Evaluation and Management of Sleep Disorders

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Project ECHO®

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Objectives

- To define insomnia
- To identify potential predisposing, precipitating and perpetuating factors of insomnia
- To discuss non-pharmacological and pharmacological management of insomnia

“A Sleepless Case…"

- 54 year old man with history of **MDD**, **PTSD** and possible PNES, multiple medical comorbidities including HTN, DM, GERD, **sleep apnea**, **chronic pain** and headaches, referred by PCP for evaluation and management of ongoing symptoms of depression, anxiety, and **insomnia**

- Patient was admitted to the **ICU with COVID** in Feb. 2020 and spent **over 1 month in the hospital**, followed by rehab facility

- Patient reports this was a deeply **traumatic experience** for him as he "almost died 3 times" and **does not recall much of his hospital admission** aside from experiencing severe pain, having a pulmonary embolus and having to start **dialysis** for renal failure

What stands out so far as possible etiologies and perpetuating factors of this patient’s insomnia?

“A Sleepless Case…” (Continued)

- Patient states that since discharge from the hospital, he has "not been the same.”
- Suffers from **chronic fatigue**, **pain** and numbness, **limited mobility**, poor sleep, **frequent nightmares** and **depressed** and **anxious** mood.
- Patient reports he feels "trapped in [his] body," and is struggling with the notion that he will **never be as active as he used to be again**.
- Patient reports he still enjoys listening to music, watching TV and growing plants in his apartment.
- He reports he is close to his roommate, but explains that **she is suffering from cancer and it is "painful to watch."**
- Patient reports he is in contact with family and enjoys talking on the phone with his niece. He also endorses faith in God, and though he admits to having fleeting passive death wishes when overwhelmed, he adamantly denies any active SI or HI.
- He denies any flashbacks or hypervigilance, is able to attend medical appointments near or in the hospital and is adherent to his medications and follow up.
- He reports **he is unable to use his CPAP machine because it "burns [his] sinuses."**
- Patient denies any audio-visual hallucinations, symptoms of mania or psychosis.
- He reports **vaping cannabis** infrequently to "relax," however, **denies use of alcohol or any illicit substances**.

Any additional factors possibly contributing to this patient’s insomnia?

“A Sleepless Case…” (Continued)

- Medications
  - Tylenol, Topamax, Keppra, **Lyrica**, **Lexapro**, **Elavil**, Lipitor, Singulair, Prilosec, Lidocaine patch, naproxen, Lisinopril
- Labs and imaging
  - **TSH wnl** in 2020, LFTs elevated, HbA1c 6.6, B12 not available, EKG last done in 2020; QTc 429 ms, MRI Brain (2019) no evidence of acute intracranial abnormality or abnormal enhancement.
- Sleep study ordered but not completed
- Diagnosis
  - Adjustment disorder with mixed anxiety and depressed mood, R/o MDD, R/o GAD, PTSD, Cannabis use disorder, mild, abuse, insomnia disorder

What would be your initial plan to address this patient’s insomnia?

