

Adult/Geriatric Drug Therapy 2020

# **Pharmacological Management of Insomnia**

*Ken He, MD*

## **Objectives for Learning Outcomes:**

1. Describe insomnia definitions and core concepts.
2. How to perform an in-depth clinical evaluation of insomnia.
3. Select most appropriate drug therapy with understanding of mechanism and side effects.



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WASHINGTON

## Pharmacological Management of Insomnia

June 3rd, 2020

Ken He, MD, PharmD  
Clinical Assistant Professor, UWSoM  
Staff, Hospital & Sleep Medicine, VA PSHCS

Adult & Geriatric Drug Therapy  
UW School of Nursing CNE  
June 3, 2020



### Ken He, MD, PharmD

- Dr. He is a staff physician in Hospital and Sleep Medicine services at the VA Puget Sound Health Care System. He obtained postgraduate training in Internal Medicine and Sleep Medicine at University of Washington.
- Dr. He spends the majority of his time providing clinical care to veterans in addition to precepting medicine residents and sleep fellows from the University of Washington.
- [Dr. He's PubMed Link](#)

### Conflict of Interest Disclosures

The presenter does not have any potential conflicts of interest to disclose

The presenter wishes to disclose the following potential conflicts of interest:

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	None
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Licensing fees	None
Educational products	None

The material presented in this lecture has no relationship with any of these potential conflicts

This talk presents material that is related to one or more of these potential conflicts, and references are provided throughout this lecture as support.

### Learning Objectives

Describe insomnia definitions and core concepts.

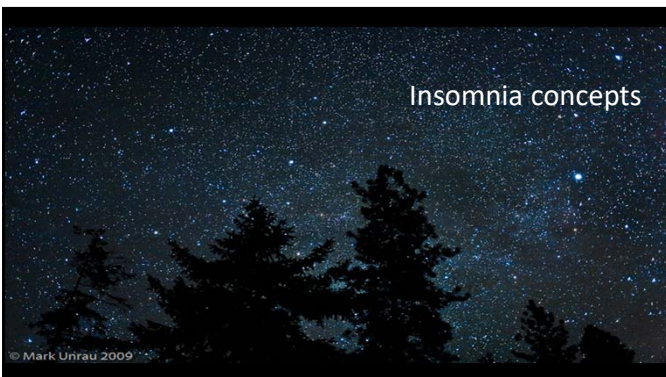


Perform an in-depth evaluation of insomnia



Select the most appropriate drug therapy

### Insomnia concepts



### Short-term vs. Chronic Insomnia

ICSD – 3 Diagnostic Criteria

Short-term insomnia

Chronic insomnia

- Less than 3 months

- Greater than 3 months

ICSD no longer differentiates between primary, secondary or insomnia subtypes



ICSD-3: International Classification of Sleep Disorders, 3<sup>rd</sup> edition, Image: Dana Farber

## Insomnia Nosology

### Primary

- Idiopathic
- Paradoxical
- Psychophysiological
- Inadequate sleep hygiene

### Secondary (comorbid)

- Due to drug or substance
- Due to medical condition
- Due to mental disorder
- Due to other sleep disorder

American Academy of Sleep Medicine ([aasm.org/resources/factsheets/insomnia.pdf](http://aasm.org/resources/factsheets/insomnia.pdf))

## Short-term\* Insomnia Disorder

ICSD – 3 Diagnostic Criteria

All criteria must be present

1. Difficulty falling or maintaining sleep, or waking too early
2. Occurs despite adequate sleep opportunity
3. **Occurs < 3 months**
4. Daytime impairment (*fatigue, sleepiness, mood, cognition, performance, preoccupation with sleep*)
5. **Cannot be better explained by another sleep disorder**



\*May be referred to as acute or adjustment insomnia

ICSD-3: International Classification of Sleep Disorders, 3<sup>rd</sup> edition

## Chronic Insomnia Disorder

ICSD – 3 Diagnostic Criteria

All criteria must be present

1. Difficulty falling or maintaining sleep, or waking too early
2. Occurs despite adequate sleep opportunity
3. **Occurs ≥3 times/week for ≥ 3 months**
4. Daytime impairment (*fatigue, sleepiness, mood, cognition, performance, preoccupation with sleep*)
5. **Cannot be better explained by another sleep disorder**



ICSD-3: International Classification of Sleep Disorders, 3<sup>rd</sup> edition

## Insomnia in General Adult Population

- The most common sleep disorder
- Estimated prevalence:
  - Any insomnia, 20% to 30%
  - Chronic insomnia, 6 to 10%
- Incidence is increasing
- More problematic in military service



Prevalence of symptoms is roughly double prevalence of disorder.

