

HMP Education

# Practical Strategies for Navigating Psychiatric Complexities in Sleep Medicine



# Faculty

**Craig Chepke, MD, DFAPA**

Medical Director, Excel  
Psychiatric Associates

**Emmanuel Mignot, MD, PhD**

Craig Reynolds Professor of  
Sleep Medicine, Stanford  
University

**Philip Gehrman, PhD, CBSM, FAASM**

Professor of Psychology, University of  
Pennsylvania School of Medicine

# Faculty Disclosures

- **Craig Chepke, MD, DFAPA:** Advisory Board - AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Compass Pathways, Corium, Eli Lilly, Idorsia, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Takeda, Teva; Consultant - AbbVie, Acadia, Alkermes, Axsome, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Cingulate, Corium, Eli Lilly, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, MedinCell, Moderna, Neurocrine, Otsuka, Sage, Sumitomo, Supernus, Teva; Research Grant/Support - Acadia, Axsome, Harmony, Neurocrine, Teva; Speaker's Bureau - AbbVie, Acadia, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular, Jazz, Johnson & Johnson, Lundbeck, Luye, Merck, Neurocrine, Otsuka, Sumitomo, Takeda, Teva
- **Philip Gehrman, PhD, CBSM, FAASM:** Consultant - Vanda Pharmaceuticals; Grant/Research Support - Jazz Pharma, Merck & Co., Inc. (Terminated)
- **Emmanuel Mignot, MD, PhD: Advisory Board** – Centessa, Jazz, Takeda; Grant/Research Support – Alkermes, Avadel, Beacon, Eisai, Harmony, Idorsia, Jazz, Sunovion, Takeda, Vanda



# Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.
- This activity has been independently reviewed for balance.
- This CME activity includes brand names for participant clarity purposes only. No product promotion or recommendation should be inferred.

# Learning Objectives

- Describe the prevalence and clinical significance of psychiatric disorders in sleep medicine practice, including their bidirectional relationships with SWDs
- Review validated screening tools and interviewing skills to detect psychiatric disorders in sleep medicine practice
- Develop integrated sleep and psychiatric treatment plans for patients with co-occurring psychiatric disorders in sleep medicine practice

# Program Information

- This program is provided by HMP Education, an HMP Global Company
- Held in partnership with:  **Psych Congress**  Sleep Research Society Foundation
- Supported by educational grants from Alkermes, Inc. and Axsome Therapeutics, Inc.



# Polling

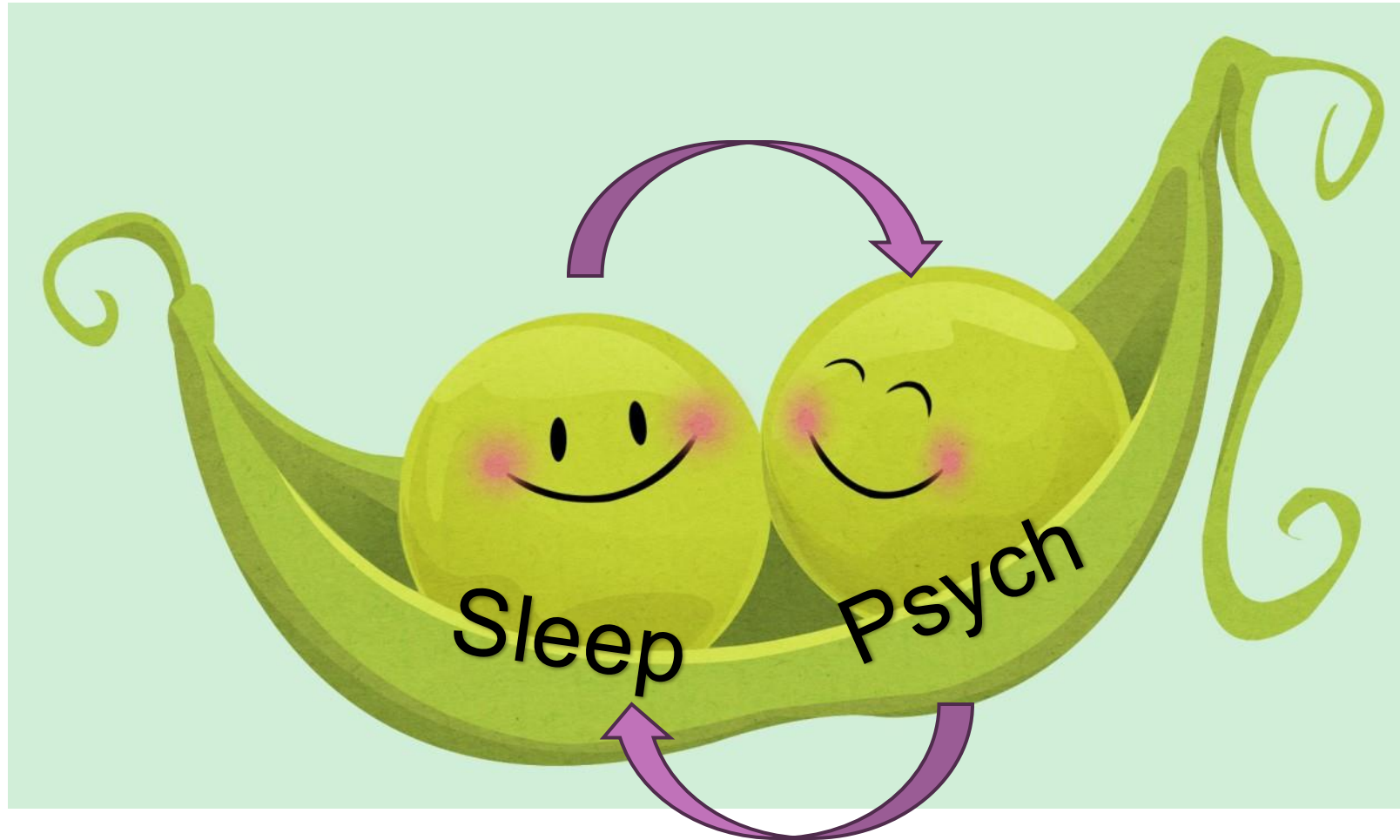
- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response.



The winner will be announced at the conclusion of the Q&A. Winner must be present to claim their prize.

# Understanding the Connections Between Psychiatric Disorders and SWDs

# Sleep Medicine and Psychiatry: Two Peas in A Pod



# Sleep Problems Are Common Across Psychiatric Diagnoses

Diagnosis	DSM-IV-TR criteria
Separation anxiety disorder	Persistent reluctance or refusal to go to sleep without being near a major attachment figure or to sleep away from home* Repeated nightmares involving the theme of separation**
Alcohol withdrawal	Insomnia**
Amphetamine withdrawal	Insomnia or hypersomnia**
Caffeine intoxication	Insomnia**
Cocaine withdrawal	Insomnia or hypersomnia**
Nicotine withdrawal	Insomnia**
Opioid withdrawal	Insomnia**
Sedative, hypnotic, or anxiolytic withdrawal	Insomnia**
Major depressive disorder	Insomnia or hypersomnia nearly every day**
Dysthymic disorder	Insomnia or hypersomnia**
Bipolar disorder	Manic or hypomanic episode = decreased need for sleep** Depressive episode = insomnia or hypersomnia**
Posttraumatic stress disorder	Recurrent distressing dreams of the event** Difficulty falling or staying asleep**
Acute stress disorder	Reexperiencing of the traumatic event in dreams** Difficulty sleeping**
Generalized anxiety disorder	Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)**

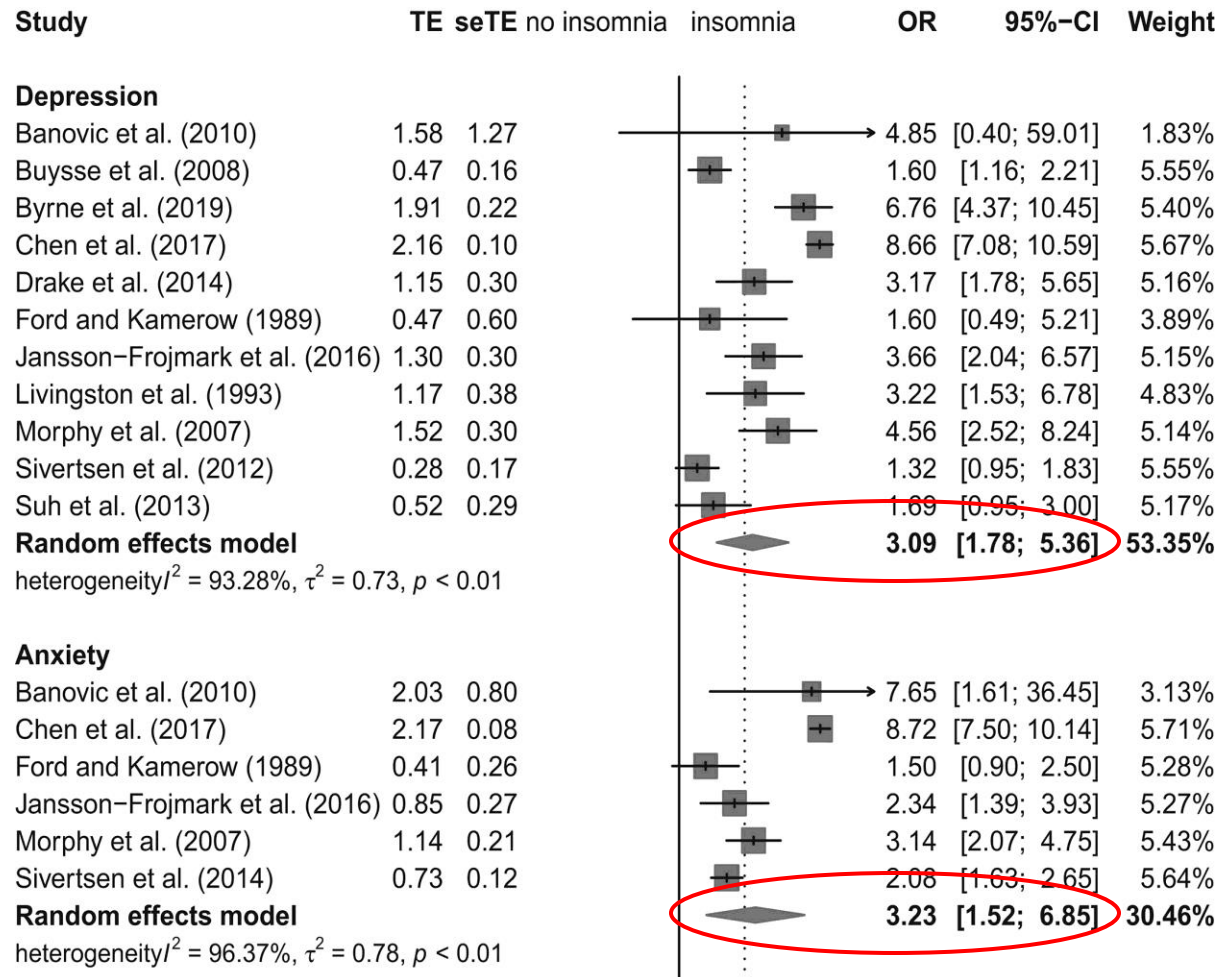
# Psychiatric Problems Are Common Across Sleep/Wake Disorders

Table 1  
Observed associations between selected psychiatric disorders and sleep disorders

