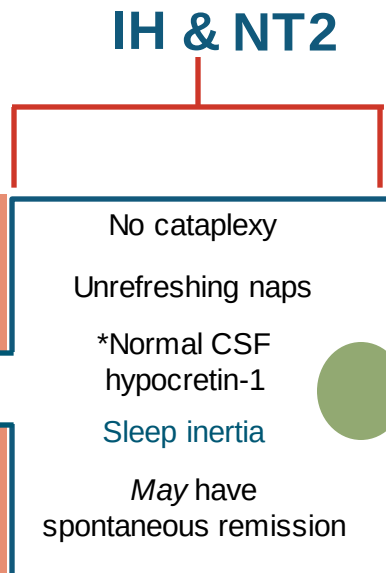
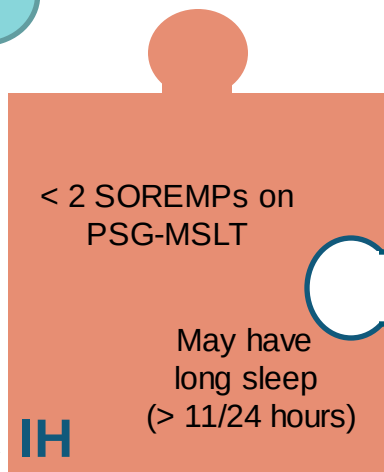
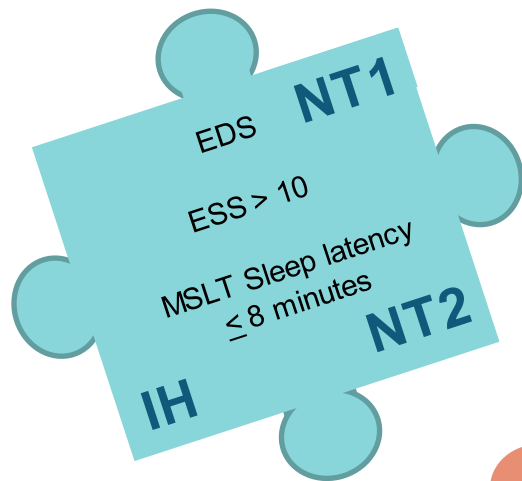
NT2

NT1 & NT2

*CSF hypocretin-1 is also known as orexin-A

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Differential Diagnosis



- ▶ EDS
 - ▶ OSAS
 - ▶ Sleep deprivation/poor sleep hygiene
 - ▶ Depression
 - ▶ Substance/drug intake
 - ▶ IH, KLS
 - ▶ PLMD
 - ▶ Circadian rhythm abnormality
 - ▶ Behavioral symptoms of EDS
 - ▶ Irritability, poor attentiveness, aggression, hallucinations



IH = idiopathic hypersomnia; KLS = Kleine-Levin syndrome; OSAS = obstructive sleep apnea syndrome; PLMD = periodic limb movement disorder

Nevsimalova S. *Curr Neurol Neurosci Rep.* 2014;14(8):469. Warman J, et al. *Neurology.* 2013;80(7 Suppl):S43.003.
Dauvilliers Y, et al. *Neurol Neurosurg Psychiatry.* 2003;74(12):1667-1673. Zhou J, et al. *Shanghai Arch Psychiatry.* 2014; 26(4):232-235.

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▶ Cataplexy

- ▶ Typical cataplexy
 - ▶ Video record if possible
- ▶ Seizure, hypotension, psychogenic



IH = idiopathic hypersomnia; KLS = Kleine-Levin syndrome; OSAS = obstructive sleep apnea syndrome; PLMD = periodic limb movement disorder

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Differential Diagnosis



▶ EDS

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- ▶ Behavioral symptoms of EDS
 - ▶ Irritability, poor attentiveness, aggression, hallucinations



▶ Cataplexy

- ▶ Typical cataplexy
 - ▶ Video record if possible
- ▶ Seizure, hypotension, psychogenic



▶ Hallucinations

- ▶ Schizophrenia
- ▶ Night terrors
- ▶ Panic attacks



IH = idiopathic hypersomnia; KLS = Kleine-Levin syndrome; OSAS = obstructive sleep apnea syndrome; PLMD = periodic limb movement disorder

Nevsimalova S. *Curr Neurol Neurosci Rep.* 2014;14(8):469. Warman J, et al. *Neurology.* 2013;80(7 Suppl):S43.003.

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Audience Response



How often do you assess treatment efficacy on functional status and QoL in your patients with narcolepsy?

- A. 0% of the time
- B. 1% - 25% of the time
- C. 26% - 50% of the time
- D. 51% - 75% of the time
- E. 76% - 100% of the time

Self-Report Measures Can Be Used in Clinical Practice



Epworth Sleepiness Scale (ESS)

- The ESS is the most frequently used, validated self-report assessment of a patient's sleepiness¹
- On a 4-point scale, patients rate their likelihood of falling asleep during 8 different situations (reading, driving, etc.)²
- The ESS can also be used to monitor the progression of or improvement in sleepiness over time³

Swiss Narcolepsy Scale (SNS)

- The SNS is a validated self-report assessment of a patient's sleepiness
- On a 5 item, 5-point scale, patients rate the frequency of individual symptoms (EDS and cataplexy)
- The SNS has a high sensitivity and specificity in identifying NT1⁴ (particularly compared to ESS)
- Each answer is weighted by a positive or negative factor; score of < 0 is suggestive of narcolepsy with cataplexy
- A two-item short form version (sSNS) also available demonstrating discriminative power for NT1⁵

Self-Report Measures Can Be Used in Clinical Practice (cont.)