Ford. Sleep Med. 2015;16:372-8.  
Morin. Lancet. 2012;379:1129-41.  
Image from [www.uniquemindcare.com](http://www.uniquemindcare.com)

## Risk Factors

- Older age
- Female gender
- Pregnancy
- Medical or psychiatric illness
- Medications
- Stressful experiences
- Social obligations

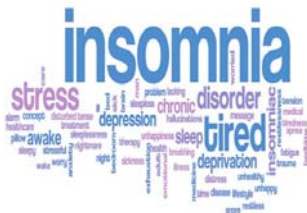


Image from [www.tribuneonline.ng](http://www.tribuneonline.ng)

## Sleep in the Era of COVID-19

- Increased stressors
- Home confinement
- Acute illness



- Increased insomnia
- Circadian rhythm disorders

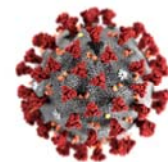


Image from [www.statnews.com](http://www.statnews.com)  
Li. JCSM. 2020;in press.  
Bryson. JCSM. 2020; in press.

Understanding these concepts helps inform medication selection

SLEEP PROMOTING

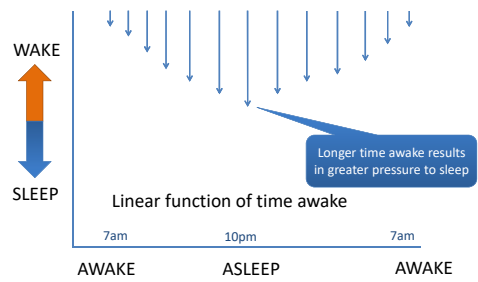
Homeostatic sleep drive

WAKE PROMOTING

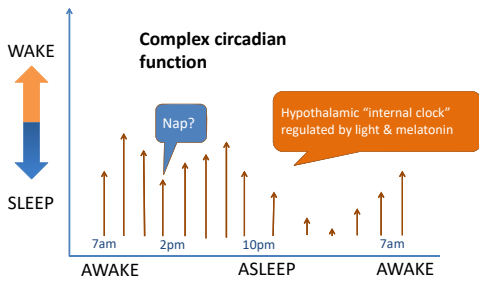
Circadian alerting drive



### Homeostatic Sleep Drive



### Circadian Alerting Drive



SLEEP PROMOTING

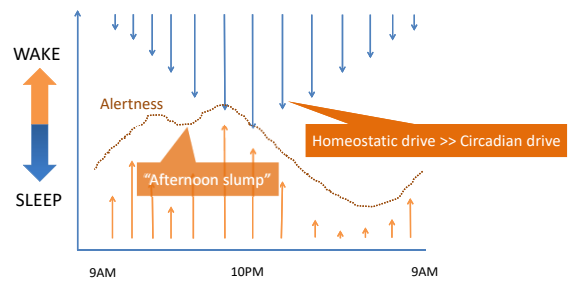
WAKE PROMOTING

Homeostatic sleep drive

Circadian alerting drive

SLEEP

### Alertness at Any Time is a Balance of these Two Processes



SLEEP PROMOTING

Homeostatic sleep drive

WAKE PROMOTING

Circadian alerting drive

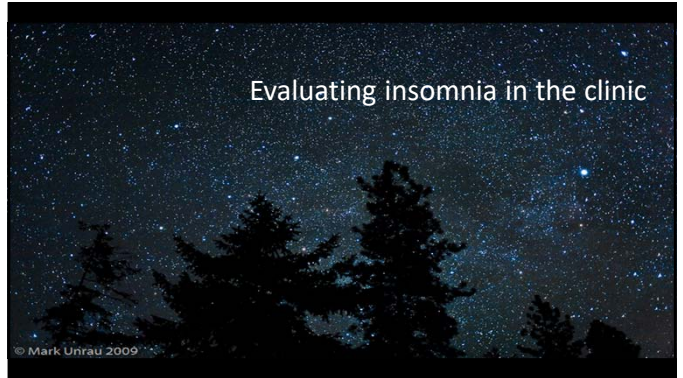
WAKE

## Effect of Insomnia

- What reduces homeostatic drive
  - Naps
  - Sleeping in
- What increases or disrupts circadian drive
  - Shift work
  - Circadian rhythm disorder
  - Light exposure
  - Cognitive or somatic hyperarousal



## Evaluating insomnia in the clinic



## Timing is Key! (the Sleep History)

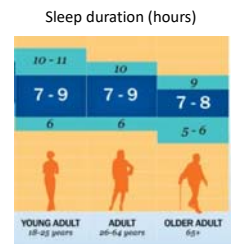
- Bedtime routine
- Time in bed & out of bed
- Initial sleep onset
- Awakenings (triggers)
- Naps
- Weekday vs. weekend changes
- Work schedule
- Sleep environment
- Sleep quality
- Symptoms of other sleep disorders
- Caffeine use



Image from Clipart.Email  
Buyssse. JAMA. 2013;309(7):706-16.