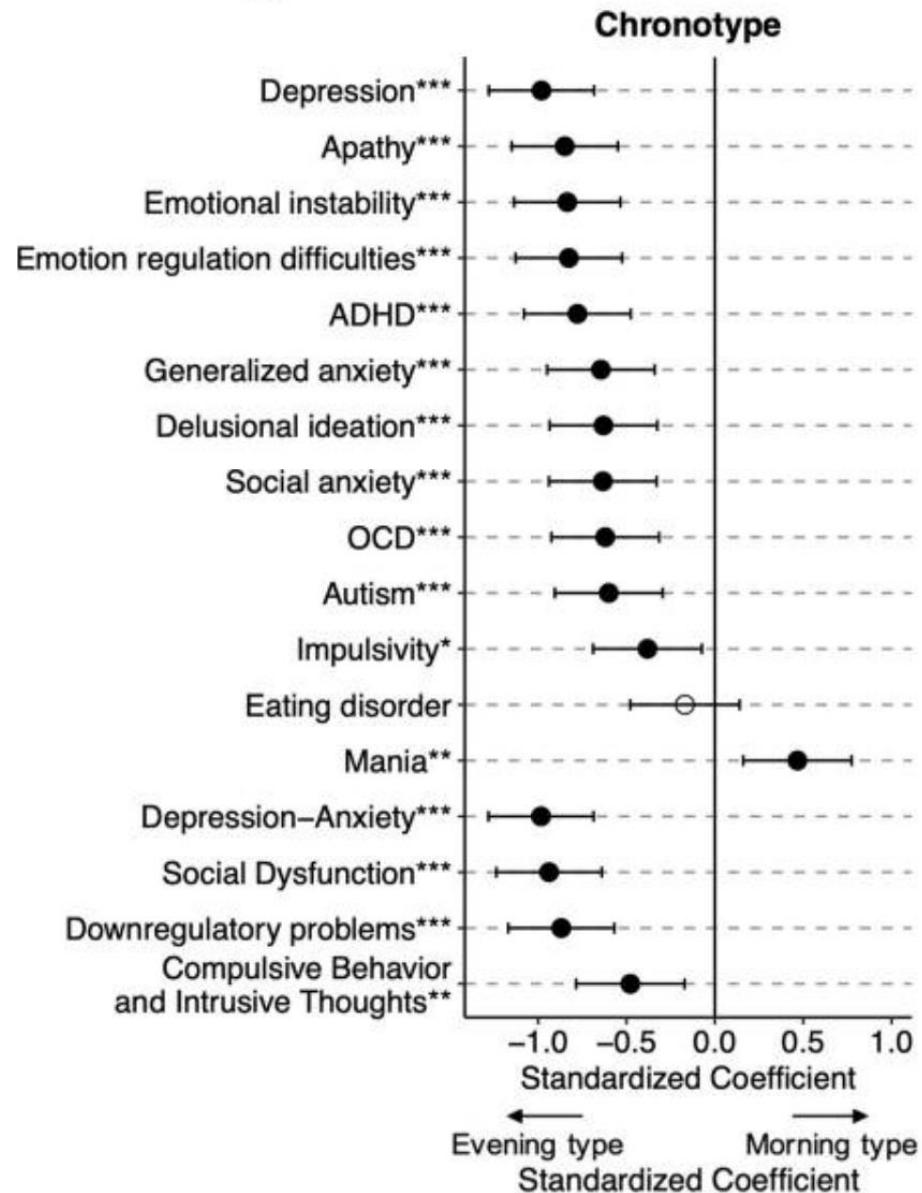
	Insomnia or Nonspecific Disrupted Sleep	Circadian Rhythm Disorder	Restless Leg Syndrome	Obstructive Sleep Apnea	Narcolepsy	Sleep Paralysis	Sleepwalking
Depressive disorders	A <sup>4</sup> B <sup>5</sup> S <sup>6</sup>	A <sup>7</sup>	A <sup>8</sup> B <sup>9</sup> PM <sup>25</sup>	A <sup>10,11</sup> M	A <sup>12</sup> S <sup>12</sup>	A <sup>13</sup>	A <sup>14</sup> PM <sup>14</sup>
Anxiety disorders	A <sup>4,15-17</sup> P <sup>4</sup> M	A (for OCD) <sup>16,18</sup>	M	A <sup>10</sup>	A <sup>12</sup>	A <sup>19,20</sup>	A (for OCD) <sup>14</sup> PM <sup>14</sup>
Posttraumatic stress disorder	A <sup>21</sup> B <sup>22</sup>				A <sup>12</sup>	A <sup>23</sup>	
Schizophrenia	A <sup>24</sup>	A <sup>24</sup>	PM <sup>25,26</sup>	PM <sup>27</sup>	S <sup>28</sup> M <sup>29</sup>		PM <sup>30</sup>
Suicidality	A <sup>31-33</sup>						
Attention-deficit/hyperactivity disorder	PM	A <sup>34</sup>	A <sup>35</sup>	A in children <sup>36</sup> Not adults <sup>37</sup>			
Impulse control disorders			SM <sup>38</sup>				

*Abbreviations:* A, association observed; B, bidirectional association observed; M, sleep condition can mimic psychiatric condition; OCD, obsessive-compulsive disorder; P, psychiatric condition precedes sleep condition; PM, psychiatric medication causes or worsens sleep condition; S, sleep condition precedes psychiatric condition; SM, sleep medication causes or worsens psychiatric condition.

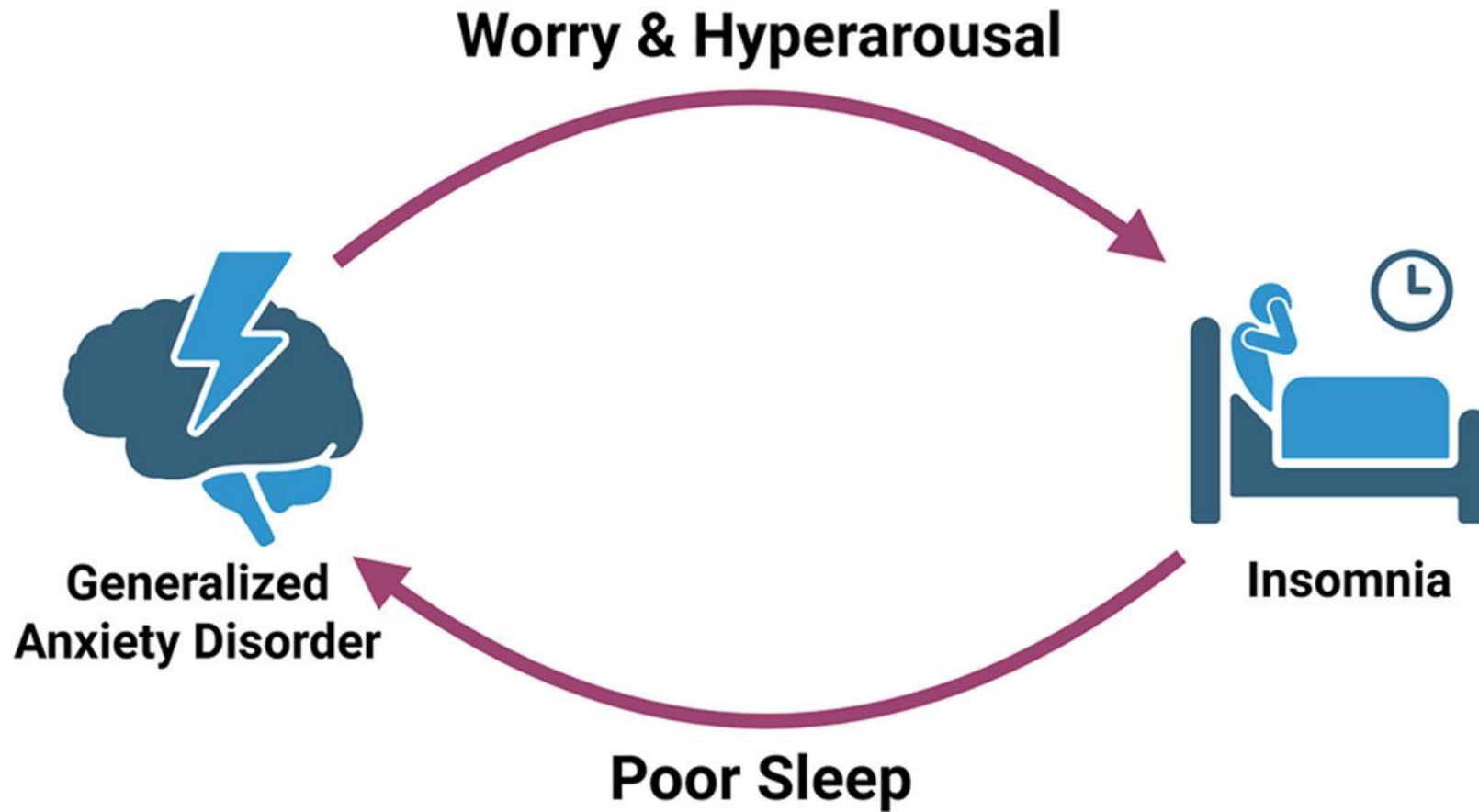
# Sleep Problems Are Not Just Symptoms of Mental Health Disorders



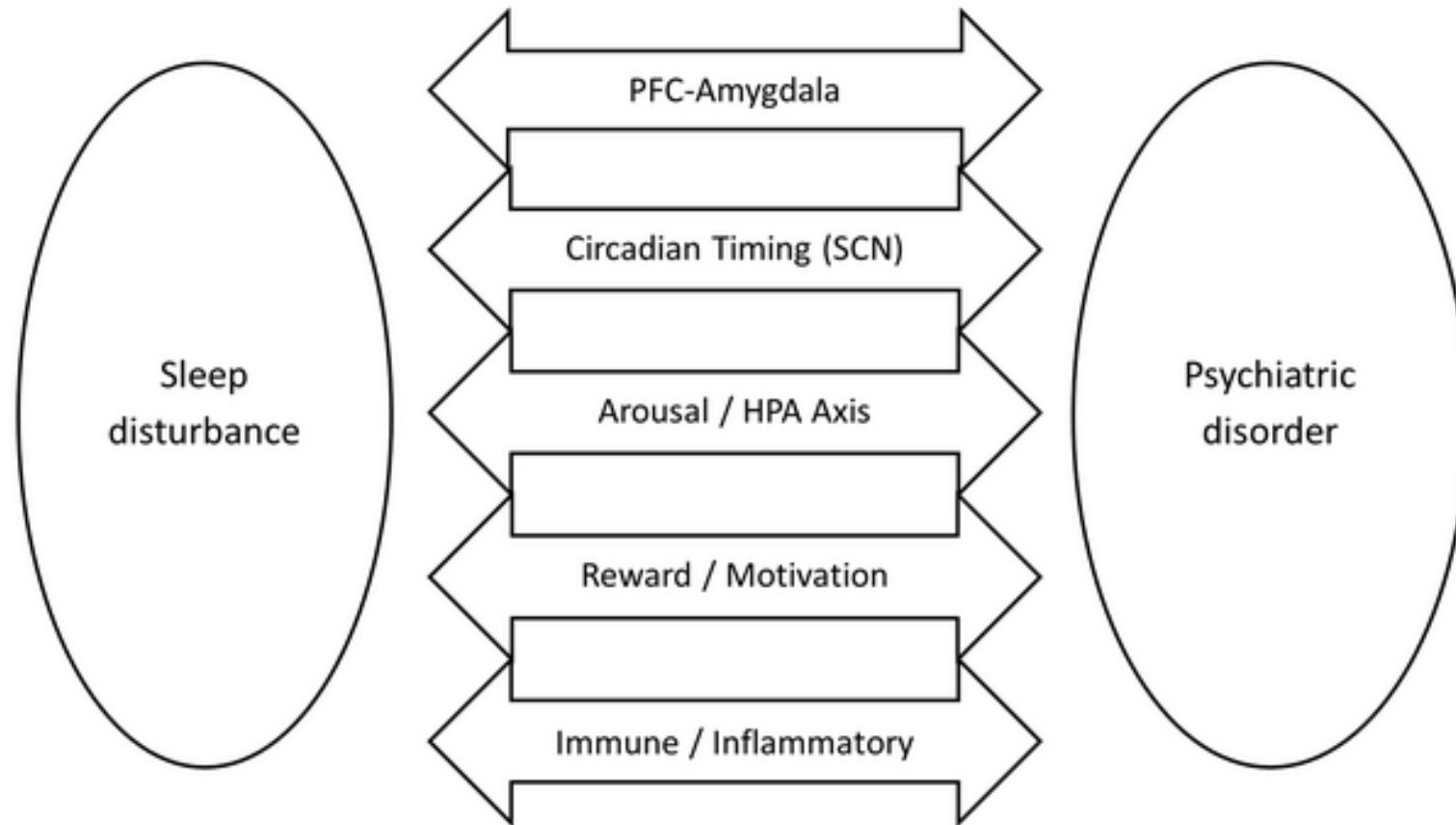
# Delayed Circadian Rhythms Are Associated With Poorer Mental Health