Functional Outcomes of Sleep Questionnaire (FOSQ)

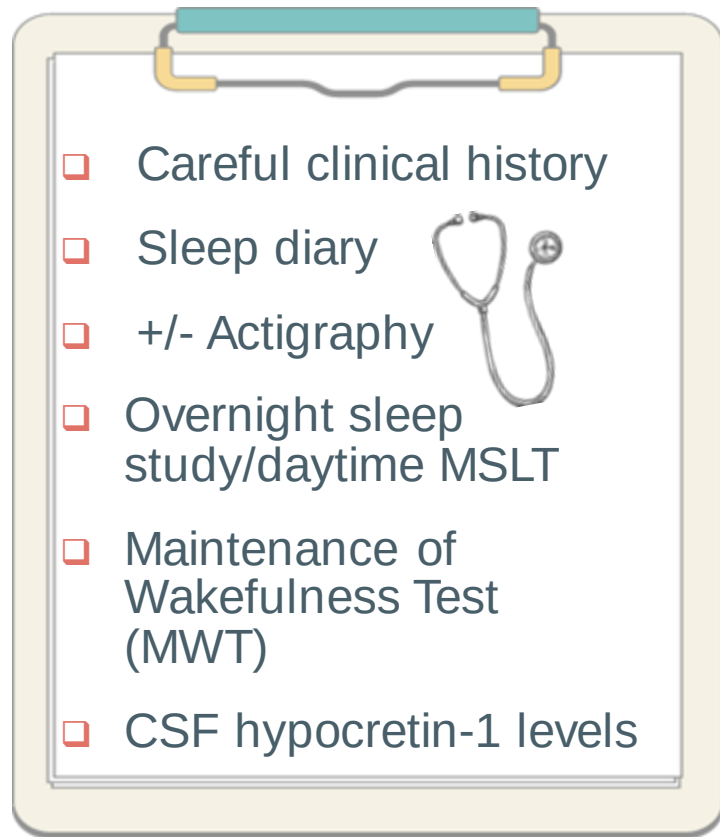
- The FOSQ (or shorter FOSQ-10) assesses the effect of sleepiness on daily functioning
- Evaluates 5 domains
 - General productivity
 - Activity level
 - Vigilance
 - Social outcomes
 - Intimate/sexual relationships



Subjective measures rely on patients to accurately report their own sleepiness; however, they are:

- Practical for monitoring progression or improvement in EDS
- Simple to administer

Narcolepsy Diagnosis and Pitfalls



- ▶ Subtleties of diagnosis
- ▶ Interpreting diagnostic tests
- ▶ Partial cataplexy
- ▶ Comorbidity with other sleep disorders is common:
 - ▶ ~25% of patients with narcolepsy also have OSA
- ▶ 82% of patients with narcolepsy receive a diagnosis ≥ 1 year from symptom onset; one-third > 10 years

Audience Response



Now, how familiar are you with best practices to implement diagnostic criteria and evidence-based screening tools into routine practice to detect and diagnose narcolepsy?

- A.** Not familiar at all
- B.** Somewhat familiar
- C.** Familiar
- D.** Extremely familiar