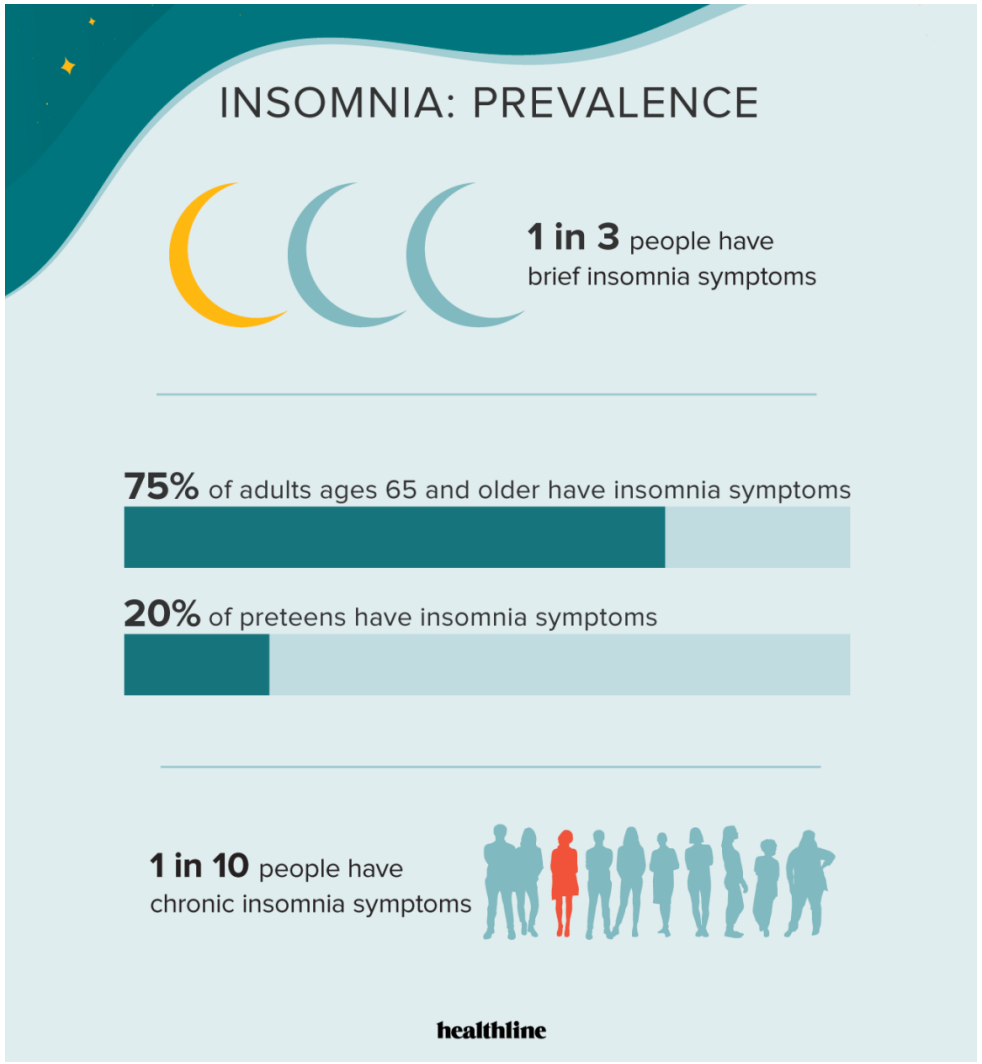
Poll Question #1

What would be your initial plan to address this patient's insomnia?

- Start a low-dose benzodiazepine
- Explore patient's bedtime routine
- Start low-dose mirtazapine
- Refer for sleep study

Defining Insomnia

- Insomnia = adequate sleep opportunity + persistent sleep difficulty + daytime dysfunction
- One of the *most common medical complaints* (6-10% adults meet diagnostic criteria for insomnia)
- Co-exists with other disorders – medical, psychiatric, neurological
- May also be associated with environmental factors, substances / medications, poor sleep hygiene
- Can be short-term or chronic (> 3 months)
- More common in women and older adults



Clinical Features of Insomnia

- Difficulty initiating or maintaining sleep
- Compromised daytime function (fatigue, poor attention, irritability, etc.)
- *Note: *excessive daytime sleepiness* (actually falling asleep at unwanted or unintended times during the day) may be indicative of comorbid sleep disorder.

Table 1. DSM-V Criteria for Insomnia Disorder

- Complaint of dissatisfaction with quantity or quality of sleep occurs at least 3 nights a week for at least 3 months, associated with one or more of the following:
  - Difficulty falling asleep
  - Difficulty staying asleep, with frequent awakenings or difficulty falling back asleep
  - Early morning awakening
- The sleep disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- The sleep disturbance occurs even when there is enough time for sleep
- The sleep disturbance does not occur exclusively during the course of narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia (an unusual behavior or event that occurs during sleep that may lead to intermittent awakenings).
- The sleep disturbance does not occur exclusively during the course of another mental disorder.
- The sleep disturbance is not due to the direct physiologic effects of a substance such as a drug of abuse or a medication, or from a general medical condition.