# Relationships Are Bidirectional

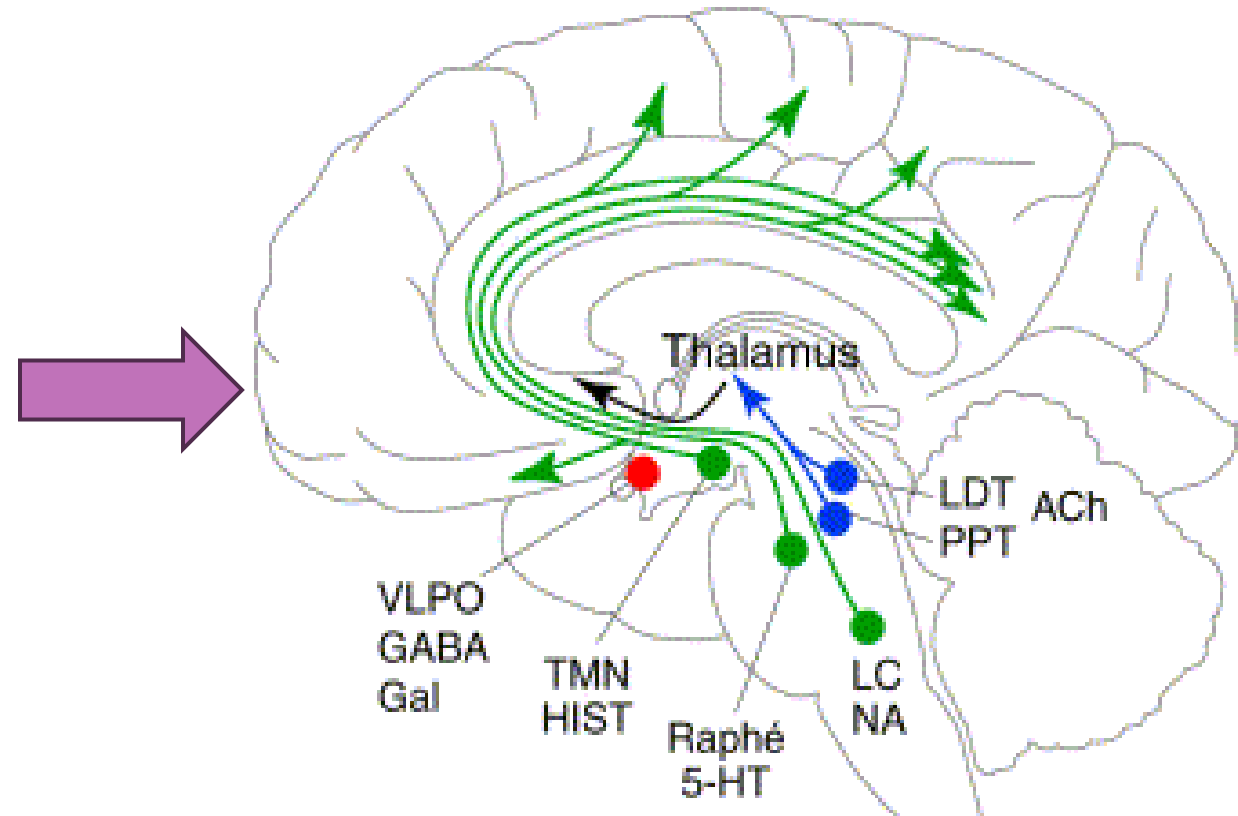


# Sleep Disturbances And Psychiatric Disorders Have Shared Biology



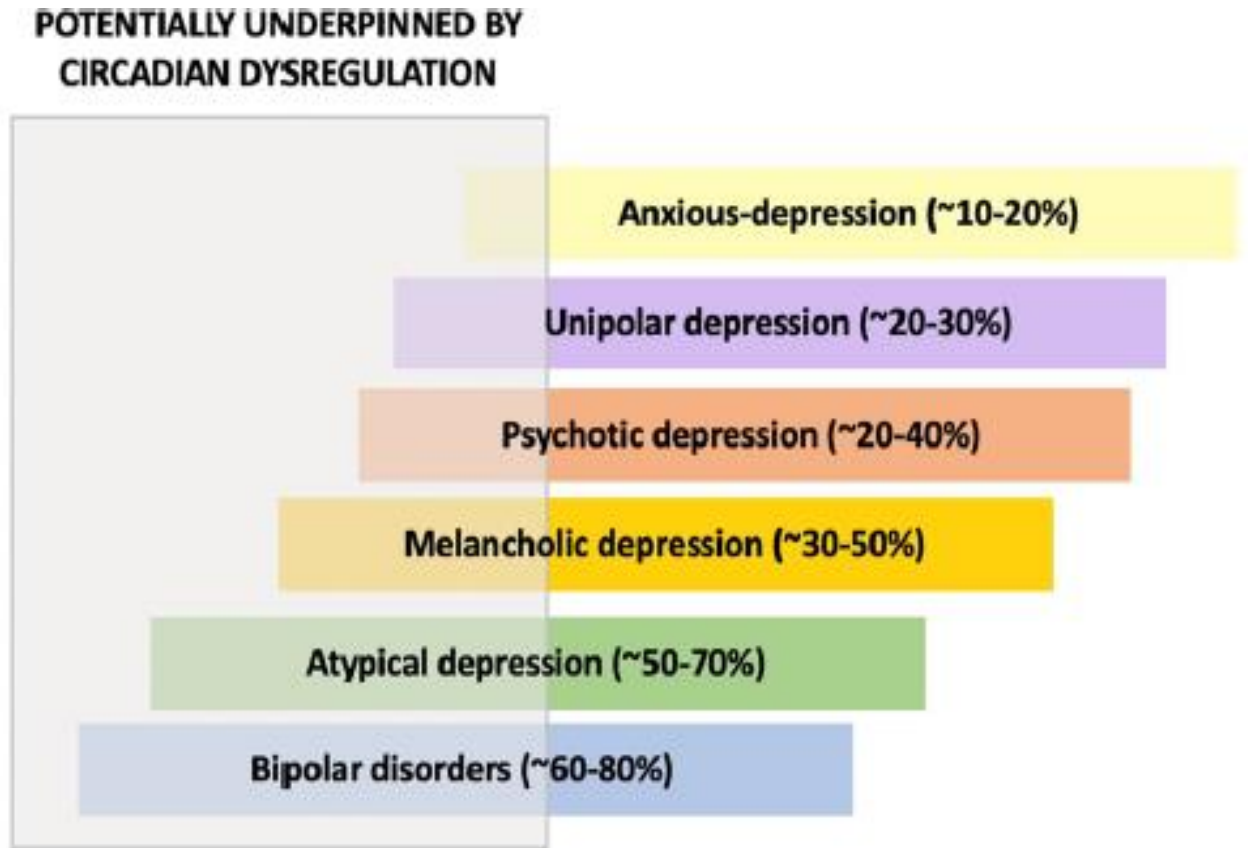
# Psychotropics And Sleep/Wake Regulation

Common  
Targets of  
psychotropic  
medications



# The Case of Bipolar Disorder...

- Significant circadian disruption
  - Blunted amplitude of rhythms
  - Phase advance or delay of rhythms
  - Late chronotype is a risk factor
  - Enhanced light sensitivity?



# Circadian Clock Genes Are Linked to Bipolar Disorder

**>50 studies**

show associations  
between clock genes  
and mood disorders

- In GWAS of Bipolar, BMAL1 (ARNTL) was among the genome-wide significant hits
- Strong genetic correlation between chronotype and Bipolar
- Mice with a mutation in the clock gene (*Clock* $\Delta$ ) have a mania-like behavioral pattern

GWAS = genome-wide association studies.

McClung CA. *Biol Psychiatry*. 2013;74(4):242-249; Stahl EA, et al. *Nat Genet*. 2019;51(5):793-803; Jones SE et al., *Nat Commun*. 2019;10(1):343; Roybal K, et al. *Proc Natl Acad Sci U S A*. 2007;104(15):6406-6411.

# Does Bipolar Disorder Reflect Circadian Dysregulation?

In cellular models, bipolar disorder is associated with:



## Longer circadian period

- Bipolar cellular models exhibit longer circadian cycles
- Lithium shortens circadian period and increases rhythm amplitude



## Enhanced light sensitivity

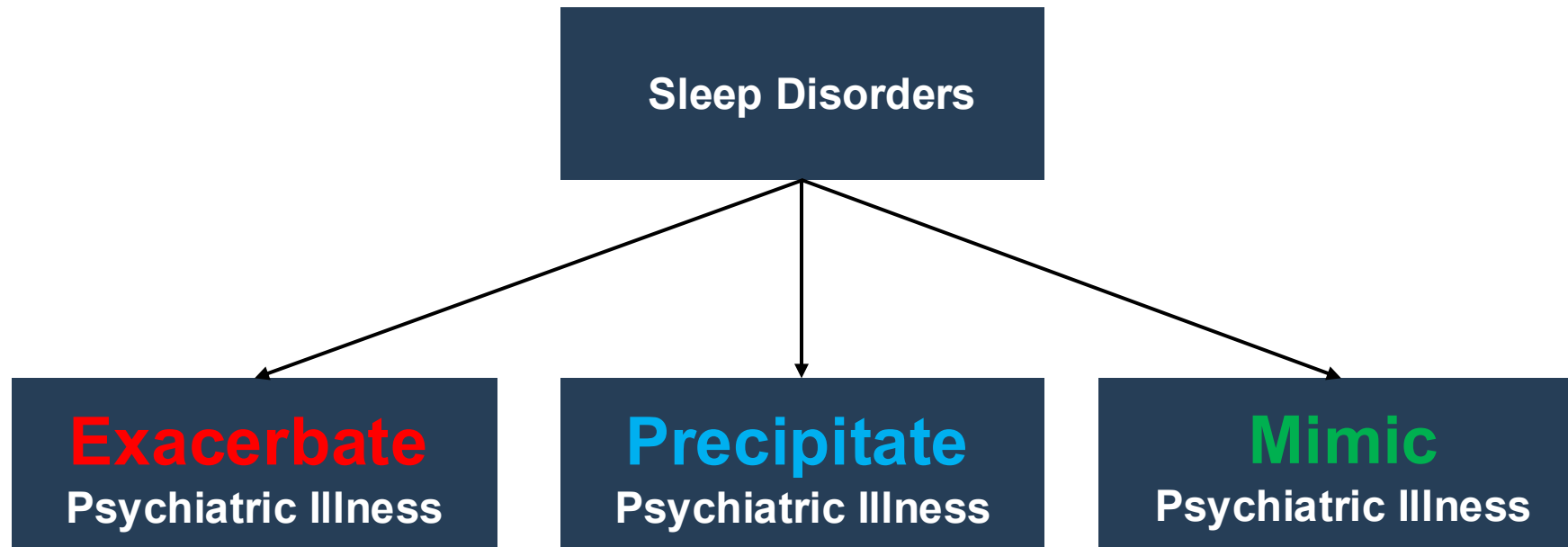
- Excessive light exposure may trigger mania
- Greater melatonin suppression after light exposure
- Increased PIPR suggests altered ipRGC responsiveness

PIPR = post-illumination pupil response; ipRGC = intrinsically photosensitive retinal ganglion cell.