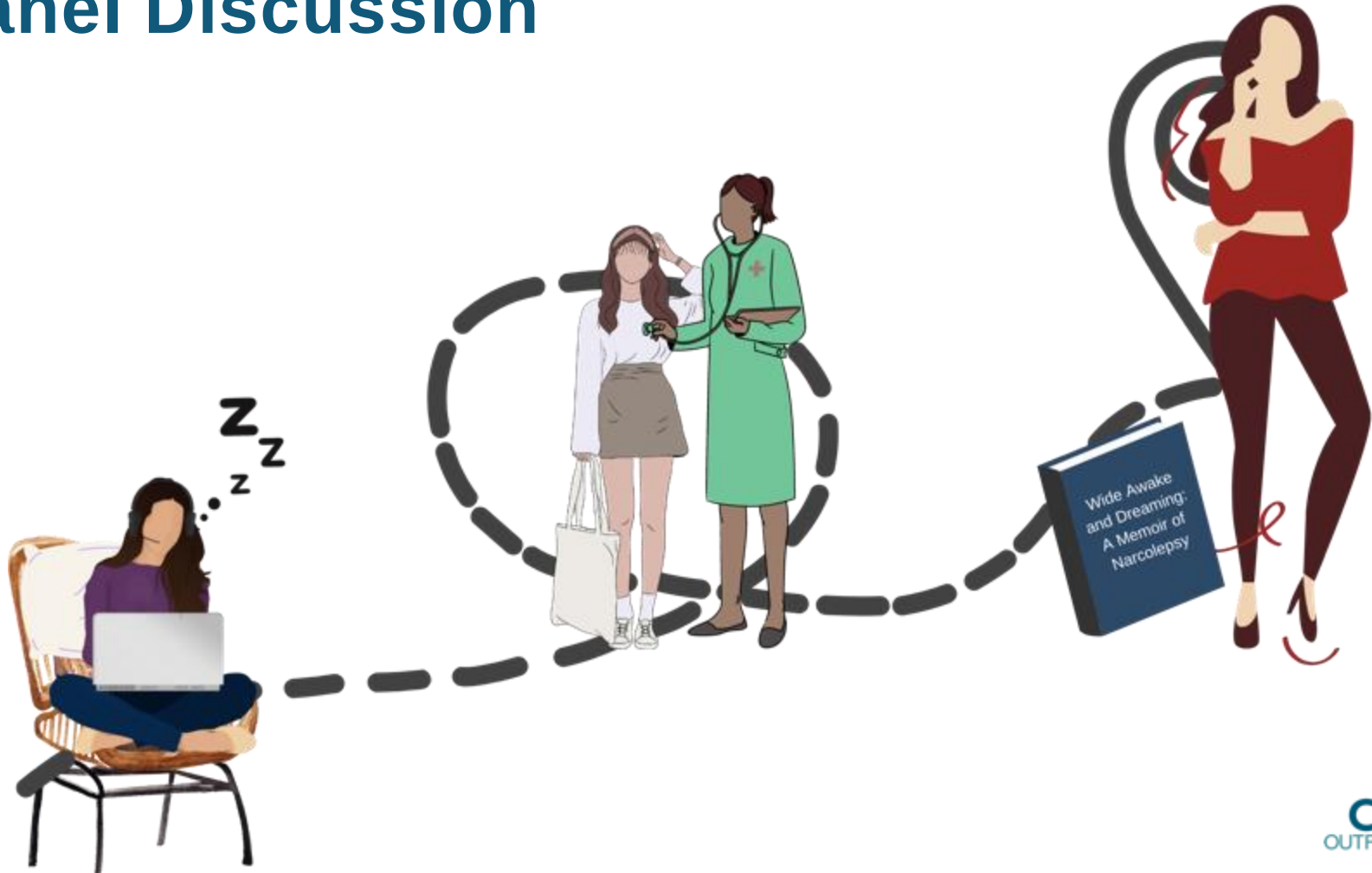
Audience Response



Now, how often will you assess treatment efficacy on functional status and QoL in your patients with narcolepsy?

- A. 0% of the time
- B. 1% - 25% of the time
- C. 26% - 50% of the time
- D. 51% - 75% of the time
- E. 76% - 100% of the time

Panel Discussion



**Integrate strategies to
mitigate CV risk
associated with
narcolepsy in treatment
decision-making.**

**LEARNING
OBJECTIVE**

3



Audience Response



How confident are you in your ability to reduce cardiovascular risks or mitigate cardiovascular burden when making treatment selections for your patients with narcolepsy?

- A. Not confident at all
- B. Somewhat confident
- C. Confident
- D. Extremely confident

Cardiovascular Impact of Narcolepsy



In patients with narcolepsy
vs. controls, higher risks of:

- ▶ Stroke¹: 2.5X
- ▶ Heart disease²: 2.1X
- ▶ Hypertension²: 1.3X
- ▶ Hypercholesterolemia²: 1.5X

In patients with narcolepsy*
(n = 12,816) vs. controls (n = 38,441)³:

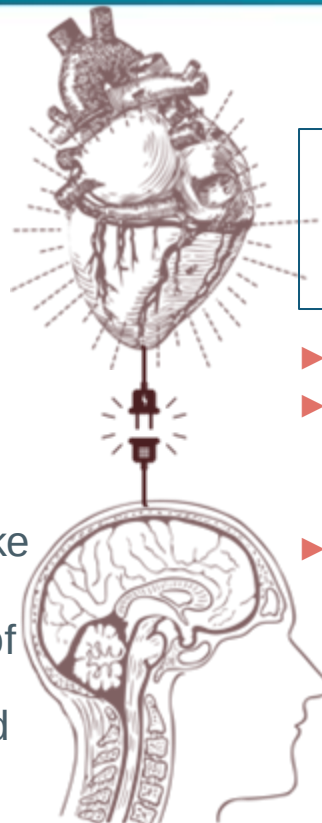
- | | |
|----------------------------|---|
| ▶ CVD without hypertension | ▶ Ischemic stroke |
| ▶ MACE | ▶ Edema |
| ▶ Heart failure | ▶ A composite of stroke, atrial fibrillation, and edema |
| ▶ Stroke | |

*per 1,000 person-years.

CVD = cardiovascular disease; MACE= major adverse cardiac event

1. Black J, et al. *Sleep Med.* 2017;33:13-18. 2. Ohayon MM. *Sleep Med.* 2013;14(6):488-492. 3. Ben-Joseph R, et al. *Neurology.* 2022;98(Suppl 18):1203.

4. Ohayon MM, et al. *Sleep.* 2014;37(3):439-444.



Mortality in narcolepsy (n = 77,616)
vs. non-narcolepsy controls
(n = 176,234,879)⁴:

- ▶ Incidence: 1.5X
- ▶ Sex differences:
 - ▶ Female, 0.99%
 - ▶ Male, 1.43%
- ▶ Higher rates stratified by age from 25-34 years to 75+ years

The Role of Orexin in Narcolepsy and CVD



- ▶ Roughly 90% of orexin-producing neurons are lost in human narcolepsy with cataplexy¹
- ▶ It's thought that an autoimmune process kills the orexin neurons¹
 - ▶ HLA linked to many autoimmune diseases; the strongest known HLA association is with narcolepsy
 - ▶ Carrying this gene increases narcolepsy risk ~200-fold
- ▶ Animal studies indicate orexin A and B and orexin receptors 1 and 2 present throughout the myocardium and centrally²
 - ▶ Increased cardiac dysfunction and myocardial scarring are associated with a deficiency in orexin 2 with narcolepsy phenotype³
- ▶ Endothelial dysfunction is induced by chronic sleep fragmentation²
 - ▶ Administering orexin decreases sleep fragmentation and severity of atherosclerosis
 - ▶ Sleep fragmentation causes orexin deficiency

HLA = human leukocyte antigens

1. Scammell TA. *N Engl J Med*. 2015;373(27):2654-2662. 2. Imperatore R, et al. *Clin Sci (Lond)*. 2019;133(7):853-857. 3. Perez MV, et al. *J Am Coll Cardiol*. 2015;66(22):2522-2533.