## What is Normal Sleep?

- Sleep timing (variable)
- Similar timing through the week
- Sleep onset latency < 30 minutes
- WASO < 30 minutes
- Awakenings (few, brief, spontaneous)
- Sleep efficiency 85% to 92%



Adapted from SleepFoundation.org

## Sleep Diaries: an Essential Tool

Blank sleep diary available on paper or electronic

- Critical in evaluation of insomnia
- More precise recording of timing and pattern of sleep
- Many formats



- Pen/paper diary ([www.yoursleep.aasmnet.org/pdf/sleepdiary.pdf](http://www.yoursleep.aasmnet.org/pdf/sleepdiary.pdf))
- E-diary – CBT-I coach ([www.mobile.va.gov/app/cbt-i-coach](http://www.mobile.va.gov/app/cbt-i-coach))
- Sleep trackers
- Actigraphy
- Polysomnography

Image from Whoop Smartwatch

## Sleep Diary Sample (insomnia)

Today's Date	Day of the week	Type of Day (work, school, off etc)	Noon	1:00 PM	2:00 PM	3:00 PM	4:00 PM	5:00 PM	6:00 PM	7:00 PM	8:00 PM	9:00 PM	10:00 PM	11:00 PM	MIDNIGHT	1:00 AM	2:00 AM	3:00 AM	4:00 AM	5:00 AM	6:00 AM	7:00 AM	8:00 AM	9:00 AM	10:00 AM	11:00 AM
8	Sun	Off																								
9	Mon	Work																								
10	Tues	Work																								
11	Wed	Work																								
12	Th	Work																								
13	Fri	Work																								
14	Sat	Off																								

E = Exercise C= Coffee/cola etc. M= Medications A= Alcohol

Awake   
  In bed   
  SLEEP   
  Out of bed

## Issue with Insomniacs...

- Distorted perceptions & beliefs about sleep
- Subjective sleep loss often exceeds objective measurements
  - Overestimate time to fall asleep
  - Underestimate total sleep time
  - Overestimate time awake after sleep onset
  - Overestimate number of awakenings

**“Catastrophizing”**

Edinger. Sleep Med Rev. 2003;7(3):203-14.

## Selecting drug therapy

© Mark Unrau 2009

## Establish Expectations

### For sleep

- Insomnia is chronic and requires time and effort to improve
- Goal is often NOT to normalize, but to **improve sleep quality and daytime function**

### For drug therapy

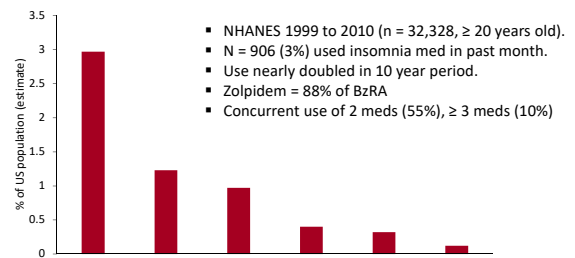
- There is NO magic drug fully effective AND safe
- Timing is KEY!
- Improves objective sleep parameters by MINUTES.



**Avoid pursuit of orthosomnia**

Baron. JCSM. 2017;13(2):351-4.

## Commonly Used Insomnia Medications



## Pharmacologic Categories

Non-BZ Benzodiazepine receptor agonists	GABA-A agonist via BZ <sub>1</sub> receptor
Benzodiazepines (traditional)	GABA-A agonist via BZ receptor
Melatonin receptor agonists	MT <sub>1</sub> and MT <sub>2</sub> receptors
Orexin (hypocretin) antagonists	OX <sub>1</sub> R and OX <sub>2</sub> R receptors
Antidepressants (sedating)	Multimodal (5HT, NE, D, H, Ach, α <sub>1</sub> )
Antihistamines	H <sub>1</sub> , Ach receptor blockade
Antipsychotics (second generation)	Multimodal (D, 5HT, Ach, H, α <sub>1</sub> )
Antiepileptics	Modulates alpha-2-delta-1 subunit
Sympatholytics	α <sub>1</sub> receptor antagonist, α <sub>2</sub> receptor agonist
Herbals and nutraceuticals	Multimodal
Substances (recreational)	Multimodal

BZ = benzodiazepine; MT = melatonin; OX<sub>1</sub>R = orexin; 5HT = serotonin; NE = norepinephrine; D = dopamine; H = histamine; Ach = acetylcholine

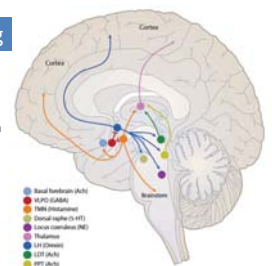
## Important Neurotransmitters

### Wake promoting

- Orexin/hypocretin
- Serotonin
- Norepinephrine
- Dopamine
- Histamine
- Acetylcholine
- Alpha-2-delta
- Glutamate

### Sleep promoting

- GABA
  - α<sub>1</sub> – sedating
  - α<sub>2</sub> – anxiolysis
  - α<sub>3</sub> – myorelaxation
  - α<sub>5</sub> – amnesia
- Adenosine
- Melatonin
- Galanin



Take note of medications with agonist v. antagonist effects

Nieblas-Beltran. J Syst Integr Neurosci. 2016. Sigol. J Biol Chem. 2012;287(48):40224-31.