Hastings MH, Goedert M. *Curr Opin Neurobiol.* 2013;23(5):880-887; McCarthy MJ, Welsh DK. *J Biol Rhythms.* 2012;27(5):339-352;

Roguski A, et al. *Br J Psychiatry.* 2024;224(5):143-146.

# Sleep and Psychiatric Disorders



# Psychiatric Stigma and Sleep Difficulties

*Under-recognition of psychiatric illness is common in sleep medicine*

**5-10%**

Board-certified sleep medicine physicians have a primary psychiatry background

**5x higher**

Depression prevalence in sleep center populations

**>40%**

Physicians treating insomnia endorse "treat psychiatry and sleep follows"

Patients and clinicians often misattribute sleep disorders to psychiatric causes, contributing to **under-referral to sleep specialists** and **under-recognition of depression**

# Barriers in Sleep Medicine



CBTi is  
unavailable  
and takes  
time



Under-  
recognition of  
psychiatric  
comorbidities  
in sleep  
clinics



General  
discomfort  
with  
psychiatric  
patients



Lack of training,  
clinician  
burnout and  
difficult patient  
encounters



Undertreatment  
due to the  
difficulties in  
coordinating  
cares



Time and  
reimbursement  
constraints



# Key Learning Points

- Sleep/wake disorders and psychiatric disorders frequently co-occur, share overlapping symptoms and biology, and often influence one another bidirectionally
  - i.e., insomnia approximately **doubles the risk** of developing depression and is also associated with increased risk of anxiety disorders, PTSD, and psychosis, independent of pre-existing psychiatric conditions
- Effective sleep medicine practice requires awareness of psychiatric comorbidities, circadian factors, medication effects, and barriers that contribute to under-recognition and undertreatment

# Recognizing Psychiatric Disorders in Sleep Medicine Practice

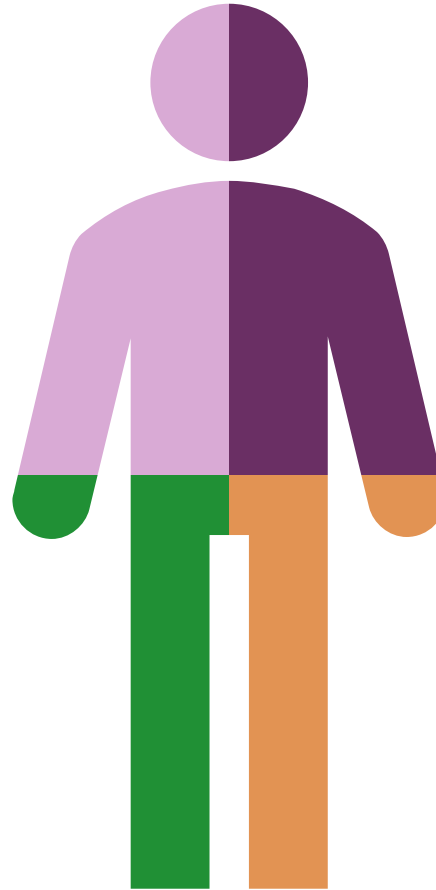
# Clinical Phenotypes of Sleepiness

## Narcolepsy Type 1 (orexin deficiency)

- Cataplexy: sudden episodes of muscle weakness with emotions, such as laughing
- Refreshing short naps
- REM sleep dissociated features; hallucinations, sleep paralysis
- Fragmented nighttime sleep
- Obesity or increased BMI
- PSG SOREMPs and MSLT SOREMPs

## Narcolepsy-type sleepiness (some orexin deficiency)

- No cataplexy
- Refreshing naps
- May have REM sleep dissociated features
- MSLT short SL +/-, SOREMPs (predicts orexin deficiency)
- Differential: insufficient sleep



## Periodic Hypersomnia (KLS)

- Teen or young adult
- Sudden episodes of 15-20 hrs of sleep lasting a few weeks (often hospitalized)
- When awake, cognitive abnormalities with feeling of derealization; mutism
- Disinhibition, infantile behavior, hyperphagia, hypersexuality
- Entirely reversible but reoccur randomly
- Spontaneously improves ~10 years after onset; disease “burns” out
- Related to bipolar (TRANK1 & circadian)

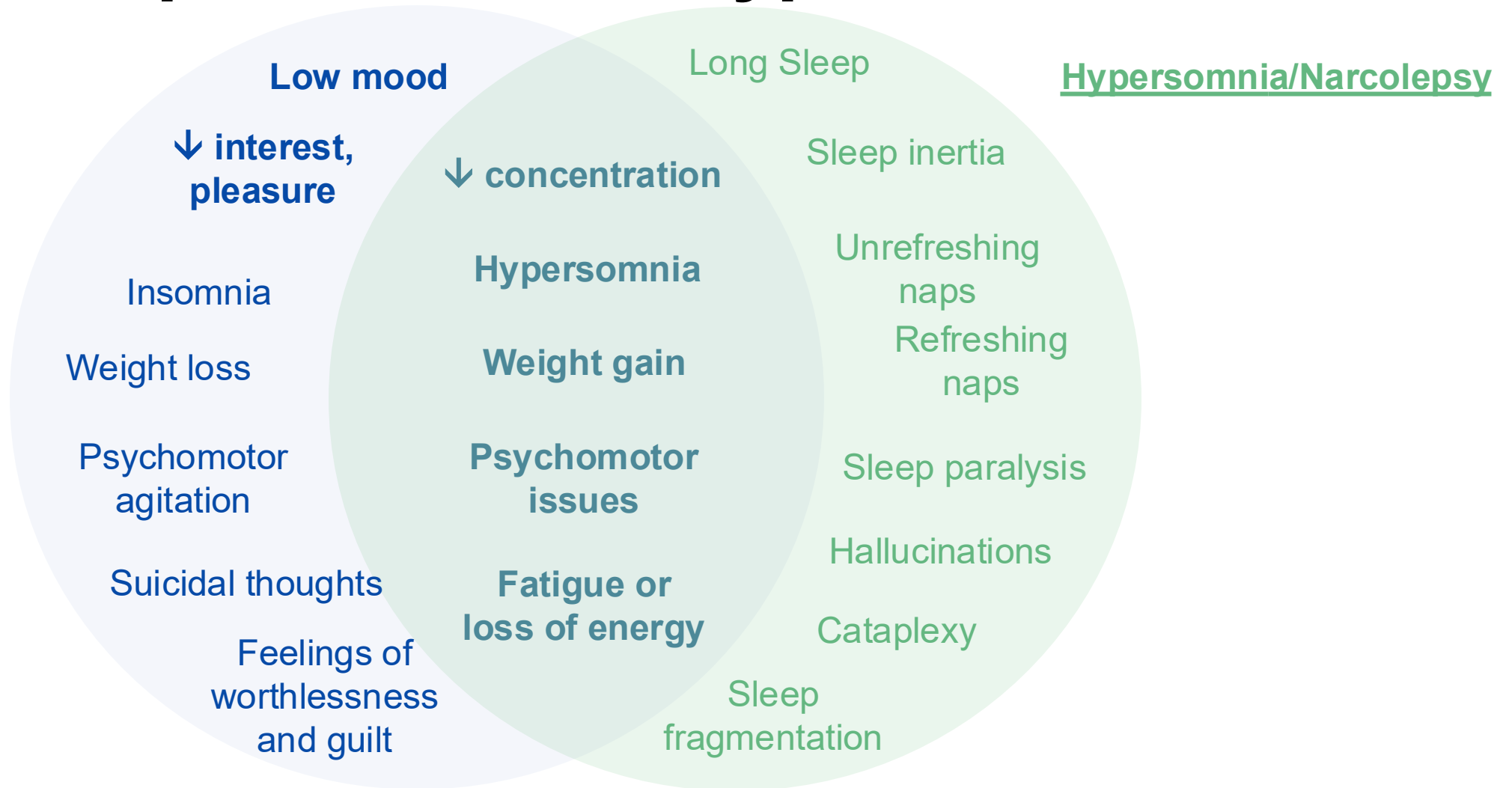
## Idiopathic Hypersomnia

- Long nocturnal sleep with sleep inertia .
- Long unrefreshing naps
- MSLT short SL +/-, SOREMPs +/-
- May have REM sleep dissociated features
- Differential: Depression, anxiety, psychiatric

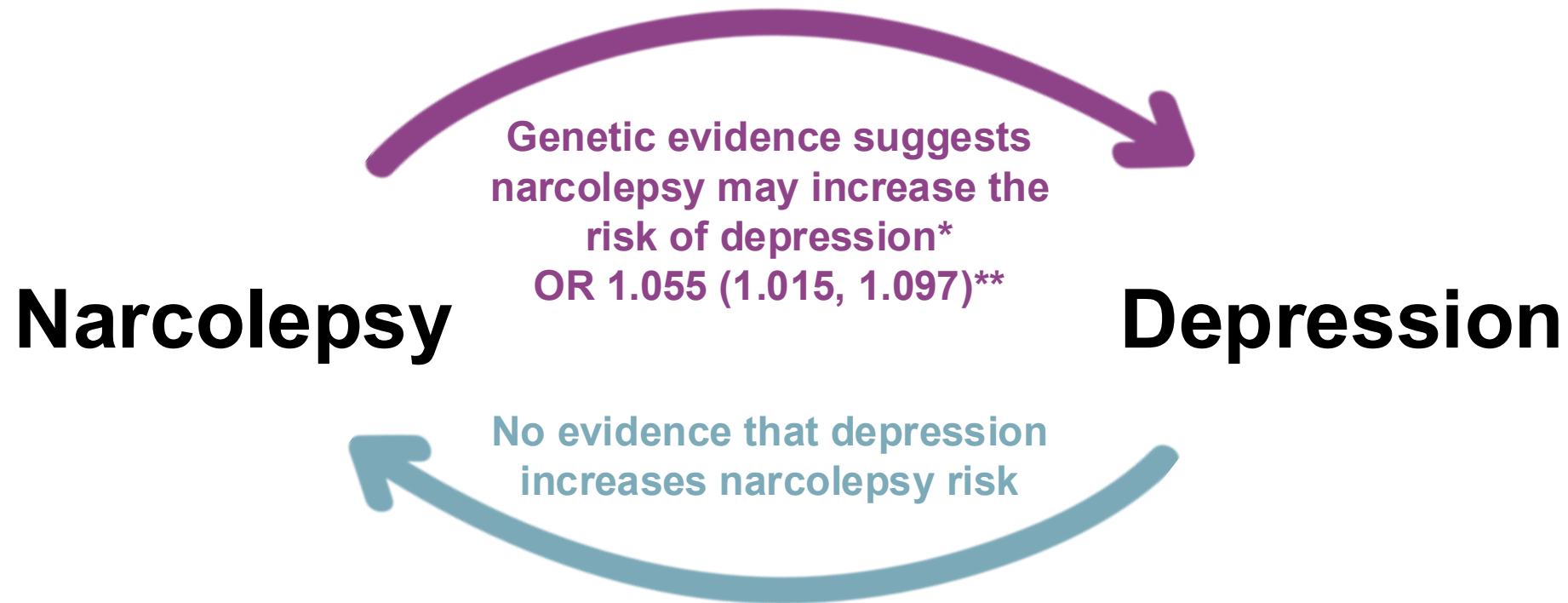
# Substantial Symptom Overlap Exists Between Depression and Hypersomnia