Narcolepsy and CVD: Take It With A Grain of Salt



- ▶ **Hypertension** is the **leading global risk factor** for disease and death¹
- ▶ One size does not fit all when it comes to recommending lower sodium diets, as methods used to assess sodium intake have been criticized for inaccuracy¹

Largest contributors to global DALYs^{1,2}

- ▶ High systolic blood pressure (212 million)
- ▶ Smoking (149 million)
- ▶ High fasting plasma glucose (143 million)
- ▶ High body mass index (120 million million)
- ▶ Childhood undernutrition (113 million)
- ▶ Alcohol use, high total cholesterol, and high sodium diets

DALYs = disability adjusted life years

1. Kjeldsen SE, et al. *Blood Pressure*. 2017;26(2):65-66. 2. GBD 2015 Risk Factors Collaborators. *Lancet*. 2016;388(10053):1659-1724.

Treatment Considerations for Patients With or At-Risk for CVD



- ▶ Improving nutrition
 - ▶ DASH diet
 - ▶ Diet lower in sodium
- ▶ Increasing physical activity
- ▶ Reducing or slowing down rise of BMI
- ▶ Anti-hypertensive agents



BMI = body mass index; DASH = Dietary Approaches to Stop Hypertension
Kjeldsen SE, et al. *Blood Pressure*. 2017;26(2):65-66.

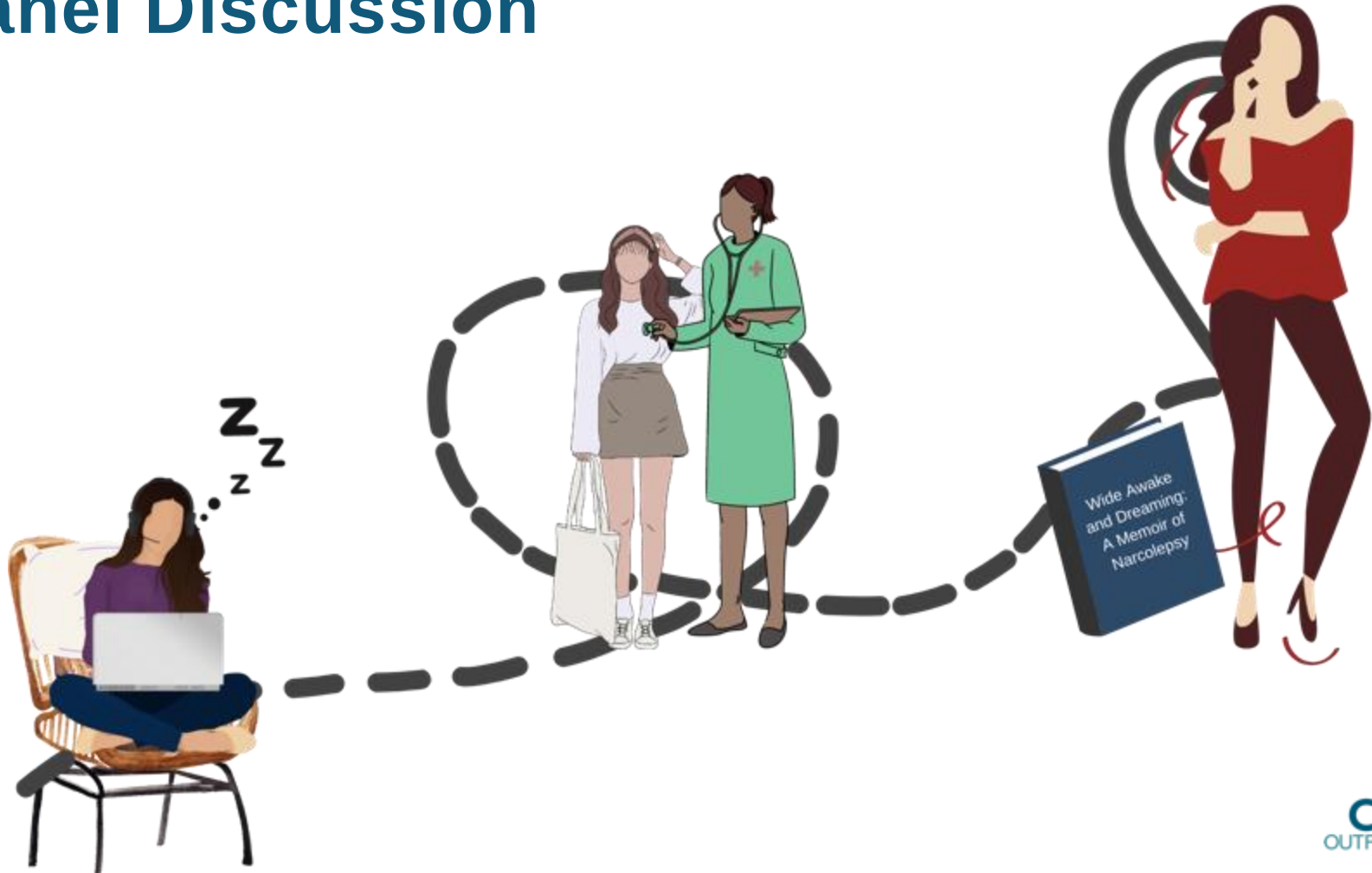
Audience Response



Now, how confident are you in your ability to reduce cardiovascular risks or mitigate cardiovascular burden when making treatment selections for your patients with narcolepsy?

- A.** Not confident at all
- B.** Somewhat confident
- C.** Confident
- D.** Extremely confident

Panel Discussion



Implement evidence-based strategies for the initiation and/or switching of therapies to improve and sustain patient QoL and psychosocial and work functioning.