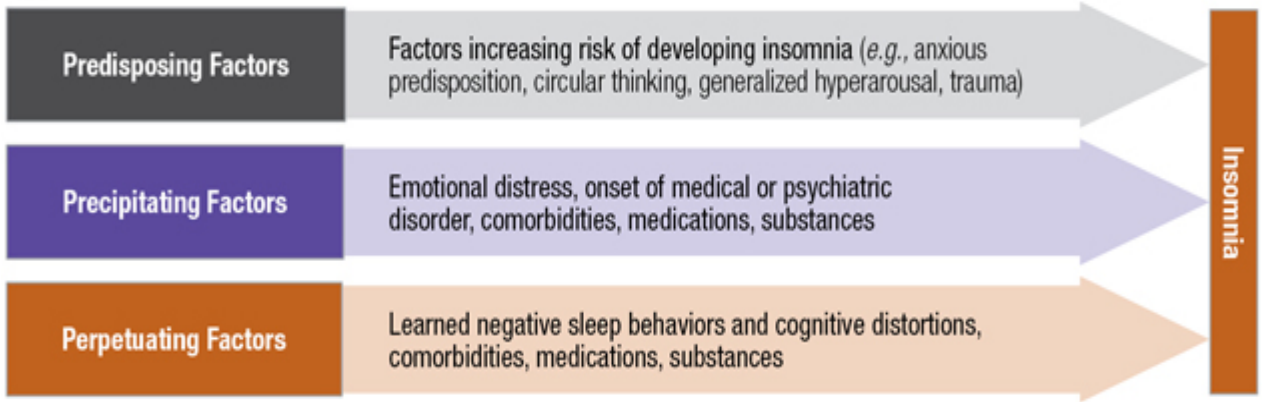
DSM-V, Diagnostic and Statistical Manual of Mental Disorders, 5th Ed.
Based on reference 4.

Evaluation

- **Sleep history**: amount, quality, timing, 'state of mind'
- Predisposing, precipitating and perpetuating factors

- International Classification of Sleep Disorders (ICSD-3)
  - Insomnia
  - Sleep-related breathing disorders (e.g. sleep apnea)
  - Central disorders of hypersomnolence (e.g. narcolepsy)
  - Circadian rhythm sleep-wake disorders (e.g. shift work disorder)
  - Parasomnias (e.g. sleep terrors, sleepwalking)
  - Sleep-related movement disorders (e.g. restless legs syndrome)
  - Others

Figure 2. **Clinical Aspects of Insomnia: The 3-P Model**[6,10]



Adapted from 1. Schutte-Rodin S, et al. J Clin Sleep Med. 2008;4(5):487-504; 2. MacFarlane J. Insomnia Rounds. 2012;1(2):1-6. 2008;4(5):487-504.

Predisposing / Precipitating Factors

- Social / medical / psychiatric events at onset of insomnia?
- Pain / nocturia / SOB → *optimize medical condition*
  - Suspected OSA → polysomnography, OSA management
- Trauma, chaotic environment, comorbid psychiatric conditions → *psychiatric and psychosocial intervention*
- **Medication side effects**
  - Stimulants
  - Antidepressants (dose SSRIs, SNRIs in the morning!)
  - Steroids
  - Opioids (though sedating, can fragment sleep with chronic use)
  - Benzodiazepines
- **Substances**

Perpetuating Factors

- **Poor sleep hygiene**
- Unrealistic expectations / perceptions of sleep
- Maladaptive coping with insomnia
- “Cycle” of anxiety

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Sleep Hygiene Guidelines

Recommendation	Details
Regular bedtime and rise time	Having a consistent bedtime and rise time leads to more regular sleep schedules and avoids periods of sleep deprivation or periods of extended wakefulness during the night.
Avoid napping	Avoid napping, especially naps lasting longer than 1 hour and naps late in the day.
Limit caffeine	Avoid caffeine after lunch. The time between lunch and bedtime represents approximately 2 half-lives for caffeine, and this time window allows for most caffeine to be metabolized before bedtime.
Limit alcohol	Recommendations are typically focused on avoiding alcohol near bedtime. Alcohol is initially sedating, but activating as it is metabolized. Alcohol also negatively impacts sleep architecture.
Avoid nicotine	Nicotine is a stimulant and should be avoided near bedtime and at night.