## Depression

DSM-5-TR:  
presence of 5  
symptoms not  
attributed to other  
medical  
conditions (must  
include core  
symptoms of low  
mood or reduced  
interest/pleasure)

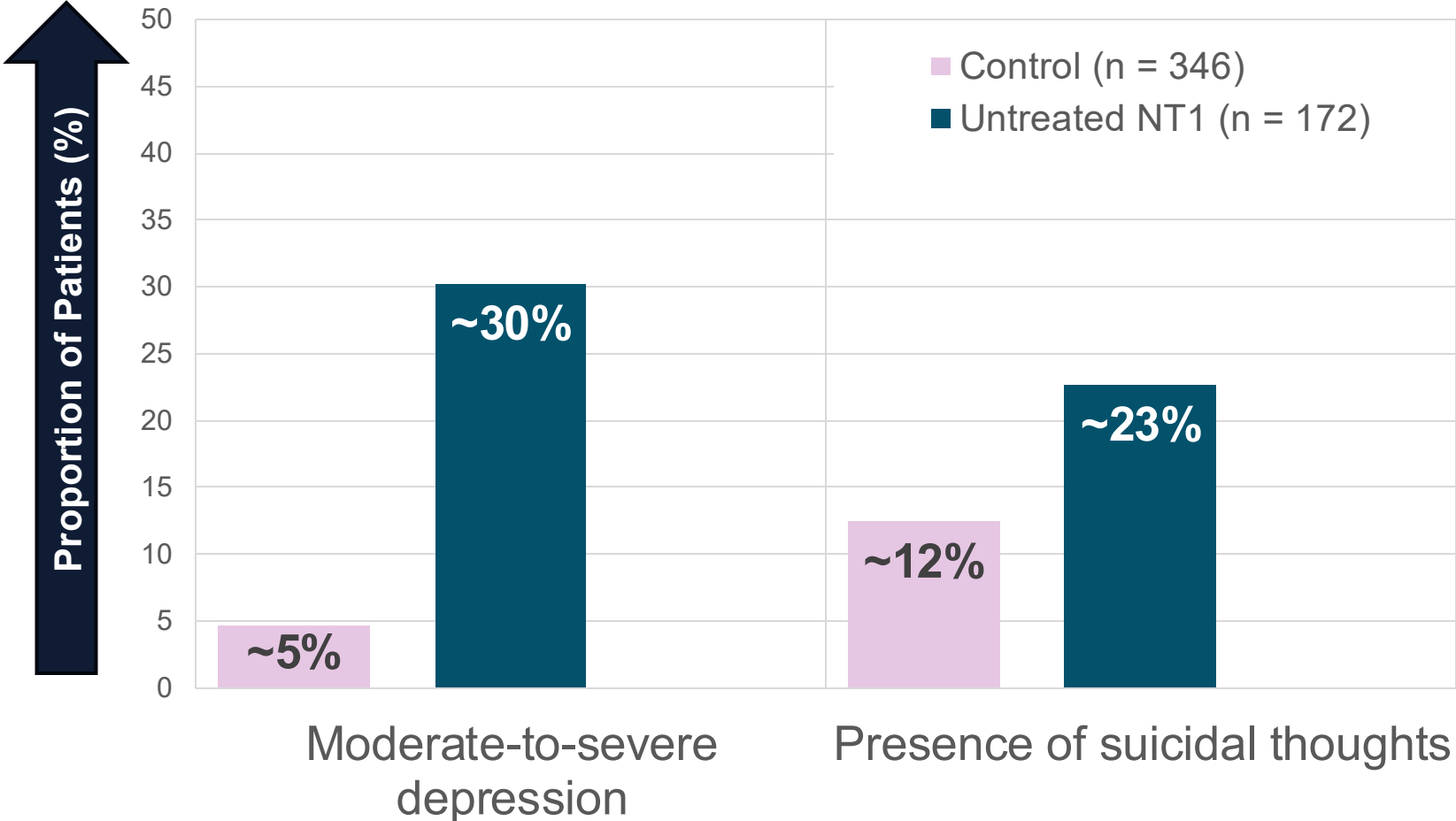


# What Is the Relationship Between Narcolepsy and Depression?



# Untreated NT1 Was Associated with Higher Rates of Depressive Symptoms and Suicidal Thoughts

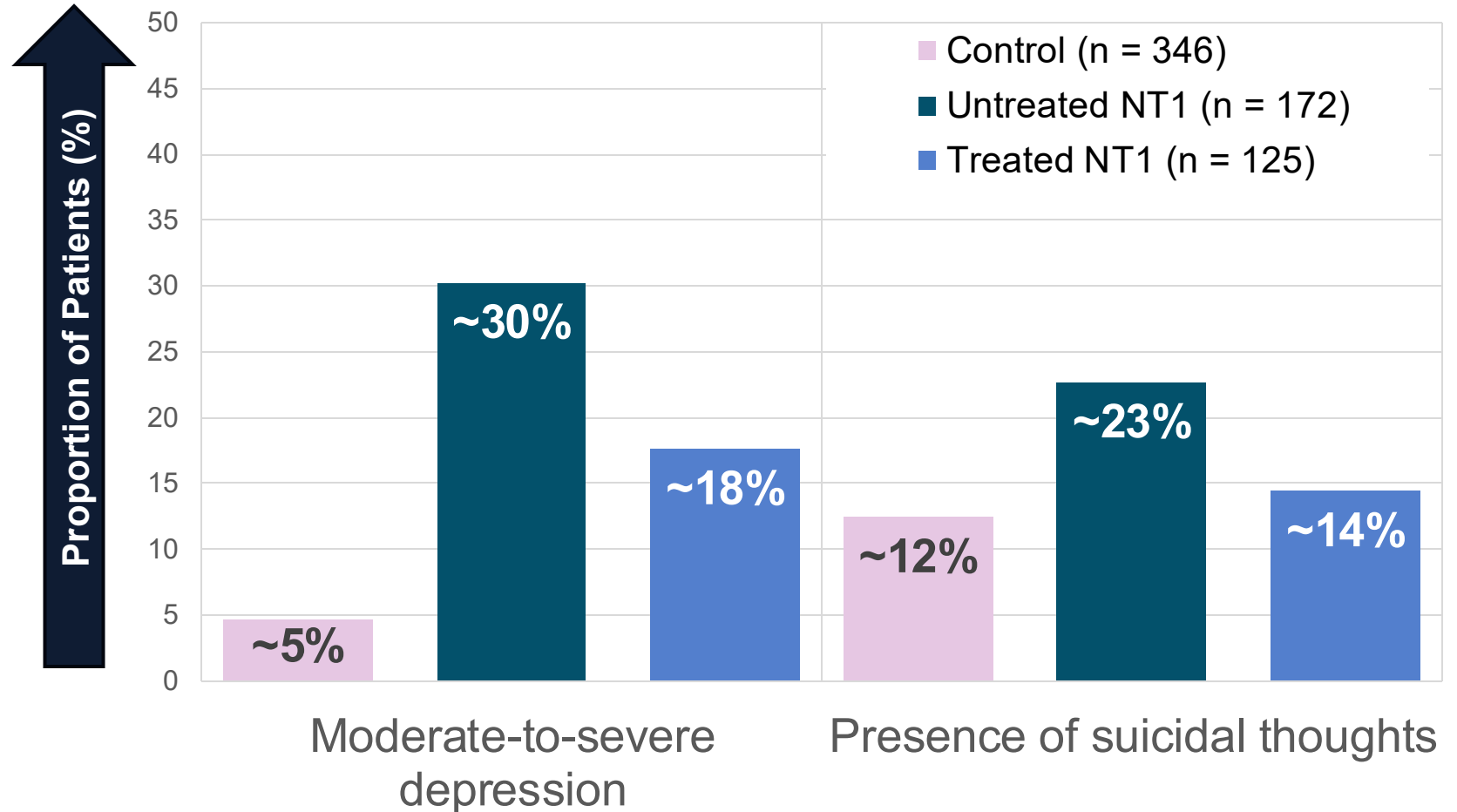
Compared to controls, untreated NT1 was associated with **~6-fold higher rates of moderate-to-severe depressive symptoms** & **nearly twice the rate of suicidal thoughts**



NT1 = narcolepsy type 1  
Barateau L, et al. Neurology. 2020;95:e2755-e2768

# However, Patients With Treated NT1 Reported Lower Rates

Patients receiving NT1 treatment reported **lower rates of moderate-to-severe depression and suicidal thoughts** than untreated patients, although rates remained higher than those observed in controls

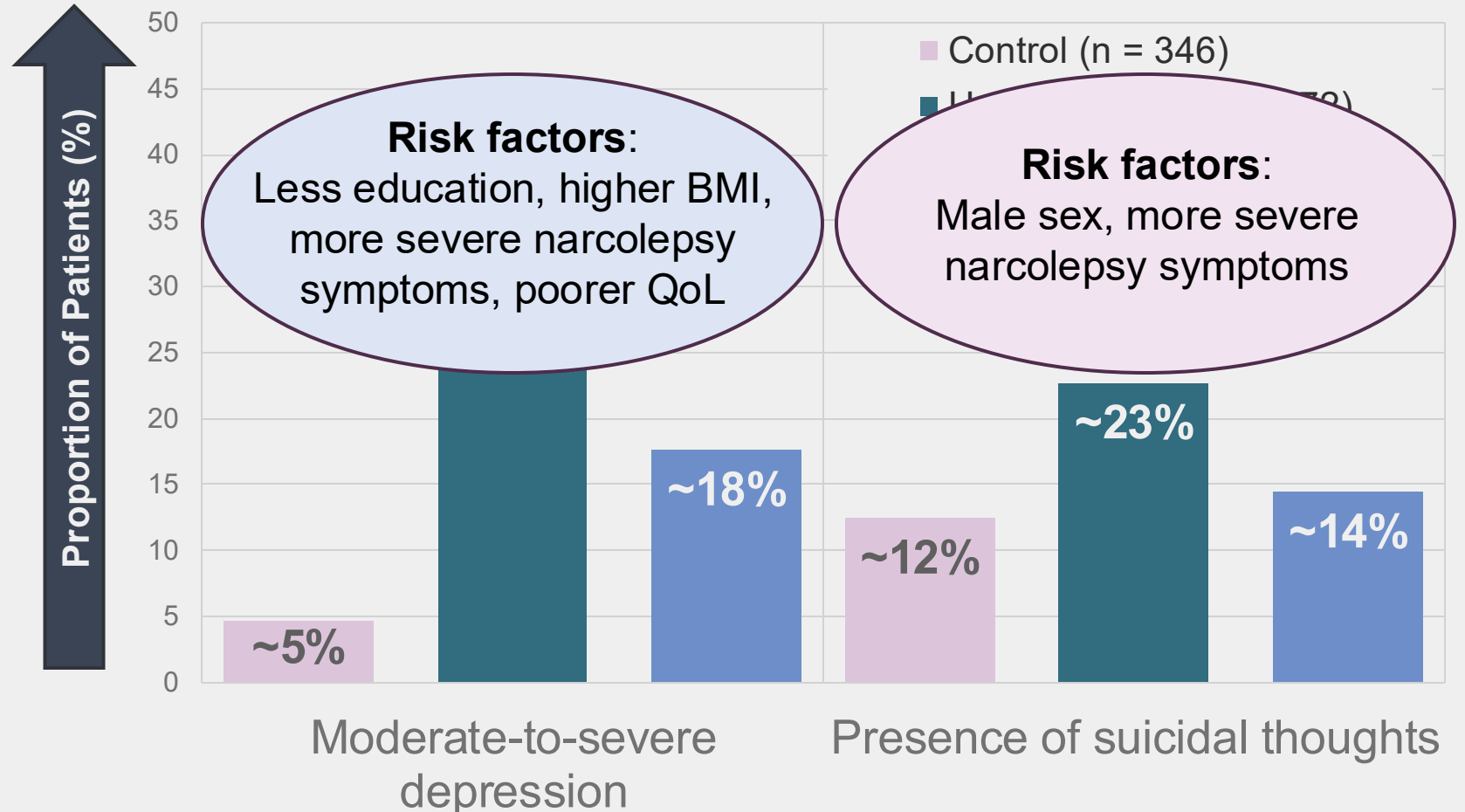


NT1 = narcolepsy type 1

Barateau L, et al. Neurology. 2020;95:e2755-e2768

# However, Patients With Treated NT1 Reported Lower Rates

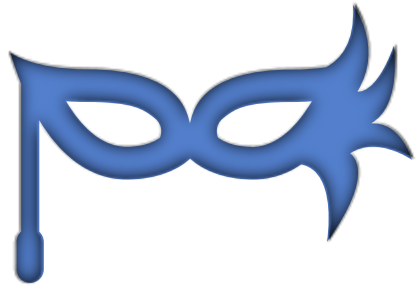
Patients receiving NT1 treatment reported **lower rates of moderate-to-severe depression and suicidal thoughts** than untreated patients, although rates remained higher than those observed in controls