LEARNING OBJECTIVE 4



Audience Response



How confident are you initiating treatment for narcolepsy in patients with medical and/or psychiatric comorbidities?

- A. Not confident at all
- B. Somewhat confident
- C. Confident
- D. Extremely confident

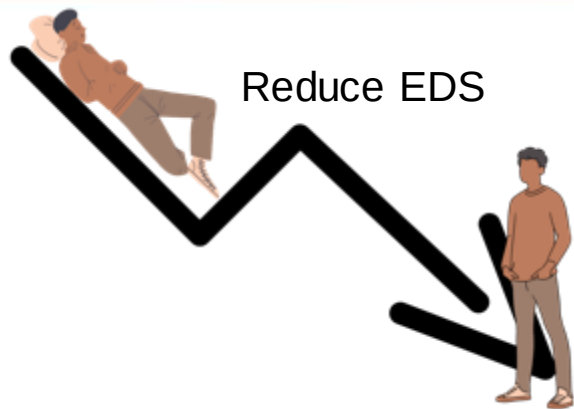
Audience Response



How confident are you switching medications (e.g., from a stimulant to a non-stimulant) for patients with narcolepsy experiencing persistent symptoms with initial therapy?

- A. Not confident at all
- B. Somewhat confident
- C. Confident
- D. Extremely confident

Treatment Goals in Narcolepsy



Reduce EDS

Optimize risk/benefit of
pharmacotherapies



Control nightmares
and hallucinations,
sleep paralysis, and DNS



Improve psychosocial
dysfunction and quality of life

Improve safety of patient
and public



Control cataplexy

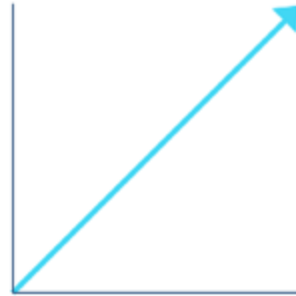


Realistic Goals for Realistic Outcomes



- ▶ What should the patient expect?
- ▶ What should the clinician expect?