## Specific Medications

Non-BZ BZRA	<i>zolpidem, zaleplon, eszopiclone</i>
BZ (traditional)	<i>temazepam, triazolam</i>
Melatonin and derivatives	melatonin, <i>ramelteon</i> , (tasimelteon)
Orexin (hypocretin) antagonists	<i>suvorexant, lemborexant</i> , (daridorexant, seltorexant)
Antidepressants (sedating)	trazodone, mirtazapine, amitriptyline, <i>doxepin</i>
Antihistamines	<i>diphenhydramine, doxylamine</i> , hydroxyzine
Antipsychotics (second generation)	olanzapine, risperidone, quetiapine, etc
Antiepileptics	gabapentin, pregabalin, tiagabine, barbiturates
Sympatholytics	prazosin, clonidine, tizanidine, guanfacine
Herbals and nutraceuticals	kava kava, valerian, chamomile
Substances (recreational)	alcohol, opioids, marijuana

BRZA = benzodiazepine receptor agonist; BZ = benzodiazepines; *italics* = FDA approved for insomnia

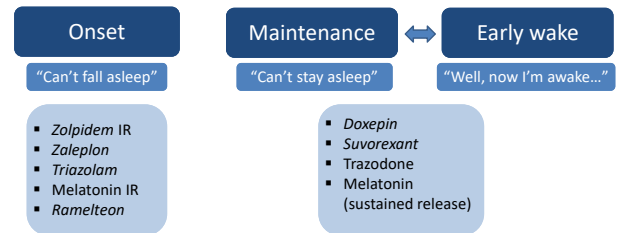
	Advantages	Disadvantages
Non-BZ BZRA & BZ (traditional)	effective, various half-lives	cognition, falls, dependence, sleep related behaviors, withdrawal
Melatonin	natural, minimal side effect	limited efficacy, not regulated
Orexin	new class	limited experience
Antidepressants	no abuse, effective for maintenance	cardiac, anticholinergic, orthostatic, suicidal thinking, serotonin syndrome
Antihistamines	easily obtained	cognition, limited efficacy
Antipsychotics	effective for psychosis	cardiac, metabolic, anticholinergic, falls, dystonia
Antiepileptics	effective for nerve pain	edema, cognition, falls, respiratory depression
Sympatholytics	effective for nightmares	falls, priapism, cardiac
Herbals and nutraceuticals	natural	liver toxicity, not regulated
Substances (recreational)	none	dependence, liver toxicity, respiratory depression

## Factors When Selecting a Drug

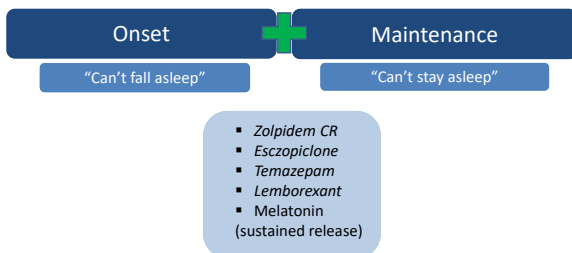
- Timing of symptoms
- Age
- Preference
- Comorbidities
- Substance use history
- Prior sedative use history
- Drug interactions



## Timing of Symptoms



## Timing of Symptoms



## What do the Guidelines Say?

### American College of Physicians (2016)

- All adults receive CBT-I as initial treatment for chronic insomnia (strong)
- Share decision making on deciding to add medications if CBT-I unsuccessful (weak)
- Limit medication use to < 4 to 5 weeks

### European Sleep Research Society (2017)

- All adults receive CBT-I as initial treatment for chronic insomnia (strong)
- Offer medications if CBT-I effective or not available (weak)
- Limit medication use to ≤ 4 weeks
- Antihistamines, antipsychotics, melatonin, alternative therapies are not recommended (strong to weak)

Qaseem. Ann Int Med. 2016;165(2):125-33.  
Riemann. J Sleep Res. 2017;26(6):675-700.

## What do the Guidelines Say?

### JAMA Clinical Guidelines (2017)

- Updates:
  - Medications most appropriate for short-term insomnia
  - Use shorter half-life agents, lower dose, intermittent dosing

### AASM Guidelines on Drug Therapy (2017)

- All recommendations are WEAK (low quality evidence)
- Sleep onset – zaleplon, triazolam, ramelteon
- Sleep maintenance – suvorexant, doxepin
- Combined – eszopiclone, zolpidem, temazepam
- Not recommended – trazodone, tiagabine, diphenhydramine, melatonin, valerian root, tryptophan**

Buyse. JAMA. 2017;318(20):1973-74.  
Medalie. JAMA. 2017;317(7):762-63.  
Sateia. JCSM. 2017;13(2):307-49.

## What do the Guidelines Say?

### VA/DoD Practice Guidelines 2019

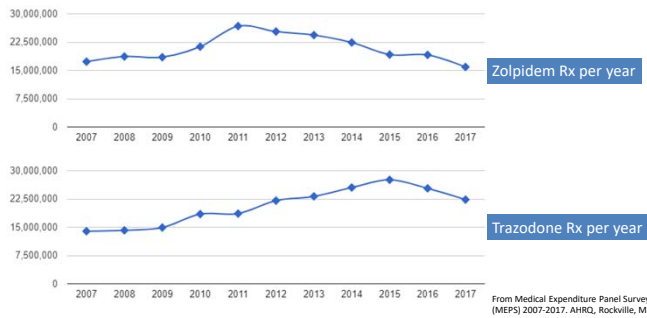
- Updates:
  - May offer BBT-I in place of CBT-I
  - Suggest against sleep hygiene as standalone treatment
  - Suggest offering auricular acupuncture

### On Drug Therapy

- Majority of recommendations are WEAK (low quality evidence)
- Recommend doxepin, BZRAs
- Recommend neither for or against ramelteon, suvorexant
- Recommend against kava, chamomile, antipsychotics, **benzodiazepines**

Mysliwiec. Ann Intern Med. 2020;172(5):325-36.