# But Not All Sleepiness Is a Sleep Disorder



# Psychiatric Disorders May *Masquerade* as Sleep Disturbances



Many patients don't say *"I'm depressed"*

*Sleep complaints are often the "mask"*

## What they might say instead:

"I'm exhausted, but I can't sleep"

"I have no energy during the day"

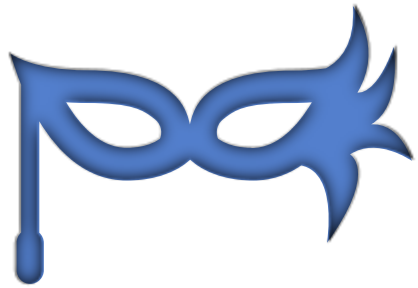
"I'm tired, but wired"

"I just can't shut my mind off at night"

"I wake up at 3 AM and can't get back to sleep"

"I just don't feel like myself"

# Psychiatric Disorders May *Masquerade* as Sleep Disturbances



Many patients don't say *"I'm depressed"*

*Sleep complaints are often the "mask"*

## Depression with Anxious Distress

"I'm exhausted, but I can't sleep"

"I wake up at 3 AM and can't get back to sleep"

"I just can't shut my mind off at night"

## Depression with Mixed Features

"I'm tired, but wired"

## Depression with Anhedonia

"I have no interest in anything"

"I just don't feel like myself"

# Looking Behind the Mask: Questions That Uncover Psychiatric Contributors to Sleep Complaints

Patient says...	Consider asking...
"I wake up at 3 AM and can't get back to sleep"	"When you wake up, what thoughts tend to be going through your mind?"
"I'm exhausted, but I can't sleep"	"How have your mood and stress levels been recently?"
"I just can't shut my mind off at night"	"Do you find yourself worrying, ruminating, or feeling anxious at bedtime? How fast do your thoughts go?"
"I'm tired, but wired"	"Do you also feel: <u>A</u> nxious? <u>A</u> gitated? <u>A</u> ngry/irritable? Have <u>A</u> ttention/concentration problems?"
"I have no energy during the day"	"If I could magically give you energy, would you do all the things you wanted to?"
"I just don't feel like myself"	"Tell me more..." / "What things are you excited about or looking forward to?"

# When Symptoms Suggest Something More: Utilizing Psychiatric Screening and Monitoring Tools

## Anxiety (GAD-7)

Over the **last two weeks**, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
	0	1	2	3
1 Feeling nervous, anxious, or on edge	0	1	2	3
2 Not being able to stop or control worrying	0	1	2	3
3 Worrying too much about different things	0	1	2	3
4 Trouble relaxing	0	1	2	3
5 Being so restless that it is hard to sit still	0	1	2	3
6 Becoming easily annoyed or irritable	0	1	2	3
7 Feeling afraid, as if something awful might happen	0	1	2	3

Column totals:  +  +  +  = Total score

0-4: Minimal anxiety  
 5-9: Mild anxiety  
 10-14: Moderate anxiety  
 15-21: Severe anxiety

## Depression (PHQ-9)

Over the **last 2 weeks**, how often have you been bothered by any of the following problems?  
 (Use  to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
	0	1	2	3
1 Little interest or pleasure in doing things	0	1	2	3
2 Feeling down, depressed, or hopeless	0	1	2	3
3 Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4 Feeling tired or having little energy	0	1	2	3
5 Poor appetite or overeating	0	1	2	3
6 Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7 Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8 Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9 Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Column totals:  +  +  +  = Total score

0-4: Minimal or no depression  
 5-9: Mild depression  
 10-14: Moderate depression  
 15-19: Moderately severe depression  
 20-27: Severe depression

## Bipolar Disorder (RMS)

Are you among the millions of people who have depressive symptoms? Answer the following questionnaire about your medical history and provide it to your doctor or nurse to assist in an important conversation about your mood.

Please select one response for each question. You can complete the RMS in less than 2 minutes.

Patient Name \_\_\_\_\_ Date \_\_\_\_\_

	YES	NO
1. Have there been at least 6 different periods of time (at least 2 weeks) when you felt deeply depressed?	<input type="checkbox"/>	<input type="checkbox"/>
2. Did you have problems with depression before the age of 18?	<input type="checkbox"/>	<input type="checkbox"/>
3. Have you ever had to stop or change your antidepressant because it made you highly irritable or hyper?	<input type="checkbox"/>	<input type="checkbox"/>
4. Have you ever had a period of at least 1 week during which you were more talkative than normal with thoughts racing in your head?	<input type="checkbox"/>	<input type="checkbox"/>
5. Have you ever had a period of at least 1 week during which you felt any of the following: unusually happy; unusually outgoing; or unusually energetic?	<input type="checkbox"/>	<input type="checkbox"/>
6. Have you ever had a period of at least 1 week during which you needed much less sleep than usual?	<input type="checkbox"/>	<input type="checkbox"/>

“YES” responses to 4 or more of the 6 items are considered a positive screen, providing high confidence for BP-I

# Adverse Childhood Experiences (ACEs) Are Also Risk Factors for Poor Sleep

## 10 ACE Domains

- Abuse (emotional, physical, sexual)
- Neglect (emotional, physical)
- Household dysfunction
  - Substance use
  - Mental illness
  - Domestic violence
  - Separation/divorce
  - Incarceration

*ACE Score = Number of adverse experiences endorsed (0-10)*

## ACEs are associated with:



↑ Insomnia symptoms



↑ Nightmare frequency



↑ Sleep fragmentation



↑ Risk of short sleep duration



↑ OSA risk



↓ Overall sleep quality

OSA = obstructive sleep apnea.

Chapman DP, et al. *Sleep Med.* 2011;12(8):773-779; Kajeepta S, et al. *Sleep Med.* 2015;16(3):320-330.

# Psychiatric Screening Tools In Practice



## WHEN TO USE

- Persistent sleep/wake symptoms despite treatment
- Any suspected mood or anxiety disorder



## WHAT THEY ADD

- Objectifies symptoms
- Enables **measurement-based care** by identifying severity and tracking response to treatment



## HOW TO USE

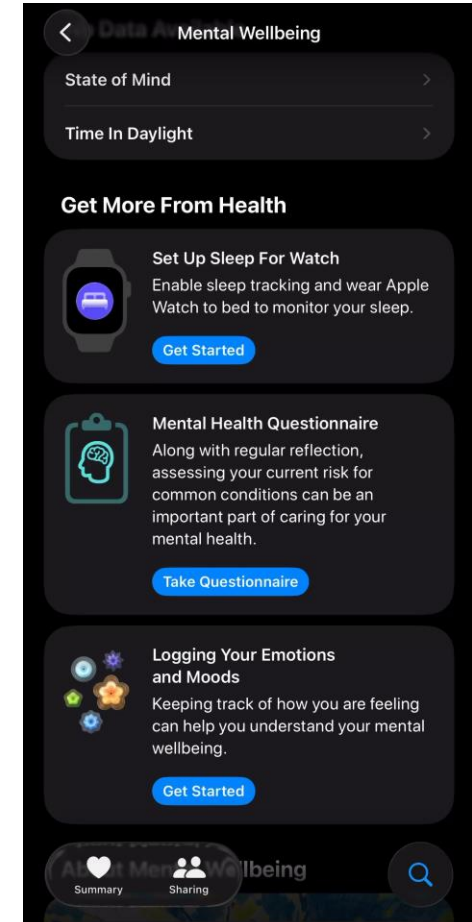
- Administer in <2 minutes (paper or digital)
- Use in waiting room or prior to visit

# Mental Health Assessments Are Integrated Mobile Devices

On an iPhone:

- Go to the Health app.
- Tap the Search 🔍 button, then tap Mental Wellbeing.
- Tap **Anxiety Risk (GAD-7)** or **Depression Risk (PHQ-9)**
  - OR scroll down to find **Mental Health Questionnaire** (includes both assessments)

**16 questions →**  
7 for anxiety and 9 for depression



Example shown: Apple Health app includes integrated PHQ-9 and GAD-7 assessments. Similar screening tools are available through many digital health platforms.



# Key Learning Points

- Diagnostic accuracy requires considering medical, psychiatric, behavioral, medication-related, and sleep-related causes of symptoms while avoiding cognitive biases
- Depression, anxiety, and bipolar disorder may be “*masked*” as sleep complaints, making targeted questioning and screening essential
- Brief validated screening tools (e.g, PHQ-9, GAD-7, RMS) can improve detection, support measurement-based care, and guide referral decisions
- In doubt, always ask about suicidal thoughts and intent

**Gaining Confidence  
with Psychotropic Agents  
in Sleep Medicine Practice**

***Psychopharmacology Is Easy...  
Right?***

Citalopram

Amitriptyline

Trimipramine

Tranylcypromine

Selegiline

Fluvoxamine

Protriptyline

Isocarboxazid

Dextromethorphan-bupropion

Sertraline

Paroxetine

Maprotiline

Phenelzine

Esketamine

Chlorpromazine

Bupropion

Fluoxetine

Clomipramine

Aripiprazole

Escitalopram

Nortriptyline

Trifluoperazine

Trazodone

Asenapine

Vortioxetine

Lurasidone

Vilazodone

Nefazodone

**Right?**

Iloperidone

Pimozide

Olanzapine

Desvenlafaxine

Duloxetine

Doxepin

Cariprazine

Pimavanserin

Venlafaxine

Mirtazapine

Imipramine

Perphenazine

Risperidone

Ziprasidone

Levomilnacipran

Amoxapine

Valproate

Paliperidone

Quetiapine

Desipramine

Fluphenazine

Haloperidol

Prochlorperazine

Lumateperone

Xanomeline/trospium

Molindone

Loxapine



Thioridazine

Brexpiprazole

Clozapine

Thiothixene



# Chepke's Choices: SSRI Advantages and Disadvantages

	Advantages	Disadvantages	My Verdict
<b>Citalopram</b>	FDA-approved for adults with MDD. Easy to switch to escitalopram.	QTc warning; Less efficacious and tolerable than escitalopram; fewest indications	No good reason to use
<b>Paroxetine</b>	Well-studied and efficacious in a variety of conditions	Strong 2D6 inhibition; mild anticholinergic effects; Worst sexual AEs and reproductive safety; Substantial withdrawal syndrome	"There's always a better choice than paroxetine for new starts"
<b>Fluvoxamine</b>	FDA-approved in and may be efficacious when others haven't in adult and pediatric OCD.	Often not as well-tolerated as others; non-linear kinetics, pervasive DDIs	For OCD, I prefer high dose sertraline
<b>Fluoxetine</b>	Extremely well-studied, with many pediatric indications. Very long half-life.	Very long half-life. Strong 2D6/2C19 and weak 3A4 inhibition	With a 5-week wash out, & many DDIs/warnings... Not 1 <sup>st</sup> line for adults
<b>Sertraline</b>	Broadly indicated, flexible dosing; Distributed metabolism mitigates effect of CYP inhibitors/PMs; Favorable reproductive profile	Prominent GI side effects; dose-dependent 2D6 inhibition & QTc prolongation	A solid medication with a lot of utility. 
<b>Escitalopram</b>	Robust efficacy (and superior to citalopram), well-tolerated (low discontinuation due to AEs); simple dosing; no QT warning; low risk of CYP inhibition.	Vulnerable to CYP 2C19 interactions; Few indications; lower, but nonzero QTc risk	I don't always prescribe SSRIs... but when I do, it's usually escitalopram 

AE=adverse event; DDI=drug-drug interaction; QTc=corrected QT interval; PM=poor metabolizer.