Feeling “better” with a chronic condition

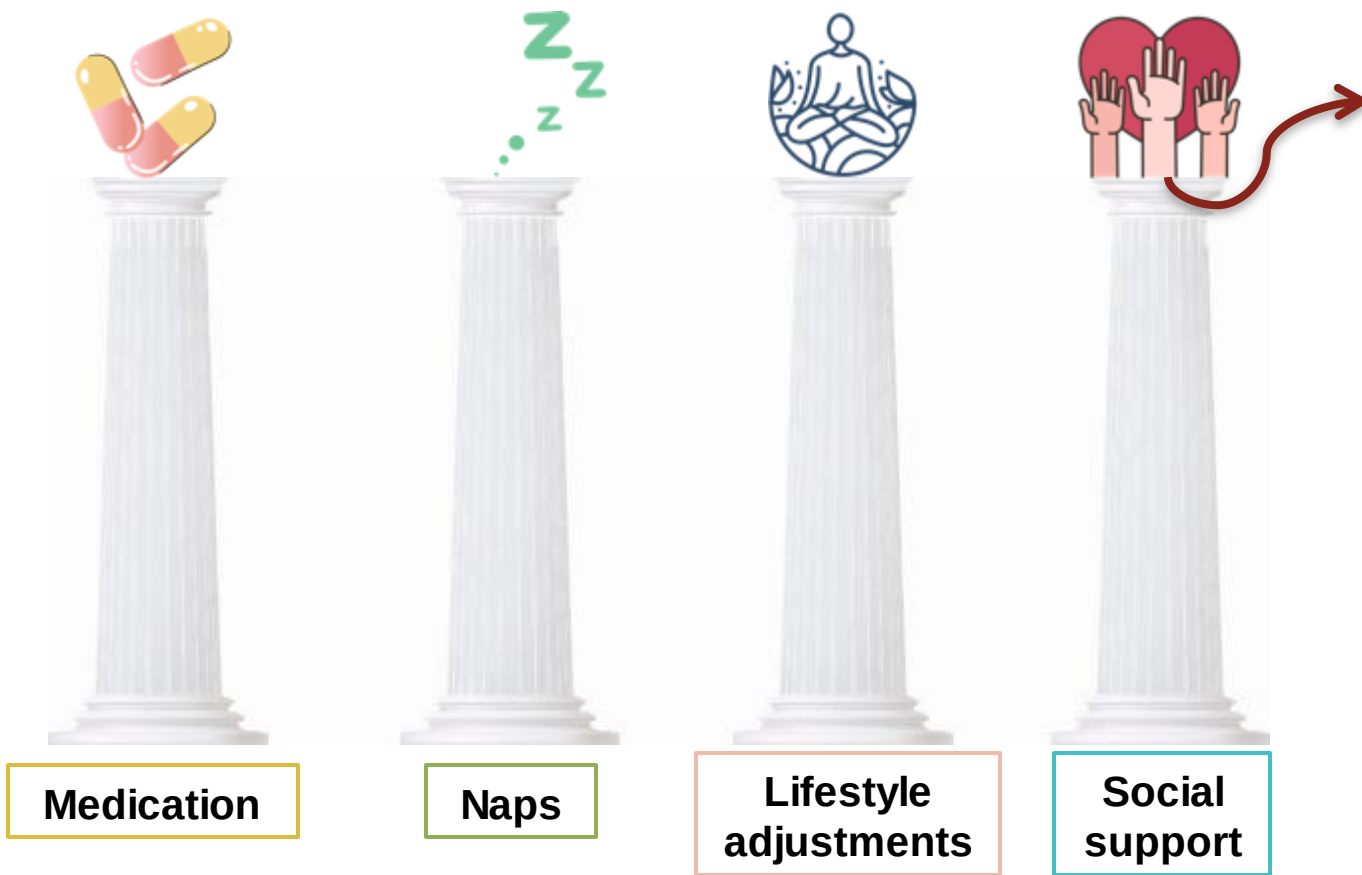


What people
think it looks like



What it actually
looks like

Narcolepsy: The Four Pillars of Treatment



Patient advocacy organizations



Strategies to Empower Patients



- ▶ Utilizing updates on the safety, efficacy, and tolerability of current therapies to personalize treatment selection^{1,2}
- ▶ Shared Decision Making^{1,2}
 - ▶ Several medications may be needed to control symptoms
 - ▶ Collaborate with the patient to establish goals, create a plan, routinely assess progress, and adjust the patient's regimen as needed
- ▶ Collaborate with the patient to determine:
 - ▶ Cataplexy triggers
 - ▶ Limitations
 - ▶ A management plan for narcolepsy and other illnesses



Encourage Questions



Am I receiving
the correct dose?



Is this medication
a good match?

In addition to medication, what else
can I do to help my symptoms?



What do I
tell my doctor?



If I experience side effects,
what should I do?

Personalizing Treatment Selection and Monitoring Patients with Narcolepsy



- ▶ Patient's needs and preferences
- ▶ Severity of EDS
- ▶ Comorbidities
- ▶ Cardiovascular risk
- ▶ Polypharmacy, including use of oral contraceptives
- ▶ Strategies for dose initiation, and modification, and cross-titration
- ▶ Adherence
- ▶ Carryover effects
- ▶ Use and interpretation of measures of patient-reported outcomes to monitor treatment efficacy



FDA-Approved* Treatments for Narcolepsy



Drug	MOA	Dose	EDS	Cataplexy	Adults	Children
Modafinil	Dopamine (DA) reuptake inhibitor	100-400 mg	X		X	
Armodafinil	DA reuptake inhibitor	50-250 mg	X		X	
Solriamfetol	DA-norepinephrine (NE) reuptake inhibitor	75-150 mg	X		X	
Pitolisant	Histamine H3 antagonist/inverse agonist	8.9-35.6 mg	X	X	X	
Sodium oxybate (SXB) / lower sodium oxybate (LXB)	GABA _B agonist	4.5-9.0 g (twice-nightly dosing)	X	X	X	X
Amphetamines / Methylphenidate	Sympathomimetic; enhance DA, NE, serotonin	Varies			X	X

* LXB is approved for narcolepsy, but it does not appear in the updated guidelines. Amphetamines and methylphenidate are approved for narcolepsy but not specifically cataplexy or EDS.

Barateau L, et al. *Ther Adv Neurol Disord*. 2019;12:1756286419875622.

Safety Considerations for FDA-Approved Treatments for EDS and Cataplexy in Narcolepsy

Drug	Schedule	Common AEs (≥ 5%) and Safety Considerations	
Modafinil / Armodafinil	IV	AEs	Anxiety, back pain, diarrhea, dizziness, dyspepsia, headache, insomnia, and nausea
		SCs	May reduce effectiveness of HC agents; may ↑ HR and diastolic and systolic BP
Solriamfetol	IV	AEs	Anxiety, decreased appetite, headache, insomnia, and nausea
		SCs	Precautions regarding BP and HR ↑; no effect on birth control
Pitolisant	—	AEs	Anxiety, insomnia, and nausea
		SCs	May ↓ effectiveness of HCs; may ↑ QTc; not a controlled substance
SXB / LXB	III	AEs	Adults: Anxiety, decreased appetite, diarrhea, dizziness, headache, hyperhidrosis, parasomnia, and vomiting; Peds: ↓ appetite, dizziness, enuresis, headache, vomiting, and weight decrease
		SCs	High sodium formulation may be contraindicated in patients at risk for CVD events; LXB formulation may be ideal in those with CVD risks; common, early onset AEs are generally of short duration and ↓ over time
Amphetamines / Methylphenidate	II	AEs	Dry mouth, upset stomach, loss of appetite, weight loss, headache, dizziness, tremors, tachycardia, elevated BP, insomnia, and mood changes
		SCs	High potential for misuse; serious cardiovascular events

↓ = decrease; ↑ = increase; AEs = adverse events; BP = blood pressure; HC = hormonal contraceptives; HR = heart rate; QTc = QT interval; SCs = safety considerations

Drugs@FDA Website. Meskill GJ, et al. *Sleep*. 2020;43(Suppl 1):A291. Setnik B, et al. *Sleep*. 2020;43(4):zs2252. Husain AM, et al. *J Clin Sleep Med*. 2020;16(9):1469-1474. Dauvilliers Y, et al. *Sleep*. 2020;43:A286.

Solriamfetol: Efficacy in Narcolepsy



- ▶ TONES trials demonstrated efficacy in reducing propensity to sleep and maintaining wakefulness (compared to PBO)
 - ▶ Significant improvements in MWT sleep latencies
 - ▶ Significant reductions in ESS
 - ▶ Significantly greater improvements in patient's and clinician's global impression of change
- ▶ Effective in treating EDS in patients with narcolepsy regardless of cataplexy status
- ▶ Long-term treatment associated with sustained improvements in functional status, work productivity, and QoL
- ▶ Common early onset TEAEs are limited in duration

PBO = single-blind placebo; QoL = quality of life; TEAEs = treatment-emergent adverse events; TONES = treatment of OSA and narcolepsy excessive sleepiness

Rosenberg R, et al. *J Clin Sleep Med*. 2022;18(1):235-244. Abad VC. *Nat Sci Sleep*. 2021;13:75–91. Dauvilliers Y, et al. *CNS Drugs*. 2020;34:773-784. Weaver TE, et al. *J Clin Sleep Med*. 2021;17(10):1995–2007.