## Prescribing Trends



## What Explains the Rx Pattern?

### Zolpidem

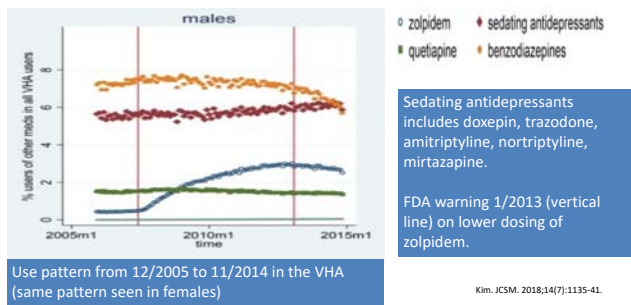
- 12/16/1992: approved for use
- 2006 to 2009: media coverage of bizarre sleep related behaviors
- 2007: FDA warns of complex sleep-related behaviors with use
- 1/10/13: FDA requests to lower initial dose by half
- 4/30/19: FDA adds boxed warning for complex sleep behaviors

### Trazodone

- 1981: approved for use
- Most commonly used insomnia medication
- Being substituted for zolpidem circa 2013

From FDA.gov Drug Safety Communication

## What Explains the Rx Pattern?



## Zolpidem Prescribing Needs Attention

### 2015 MEPS in adults

- 3.8 million adults (18 to 85 years old) reported zolpidem use.
- 65% female
- 78% users ≥ 45 years old
- Sustained use is >60 days

Table 2. Increased Risks Among Zolpidem Users

Increased Risk	Zolpidem Users, % (95% CI)
Sustained use	68.2 (62.5-73.9)
Higher dose	
Female	68.0 (60.7-75.3)
Age ≥65 y	64.0 (53.0-75.0)
Other CNS depressant use <sup>a</sup>	41.4 (34.9-47.9)
Opioid	26.5 (21.8-31.2)
Benzodiazepine	20.3 (16.8-23.8)
≥2 Safety issues	77.4 (70.5-84.3)

Abbreviation: CNS, central nervous system.

<sup>a</sup> Sustained use: more than 1 medication possible.

Moore. JAMA Intern Med. 2018;178(9):1275-77.



## Non-BZ BZRA vs. Traditional BZ

### Non-BZ BZRA

- FDA indication for insomnia
- "Safer" side effect profile
- Less adverse effect on sleep architecture
- Less rebound insomnia on discontinuation
- Be cognizant of parasomnias

### Traditional BZ

- FDA indication for insomnia
- Avoid per guidelines
- Unfavorable effect on sleep architecture
- Greater risk of falls, motor & cognitive impairment (Alzheimer's association), respiratory depression, rebound insomnia

Association with mortality or cancer (stronger at higher doses).

Billotti de Gage. *BMJ*. 2014;349. Kripke. *BMJ Open*. 2012;2(1).

## Non-BZ Benzodiazepine Receptor Agonists

Drug	T <sub>max</sub> (hours)	Elimination T <sub>1/2</sub> (hours)	Usual Dose (mg)	Approved for Insomnia	Comments
Zaleplon	1 (0.5–2)	1 (0.8–1.3)	5–20	Yes	Shortest-acting BzRA. ~30% may have unpleasant taste
Eszopiclone	1.5 (0.5–2)	6 (5–8)	1–3	Yes	
Zolpidem	1.6 (0.5–1.5)	2.5 (1.4–4.5)	5–10	Yes	Most widely-prescribed
Zolpidem: Extended Release	1.5 (1.5–2.0)	2.8 (1.6–4.5)	6.25–12.5	Yes	Higher concentrations 3–8 hours post dose than regular zolpidem
Zolpidem: Sublingual (Intermezzo®)	0.6 (0.6–1.3)	2.5 (1.4–3.6)	1.75–3.5	Yes	Use after middle of night awakening (2-4h remaining sleep time)
Zolpidem: Sublingual (Eduar®)	1.4 (0.5–3.0)	2.7 (1.5–6.7)	5–10	Yes	Mainly absorbed via GI tract
Zolpidem: Oral Spray (Zolpimist®)	0.9	2.8 (1.7–8.4)	5–10	Yes	Bioequivalent to tablets in terms of C <sub>max</sub> , T <sub>max</sub> , T <sub>1/2</sub>

Buyse. *JAMA*. 2013;309(7):706-16.