US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. [www.accessdata.fda.gov/scripts/cder/daf/](http://www.accessdata.fda.gov/scripts/cder/daf/). Macaluso M, et al (eds.) *Antidepressants: From Biogenic Amines to New Mechanisms of Action. Vol. 250*. Springer;2019. Katzung. Chapter 30, in *Basic & Clinical Pharmacology 15th Edition*. McGraw Hill; 2020.



# Chepke's Choices: SNRI Advantages and Disadvantages

	Advantages	Disadvantages	My Verdict
<b>Venlafaxine ER</b>	Well-studied; the most psychiatric indications among SNRIs; Has a dose-response relationship	Basically acts an SSRI at lower doses; Substantial side-effect burden and withdrawal syndrome. CYP liabilities.	Do not pass go, proceed directly to desvenlafaxine for new starts
<b>Duloxetine ER</b>	Well-studied for multiple symptom clusters, and has peds GAD and multiple pain indications	No clear dose-response relationship; Side-effect burden; Multiple somatic warnings (liver, skin, glucose); Moderate CYP 2D6 inhibitor.	Useful for those with selected pain conditions and pediatric GAD
<b>Milnacipran</b>	Very few DDIs; FDA approved for FM	Only indicated for FM in the US; Side-effect burden	Works well for FM... but so do a lot of other things
<b>Desvenlafaxine ER</b>	Anecdotally less prone to discontinuation syndrome than venlafaxine. Virtually no DDIs. May help vasomotor spasm (off-label)	Only indicated for MDD. Side-effect burden; FDA-approved maximum is too low for many patients.	Probably the best classic "SNRI" pharmacologically... if you want one 
<b>Levomilnacipran ER</b>	It's distinct: an "NSRI", not an SNRI. Very few DDIs. Improves function on SDS. May help FM (off-label)	Only indicated for MDD. Side-effect burden.	I don't always prescribe SNRIs... but when I do, it's usually levomilnacipran 

FM = fibromyalgia; DDI= drug-drug interaction; SDS = Sheehan Disability Scale.

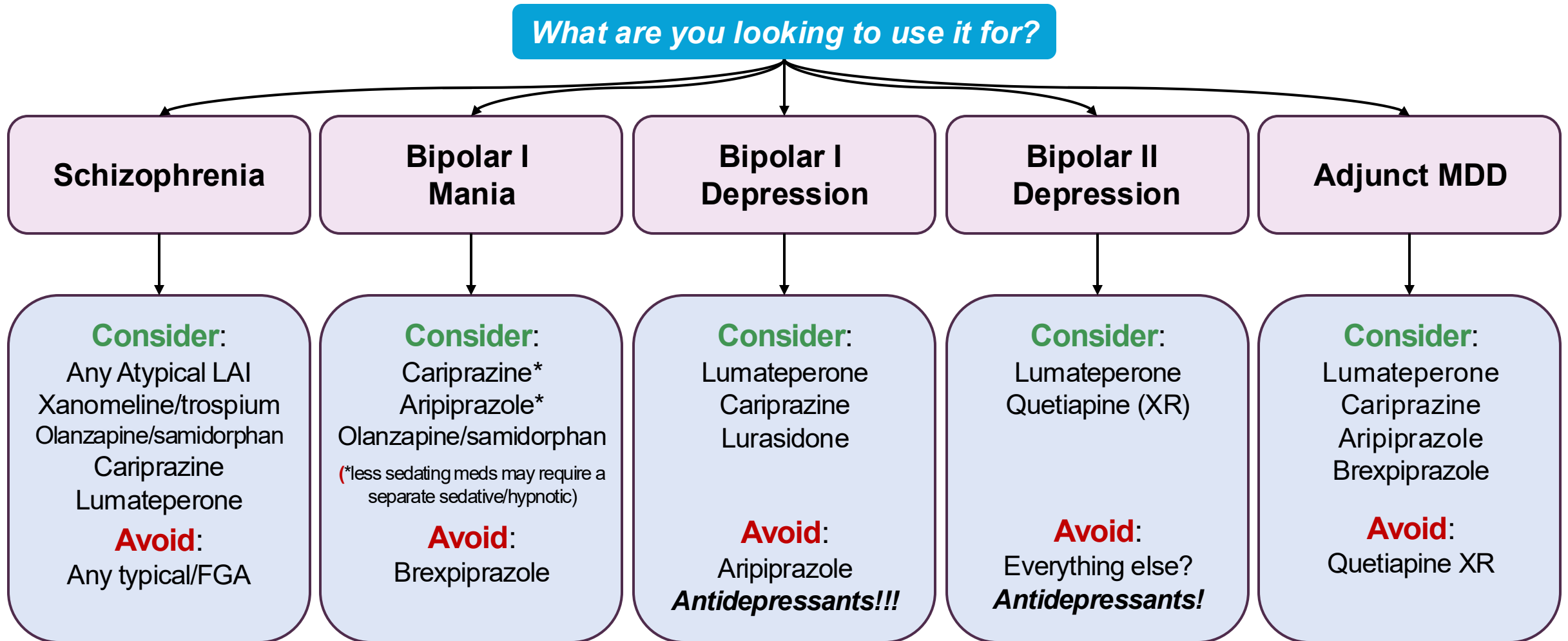
US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. [www.accessdata.fda.gov/scripts/cder/daf/](http://www.accessdata.fda.gov/scripts/cder/daf/). Macaluso M, et al (eds.). *Antidepressants: From Biogenic Amines to New Mechanisms of Action. Vol. 250*. Springer, 2019. Katzung. Chapter 30. In *Basic & Clinical Pharmacology, 15th Edition*. McGraw Hill; 2020.

# Chepke's Choices: Advantages & Disadvantages of Other Antidepressants



	Advantages	Disadvantages	My Verdict
<b>Bupropion</b>	Low risk of weight gain or sexual side effects. Can help smoking cessation.	Low chance of meaningful efficacy. Can worsen anxiety, insomnia, irritability, or tremor. Avoid in seizure disorder. Doesn't help sexual dysfunction.	Controversial opinion, but I think it's the most overrated psychiatric med ever
<b>Mirtazapine</b>	Specifically helps low appetite and insomnia symptoms. Low risk of sexual side effects.	Weight gain and sedation are very often treatment-limiting.	Great for elderly people who can't sleep or eat...
<b>Vilazodone</b>	An SSRI with 5-HT1a partial agonism	GI side effects are common (especially diarrhea) and <u>MUST</u> take with food	Not much reason to use this over many other alternatives
<b>Vortioxetine</b>	Evidence for cognitive symptoms of MDD. Favorable weight and sexual tolerability.	Early nausea common if titrated too quickly (can manage w/PRN anti-emetics). Occasional coverage challenges until generics appear in 2027.	The best pure serotonergic antidepressant that exists. 
<b>Dextromethorphan-Bupropion</b>	Rapid antidepressant and anti-anhedonia effect via NMDA-R antagonism/sigma-1 agonism. Favorable weight/sexual tolerability. Also approved for Alzheimer's Agitation.	Transient dizziness and nausea on initiation for some. CYP2D6 DDIs. Newer med, so coverage still emerging.	The best oral antidepressant that currently exists. 

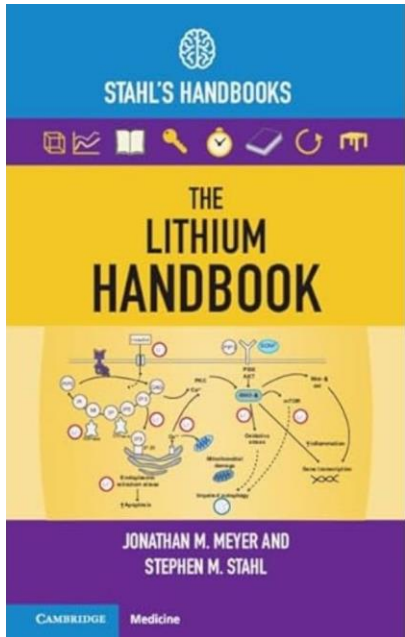
# Chepke's Choices:

## Recommended First-Line Antipsychotic Choices



# Chepke's Choices: Mood Stabilizers Advantages and Disadvantages

	Advantages	Disadvantages	My Verdict
<b>Carbamazepine</b>	Strong antimanic. Some anti-aggressive effects. Potentially useful in rapid cycling.	Risk of SJS/TEN, Aplastic anemia, agranulocytosis, Teratogenic, Extensive DDIs	Unless necessary for seizure disorder, only use as a last-resort
<b>Valproate</b>	Strong acute antimanic. Useful in Mixed Features. Can be loaded quickly.	Hepatotoxicity, Pancreatitis, teratogenic, blood levels, Tremor, Weight gain, GI issues, Hair loss	Do <b>not</b> prescribe to females <b>OR</b> males of child-bearing age.
<b>Lamotrigine</b>	One of few meds with known prevention of BP depressive episodes. Favorable tolerability.	Risk of SJS/TEN*, Slow titration (restart if >5d missed), Hormonal treatment DDI, Only approved in BPI, <b>Only</b> prevents depression,	Not the panacea that some believe, but useful for maintaining stability in BPI 
<b>Lithium</b>	Strongest evidence for relapse prevention. Anti-suicide benefit. Possible disease-modifying and neuroprotective effects.	Narrow therapeutic index* Long-term thyroid/kidney damage, Tremor, Weight gain, GI issues	Lithium is the gold Standard for Bipolar I Disorder... if the patient will agree to it 



\*boxed warning in USPI. GI=gastrointestinal; SI=suicidal ideation; DDI=Drug-Drug Interactions; SJS/TEN=Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis.US Food and Drug Administration. Drugs@FDA: FDAApproved Drug Products. [www.accessdata.fda.gov/scripts/cder/daf/](http://www.accessdata.fda.gov/scripts/cder/daf/). Ghaemi SN. *Clinical Psychopharmacology: Principles and Practice*. Oxford University Press; 2019. Suppes T, et al. *Arch Gen Psychiatry*. 1991;48(12):1082-1088. Meyer, JM, and SM Stahl. *The Lithium Handbook: Stahl's Handbooks*. Cambridge University Press, 2023. Fountoulakis KN. *Bipolar disorder: an evidence-based guide to manic depression*. Springer, 2014.

# When to Manage vs When to Refer

Patient presents with sleep complaint  
+ possible psychiatric symptoms

Initial Assessment: Screen + brief history  
(mood, anxiety, substance use)  
Consider PHQ-9, GAD-7, and RMS

Are symptoms  
mild and stable?