Pitolisant: Efficacy in Narcolepsy



- ▶ HARMONY trials demonstrated robust therapeutic effects in EDS and cataplexy attacks (vs PBO)
 - ▶ Significant reductions in ESS scores
 - ▶ Significant $\geq 50\%$ in weekly cataplexy attacks
 - ▶ Initial treatment response within 2-3 weeks of starting treatment
- ▶ In patients with high EDS burden, significant reductions in EDS and cataplexy observed

Sodium Oxybate: Efficacy in Narcolepsy



- ▶ Comparable efficacy of SXB for EDS and cataplexy shown in pediatric and adult populations
- ▶ LXB later $t_{\max}$, and a lower $C_{\max}$, but a similar AUC compared with SXB
 - ▶ Pharmacokinetic properties similar in adults and children with narcolepsy
- ▶ In pediatrics:
 - ▶ In double-blind, PBO-controlled, randomized withdrawal study, participants assigned to PBO and withdrawn from SXB had significant worsening of cataplexy and EDS compared to those continuing SXB

AUC = area under the curve

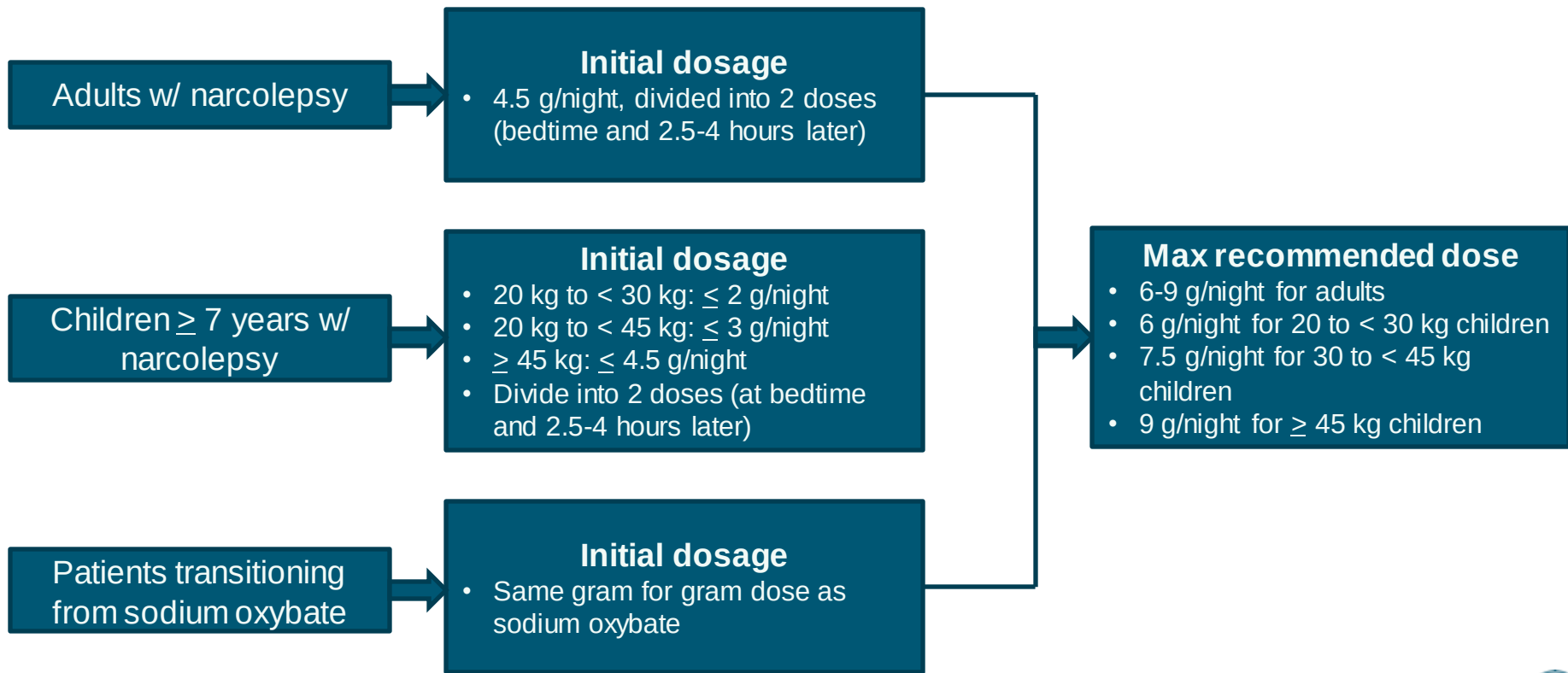
Chen C, et al. *Clin Transl Sci*. 2021;14(6):2278–2287. Chen C, et al. *Clin Transl Sci*. 2020;13(5):932–940. Plazzi G, et al. *Lancet Child Adolesc Health*. 2018;2(7):483–494. Dauvilliers Y, et al. *Nat Sci Sleep*. 2022;14:531–546.

Lower-Sodium Oxybate: Efficacy



- ▶ In double-blind randomized withdrawal study, cataplexy attacks and EDS worsened significantly in PBO group but remained stable in those who continued LXB
 - ▶ Significant reductions in ESS scores in LXB group vs PBO
 - ▶ Significant reductions in frequency of cataplexy attacks and increase of cataplexy-free days in LXB group vs PBO
 - ▶ Significant worsening of Patient Global Impression of Change, Clinical Global Impression of Change, and QoL measures in PBO group vs LXB group
- ▶ Reduction in cataplexy and increased cataplexy-free days observed during initiation/optimization of LXB and taper/discontinuation of prior antidepressants/anticataplectics

Dosing Regimens for LXB in Narcolepsy



When Initial Treatment Fails...