## Traditional Benzodiazepines

Drug	T <sub>max</sub> (hours)	Elimination T <sub>1/2</sub> (hours)	Usual Dose (mg)	Approved for Insomnia
Triazolam	1–2	2–6	0.125–0.25	Yes
Temazepam	1–2	8–22	7.5–30	Yes
Estazolam	1.5–2	10–24	0.5–2	Yes
Quazepam	2–3	48–120	7.5–15	Yes
Flurazepam	1.5–4.5	48–120	15–30	Yes
Alprazolam	0.6–1.4	6–20	0.25–1	No
Lorazepam	0.7–1	10–20	0.5–2	No
Clonazepam	1–2.5	20–40	0.5–2	No

Buyse. *JAMA*. 2013;309(7):706-16.

## Antidepressants

### Trazodone

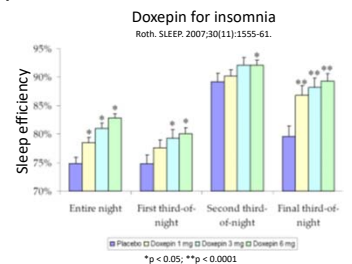
- Most commonly prescribed
- Low quality evidence on efficacy outweighed by risks

### Doxepin

- First approved in 1969
- Sleep maintenance indication in 2010
- Fair quality evidence with small to medium effect size vs. placebo

### Mirtazapine

- Exacerbates restless legs and sleep apnea (weight gain)



Yi. *Sleep Med*. 2018;45:25-32. Yeung. *Sleep Med Rev*. 2015;19:75-83.

## Sedating Antidepressants

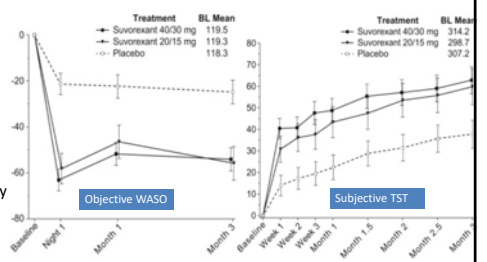
Drug	Drug class	t <sub>max</sub> (hours)	Receptor effects	t <sub>1/2</sub> in hours (range)	Usual dose (mg)	
					Antidepressant	Hypnotic
Doxepin	Tricyclic	1.5-4	Major: H <sub>1</sub> , α <sub>1</sub> Minor: M <sub>1</sub>	15 (10-30)	100-300	3-6 10-50
Amitriptyline	Tricyclic	2-5	Major: α <sub>1</sub> , M <sub>1</sub> Minor: H <sub>1</sub> , 5HT	30 (5-45)	100-300	10-100
Trimipramine	Tricyclic	2-8	Major: H <sub>1</sub> , α <sub>1</sub> Minor: M <sub>1</sub>	25 (7-15)	100-300	25-150
Trazodone	Phenylpiperazine	1-2	α <sub>1</sub> , 5HT	9 (7-15)	200-600	25-100
Nefazodone	Phenylpiperazine	1	α <sub>1</sub> , 5HT	3 (6-18)	150-600	50-150
Mirtazapine	Noradrenergic and specific serotonergic	1-3	Major: H <sub>1</sub> Minor: 5HT	30 (20-40)	15-45	7.5-15

Adapted from Buyse. *JAMA*. 2013;309(7):706-16 and Tyagi & Buyse, Chapter in PPSM 6<sup>th</sup> Edition.

## The Dual Orexin Receptor Antagonists (DORA)

### Suvorexant

- First in class
- Well tolerated (side effects are fatigue and headache)
- Avoid with other CNS depressants
- Contraindicated in narcolepsy (exceedingly rare side effect)
- Class IV controlled substance (theoretical low abuse potential)

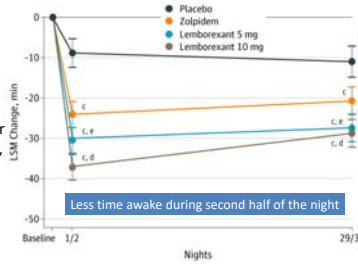


Patel. *Ann Pharmacother*. 2015;49(4):477-83. Herring. *Biol Psychiatry*. 2016;79(2):136-48.

## The Dual Orexin Receptor Antagonists (DORA)

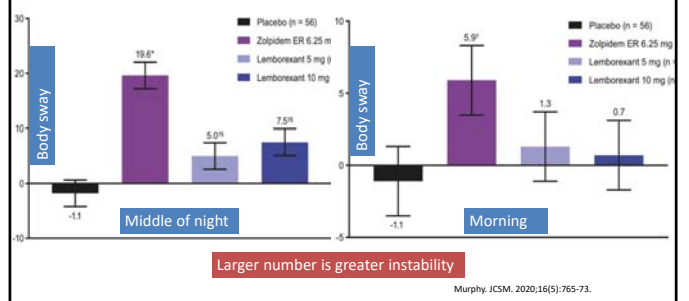
### Lemborexant

- Pivotal SUNRISE 1 phase 3 trial (n = 1,006) over 1 month showed sustained improvement in objective and subjective measures of sleep onset and maintenance without major adverse events (sleepiness, headache, abnormal dreams, sleep paralysis)
- Small study of n = 39 showed no worsening of mild OSA after lemborexant 10 mg vs. placebo
- Take at least 7 hours before planned wake time



Rosenberg. JAMA Netw Open. 2019;2(12):e1918254.  
Cheng. J Sleep Res. 2020:e13021.