YES

## Manage in Sleep Clinic

- Mild depression/anxiety symptoms
- No safety concerns
- No history suggestive of bipolar disorder
- Minimal functional impairment



- CBT-I & behavioral strategies
- Monitor symptoms over time
- Reassess with screening tools

NO

Are there red flags  
or diagnostic  
complexity?

SOME

## Collaborate/Co-Manage

Moderate symptoms without  
red flags



- Continue sleep treatment
- Coordinate with PCP or psychiatry
- Monitor closely

YES

## Refer/Collaborate with Psychiatry

If any of the following are present:

- Active/Serious Suicidal ideation
- Severe depression/anxiety
- Significant PTSD
- Substance use disorder
- Complex psychiatric med regimen

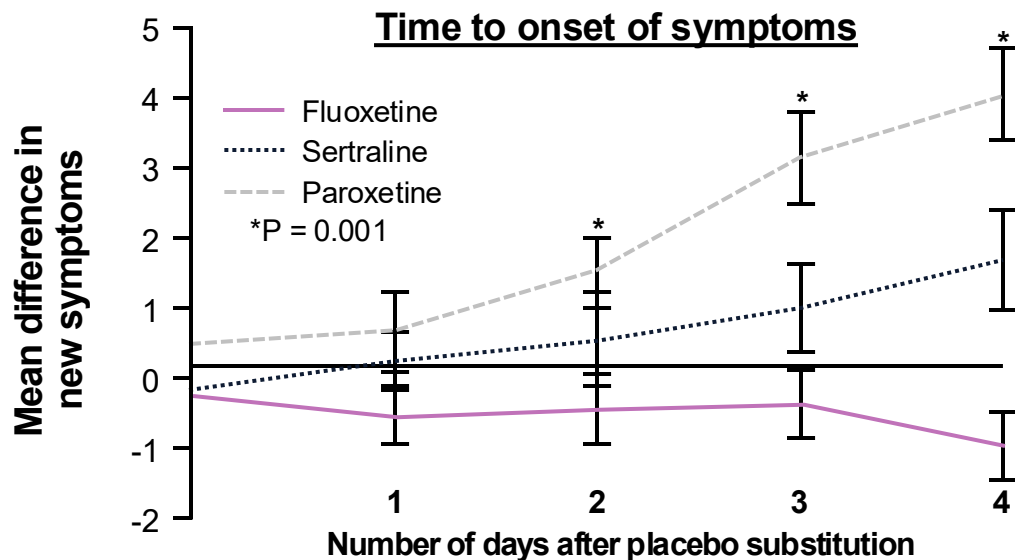
# Antidepressant Discontinuation Syndrome

Flu-like sx  
Insomnia  
Nausea  
Imbalance  
Sensory disturbances  
Hyperarousal

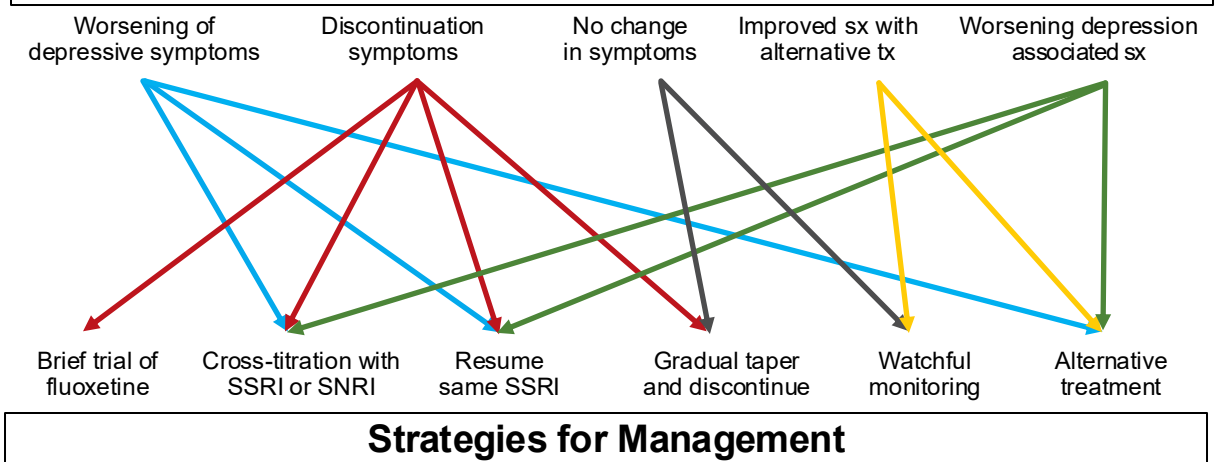
- May occur after abrupt discontinuation or overly rapid taper in up to 40%.
- Discontinuation symptoms typically resolve spontaneously over 2–3 wks
- Most common with **paroxetine** among SSRIs and **venlafaxine** among SNRIs
- Lowest likelihood with fluoxetine

## Risk Factors

Earlier age at depression onset  
 Comorbidities (eg, panic disorder)  
 Past history of discontinuation sx



## Consequences of Antidepressant Dose Decrease or Discontinuation



# Key Learning Points

- Psychotropic medications vary widely in their effects on sleep and wakefulness, making medication selection an important consideration in patients with sleep disorders
- Regular PHQ-9 monitoring can help avoid unnecessary antidepressant changes
  - *SSRIs are much more alike than they are different*; try a couple and then move on. They also don't have a dose-response relationship for efficacy, but they do for adverse reactions!
- Sleep clinicians should recognize when psychiatric symptoms can be managed within the sleep clinic, when collaborative care is appropriate, and when referral to psychiatry is warranted

# Planning Sleep Medicine Treatment for Patients with Psychiatric Disorders

# Spectrum of Psychiatric Medications



*sedating*

- **GABAergic agents:** benzodiazepines, barbiturates, baclofen
- **Tricyclic antidepressants:** amitriptyline, doxepin
- **Atypical antidepressants:** mirtazapine, trazodone
- **Orexin receptor antagonists:** daridorexant, lemborexant, suvorexant
- **Many antipsychotics:** quetiapine, olanzapine, clozapine
- **Mood stabilizers/antiepileptics:** valproate
- **Gabapentin, pregabalin**
- **Antihistamines:** diphenhydramine, hydroxyzine
- **Alpha-2 agonists:** clonidine, dexmedetomidine
- **Opioids and other CNS depressants**

# Spectrum of Psychiatric Medications



*sedating*

- **GABAergic agents:** benzodiazepines, barbiturates, baclofen
- **Tricyclic antidepressants:** amitriptyline, doxepin
- **Atypical antidepressants:** mirtazapine, trazodone
- **Orexin receptor antagonists:** daridorexant, lemborexant, suvorexant
- **Many antipsychotics:** quetiapine, olanzapine, clozapine
- **Mood stabilizers/antiepileptics:** valproate
- **Gabapentin, pregabalin**
- **Antihistamines:** diphenhydramine, hydroxyzine
- **Alpha-2 agonists:** clonidine, dexmedetomidine
- **Opioids and other CNS depressants**

*neutral/variable*

- **Some atypical antipsychotics:** aripiprazole, ziprasidone, lurasidone, cariprazine
- **Some mood stabilizers:** lithium, lamotrigine, carbamazepine
- **Many SSRIs:** fluoxetine, sertraline, citalopram, escitalopram
- Topiramate

# Spectrum of Psychiatric Medications



*sedating*

- **GABAergic agents:** benzodiazepines, barbiturates, baclofen
- **Tricyclic antidepressants:** amitriptyline, doxepin
- **Atypical antidepressants:** mirtazapine, trazodone
- **Orexin receptor antagonists:** daridorexant, lemborexant, suvorexant
- **Many antipsychotics:** quetiapine, olanzapine, clozapine
- **Mood stabilizers/antiepileptics:** valproate
- **Gabapentin, pregabalin**
- **Antihistamines:** diphenhydramine, hydroxyzine
- **Alpha-2 agonists:** clonidine, dexmedetomidine
- **Opioids and other CNS depressants**

*neutral/variable*

- **Some atypical antipsychotics:** aripiprazole, ziprasidone, lurasidone, cariprazine
- **Some mood stabilizers:** lithium, lamotrigine, carbamazepine
- **Many SSRIs:** fluoxetine, sertraline, citalopram, escitalopram
- **Topiramate**

*activating*

- **Bupropion** (DA/NE reuptake inhibitor)
- **SNRIs:** venlafaxine, duloxetine
- **Atomoxetine** (NRI)
- **Stimulants:** methylphenidate, amphetamines
- **Emerging orexin agonists:** oreporexton, alixorexton, danavorexton/related agents\*

*Stimulants are sometimes used off-label for treatment-resistant depression*

# Planning Sleep Medicine Treatment for Patients with Psychiatric Disorders

## Maximize Sleep/Wake Benefits and Psychiatric Effects

Initial Agent Selection and Dose Optimization (sedative vs activating)  
SSRI (treatment for anxiety) with oxybate (increases anxiety)  
Tapering Off vs Switching Medications (antidepressants)

## Consider Patient Preferences and Lifestyles

Convenience and Adherence (day vs night)  
Speed and Duration of Action (explain delay for antidepressant)  
Avoidance of Specific Side Effects (sedative, increased sexual side effects)

## Avoid drug-drug interactions

QT prolongation and Pitolisant (beware of cumulative effects)  
Contraception, modafinil and Pitolisant  
Avoid oxybate and sedatives, notably respiratory depressants (opioids)



# Key Learning Points

- Psychiatric medications exist on a spectrum from sedating to activating and can significantly influence sleep quality, daytime alertness, and treatment adherence
  - i.e., bupropion (**activating**) may improve EDS, whereas mirtazapine (**sedating**) may worsen EDS
- Monitor for medication-related sleep disturbances, withdrawal effects, and drug-drug interactions that may affect both psychiatric and sleep outcomes
- Use a collaborative, patient-centered approach that incorporates psychiatric screening, ongoing monitoring, and timely referral when symptoms exceed the scope of sleep medicine practice

# Faculty Panel Discussion

# Case #1

- A 52-year-old woman developed depression and insomnia during menopause
  - Both mood and sleep problems have persisted for the past 5 years
- Her PCP prescribed mirtazapine for depression and sedating properties
- Her mood gradually improved, but her insomnia persisted
- *“I thought I would sleep better once my depression got better.”*



# Case #2

- A 28-year-old man with schizophrenia, stable on an antipsychotic managed through a community mental health center
  - Referred to the sleep clinic for severe daytime sleepiness, attributed for years to his medication
- PSG with MSLT confirms a diagnosis of narcolepsy type 1
- Wake-promoting agents raise concern for exacerbating psychosis, and his antipsychotic contributes to sedation
- Treatment requires coordination between the sleep specialist and his psychiatry team across care settings
- *“Everyone always told me I was sleepy because of my meds.”*

# Case #3

- A 45-year-old man is convinced he has a serious sleep disorder
  - Reports several years of unrefreshing sleep and daytime exhaustion
- PSG and actigraphy are all normal — no sleep disorder can be diagnostically confirmed
- Screening reveals moderate depressive and anxiety symptoms and a significant ACE history
- He has no psychiatric provider and declines referral, citing stigma and cost — the sleep clinician must initiate management using available psychiatric education resources
- *“The tests say I’m fine, but I know something is wrong with my sleep.”*



# Polling

- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response.



The winner will be announced at the conclusion of the Q&A. Winner must be present to claim their prize.

HMP Education

# Practical Strategies for Navigating Psychiatric Complexities in Sleep Medicine



# Credit Claim Information

- Scan this QR code to claim credit after the session.
- Participants who complete the evaluation online within 30 days of the event will receive documentation of credit.