- ▶ Reasons for treatment modification:
 - ▶ Suboptimal efficacy
 - ▶ Coexisting medical and/or psychiatric comorbidities
 - ▶ Insurance costs
- ▶ Strategies to modify treatment
 - ▶ Dose titration
 - ▶ Direct switch
 - ▶ Adjunctive
 - ▶ Taper and switch
 - ▶ Cross-taper



Audience Response



Now, how confident are you initiating treatment for narcolepsy in patients with medical and/or psychiatric comorbidities?

- A. Not confident at all
- B. Somewhat confident
- C. Confident
- D. Extremely confident

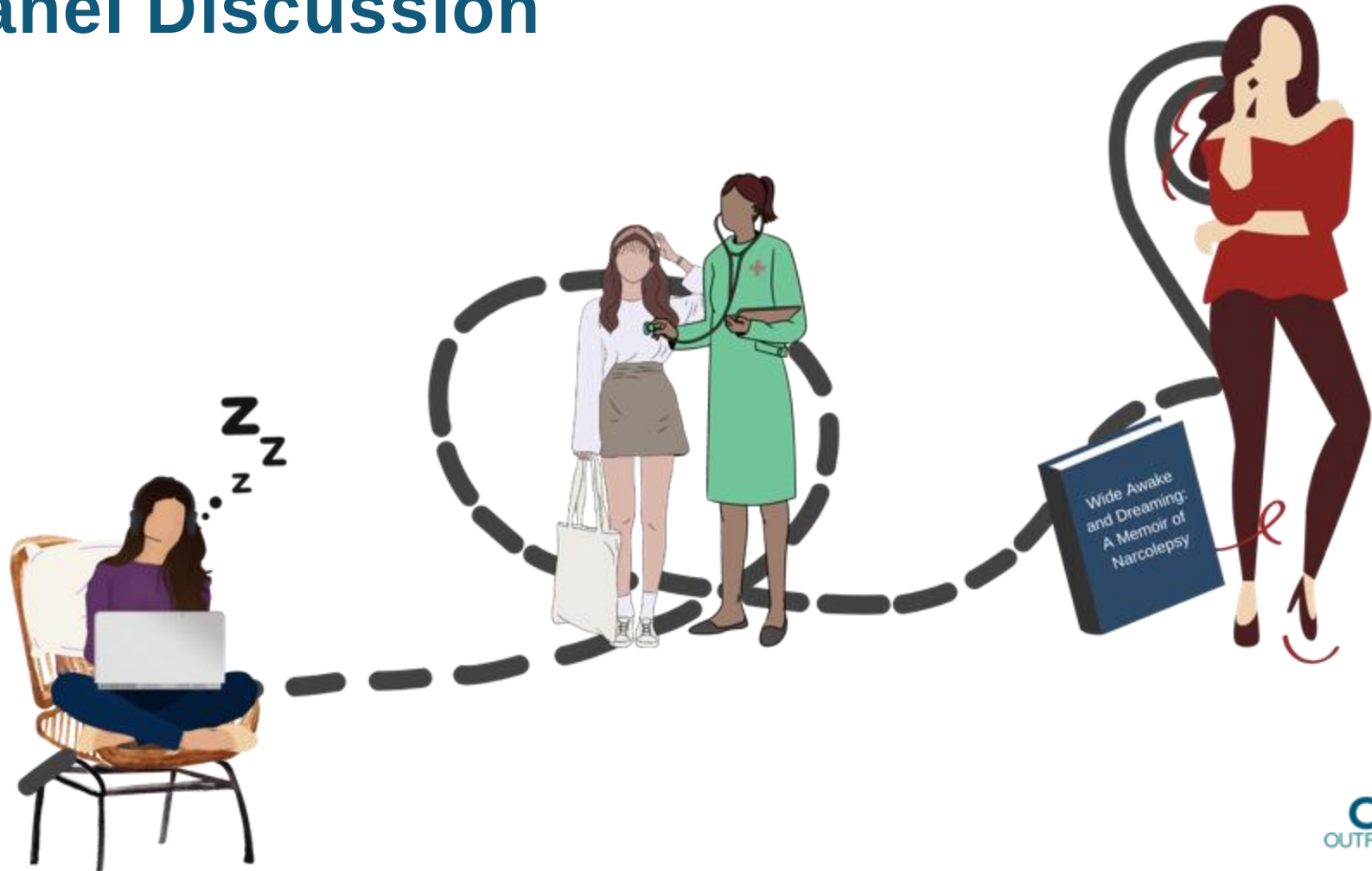
Audience Response



Now, how confident are you switching medications (e.g., from a stimulant to a non-stimulant) for patients with narcolepsy experiencing persistent symptoms with initial therapy?

- A.** Not confident at all
- B.** Somewhat confident
- C.** Confident
- D.** Extremely confident

Panel Discussion



SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- ▶ At each visit, actively engage patients to share their lived experience with narcolepsy and the impact of treatment on their psychosocial functioning and QoL
- ▶ Use evidence-based tools and diagnostic criteria to improve the detection and accurate diagnosis of narcolepsy in children and adults
- ▶ Take a patient-centric approach to the management of narcolepsy
- ▶ Implement best practices to mitigate CV risks initiating treatment for narcolepsy, monitoring for treatment effectiveness, and switching when initial therapy fails



QUESTIONS ANSWERS &

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