## Postural Sway from Lemborexant vs. Zolpidem



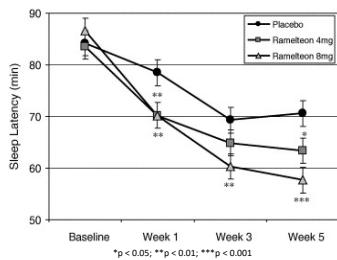
## What About Melatonin?

### Melatonin

- Most commonly used OTC agent in USA
- Endogenous hormone secreted at night
- No definitive dose (0.1 to 10 mg) or formulation (IR, SR/CR, PO, sublingual)
- Low potency, rare side effects

### Ramelteon

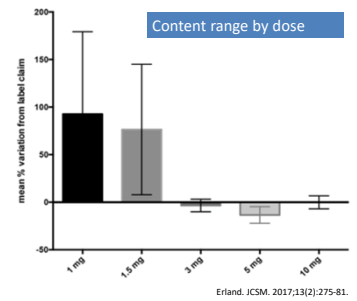
- Approved for insomnia in 7/22/05
- Improves sleep latency only
- No withdrawal
- Side effects mild (headache, dizziness, GI upset, taste disturbance)



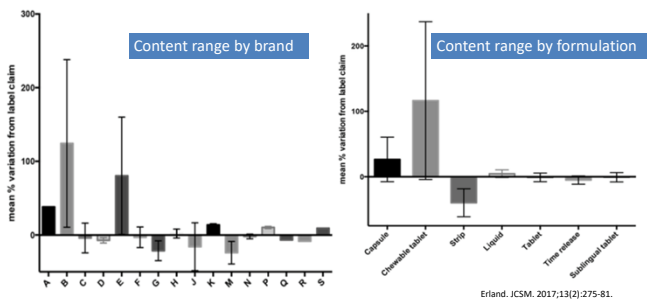
Roth. Sleep Med. 2005;7(4):312-8.

## Melatonin - an Unregulated Dietary Supplement

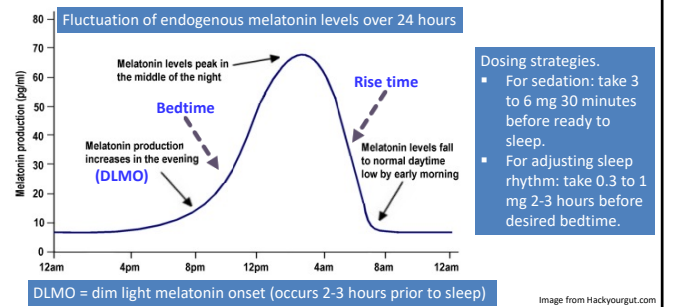
- Analysis of 31 supplements from 30 commercial sources.
- 71% of products did not meet label claim.
- 26% of products contained serotonin.
- Other ingredients may include lavender, chamomile, lemon balm, valerian, passion flower, skullcap, hops.



## Melatonin - an Unregulated Dietary Supplement



## What Time to Take Melatonin?



## Sedating Antihistamines

- Widely available as OTC or prescription
- Centrally acting agents on Beers criteria
- Little data to support use
- Anticholinergic side effects most profound in older patients

Avoid in patients ≥ 65 years old



Diphenhydramine, doxylamine, dimenhydrinate, hydroxyzine\*, meclizine, etc

## Miscellaneous Drugs

Drug	T <sub>max</sub> (hours)	Elimination T <sub>1/2</sub> (hours)	Usual Dose (mg)	Drug class	Comments
Suvorexant	2 (0.5–6)	9–13	10–20	DORA	First in class, 8/2014
Lemborexant	1–3	17–19	5–10	DORA	Approved 12/2019
Melatonin	0.3–1	0.6–1	0.5–6	MT <sub>1</sub> RA, MT <sub>2</sub> RA	Dietary supplement, <b>chronotropic agent</b>
Ramelteon	0.75 (0.5–1.5)	1–2.6	8	MT <sub>1</sub> RA >> MT <sub>2</sub> RA	Improves sleep latency
Diphenhydramine	2–2.5	4–8	25–50	H <sub>1</sub> RAnt, M <sub>1</sub> RAnt	Anticholinergic effect
Doxylamine	2–3	10	25	H <sub>1</sub> RAnt, M <sub>1</sub> RAnt	Anticholinergic effect
Hydroxyzine	2	20	25–50	H <sub>1</sub> RAnt	Minimal effect on M <sub>1</sub> RAnt
Quetiapine	1–2	6	25–50	Dibenzothiazepine atypical antipsychotic	Anticholinergic, weight gain, metabolic disturbance

Adapted from Buysse. JAMA. 2013;309(7):706-16.

## What's Not Recommended



Kava kava (significant risk of liver toxicity)

Chamomile (common tea preparations)



Valerian root (liver toxicity, withdrawal)



Alcohol (acute use reduces sleep latency, chronic use without benefits, resp. depression)



Opioids (addiction, resp. depression, drug interactions, disrupts sleep architecture)

Images from: nccih.nih.gov; seedcorner.com; salembotanicals.com; mumbaiirelandindiatimes.com; pilotonline.com

## Marijuana

### Cannabinoids

- Cannabidiol (CBD) promotes relaxation
- Cannabinol (CBN) has sedative effects
- Tetrahydrocannabinol (THC) is psychoactive

### Strains

- Sativa stimulates and energizes
- Indica relaxes and promotes sleep
- Hybrid strains

### Terpenes

- Give cannabis its smell and taste
- Ubiquitous in natural plants and fruits
- May enhance effects of cannabinoids and sleep

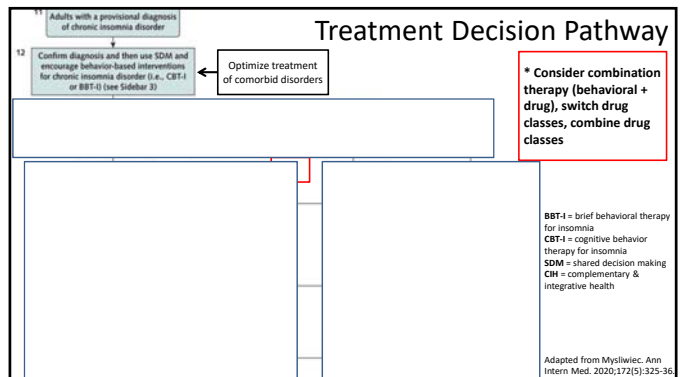
### Formulations

- Vaporized
- Edibles & beverages
- Oils & tinctures
- Pills & topicals

Images from: livescience.com; vectorstock.com

## Final words

## Treatment Decision Pathway



## Clinical Pearls

### For insomnia

- Very common diagnosis
- Sleep diary and trackers are very useful
- Effective treatment takes a concerted effort from patient and provider**
- Do NOT forget to address secondary or comorbid conditions

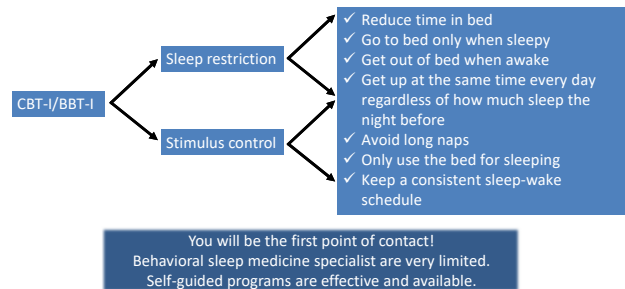
### For medications

- Tailor to patient preference, timing of symptoms, comorbidities
- Strive for shortest duration, lowest dose, shorter half-life drug**
- OK for sustained use (acute insomnia), intermittent use (if chronic user)
- Low dose combination therapy is OK
- Be cognizant of side effects

### For CBT-I/BBT-I

- First line intervention with most robust evidence**
- Consider concurrent CBT-I with drug therapy
- Taper drugs during or after CBT-I
- CBT-I may simultaneously improve comorbid mood disorders

## Final Thoughts...



## Provider & Patient Education Materials

Resource	URL
Annals of Internal Medicine: Summary of Veterans Affairs and Department of Defense Practice Guidelines (2019)	<a href="https://www.acpjournals.org/doi/10.7326/M19-3573">https://www.acpjournals.org/doi/10.7326/M19-3573</a>
AASM Practice Guidelines for Pharmacologic Treatment of Insomnia (2017)	<a href="https://aasm.org/resources/pdf/pharmacologic_treatment_of_insomnia.pdf">https://aasm.org/resources/pdf/pharmacologic_treatment_of_insomnia.pdf</a>
JAMA Clinical Review of Insomnia Diagnosis and Treatment (2013)	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC362369/#R49">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC362369/#R49</a>
Patient Education on Insomnia from American Thoracic Society (ATS)	<a href="http://www.thoracic.org/patients/patient-resources/resources/insomnia.pdf">http://www.thoracic.org/patients/patient-resources/resources/insomnia.pdf</a>
CBT-I Slide Set (from Anxiety and Depression Association of American )	<a href="https://adaa.org/sites/default/files/Bunko_177.pdf">https://adaa.org/sites/default/files/Bunko_177.pdf</a>
CBT-I coach (phone based application)	<a href="https://mobile.va.gov/app/cbt-i-coach">https://mobile.va.gov/app/cbt-i-coach</a>
Self-guided CBT-I workbook for Veterans (companion to CBT-I coach app)	<a href="https://www.mirecc.va.gov/docs/vism6/Improve_Your_Sleep_Self-Guided_Approach_for_Veterans_with_Insomnia-March-2017.pdf">https://www.mirecc.va.gov/docs/vism6/Improve_Your_Sleep_Self-Guided_Approach_for_Veterans_with_Insomnia-March-2017.pdf</a>

Thank You & Questions?

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