Source: UpToDate

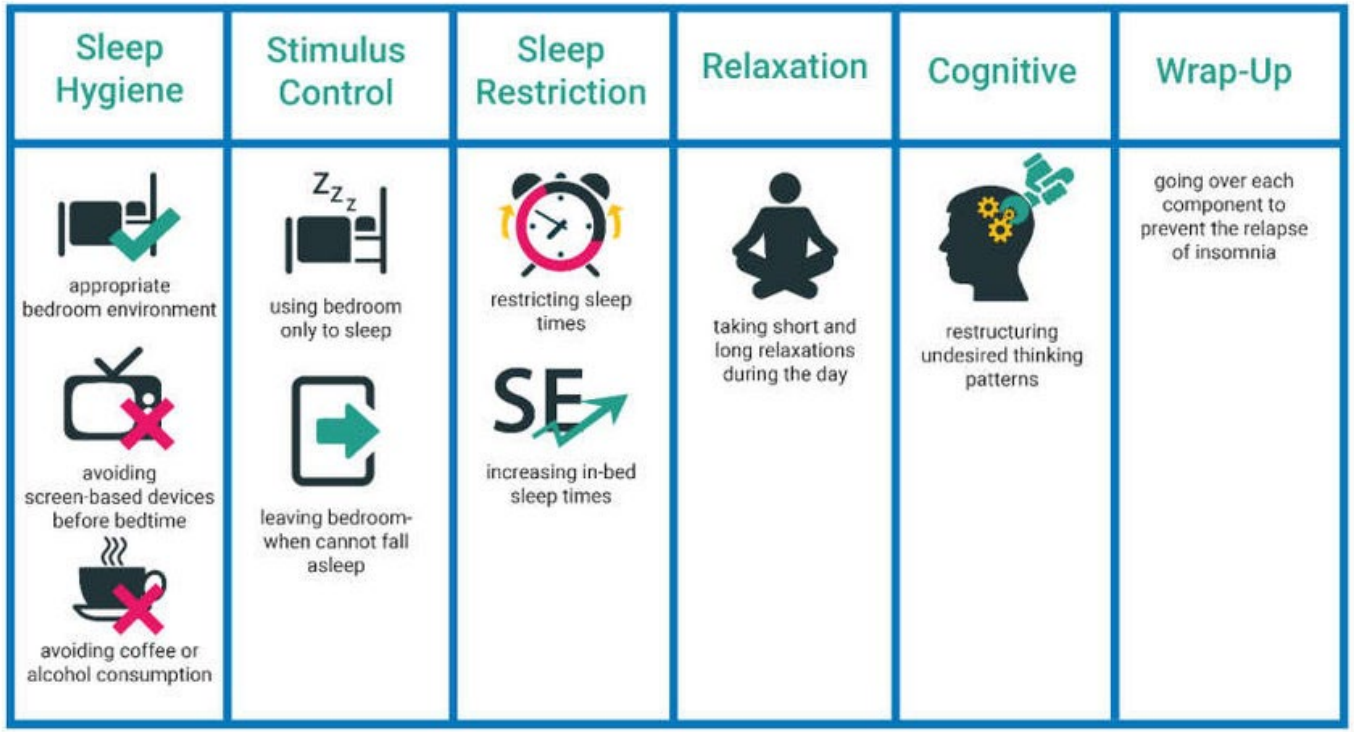
Sleep Hygiene Guidelines (continued)

Recommendation	Details
Exercise	Daytime physical activity is encouraged, in particular 4 to 6 hours before bedtime, as this may facilitate sleep onset. Rigorous exercise within 2 hours of bedtime is discouraged.
Keep the sleep environment quiet and dark	Noise and light exposure during the night can disrupt sleep. White noise or ear plugs are often recommended to reduce noise. Using blackout shades or an eye mask is commonly recommended to reduce light. This may also include avoiding exposure to television or technology near bedtime, as this can have an impact on circadian rhythms by shifting sleep timing later.
Bedroom clock	Avoid checking the time at night. This includes alarm clocks and other time pieces (e.g., watches and smart phones). Checking the time increases cognitive arousal and prolongs wakefulness.
Evening eating	Avoid a large meal near bedtime, but don't go to bed hungry. Eat a healthy and filling meal in the evening and avoid late-night snacks.

Source: UpToDate

When all of the above has been addressed…

- Consider psychotherapy +/- pharmacotherapy.
- **Cognitive behavioral therapy for insomnia (CBT-I)** generally safer and more effective than medications!
  - The American College of Physicians "… *recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder."*
  - Online apps available, e.g. ***CBT-I Coach*** from the National Center for PTSD



American College of Physicians Guidelines

This guideline is based on a systematic review of randomized, controlled trials published in English from 2004 through September 2015.

Recommendation 1

ACP recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder.

*(Grade: **strong recommendation, moderate-quality evidence**)*

Recommendation 2

ACP recommends that clinicians use a shared decision-making approach, including a discussion of the benefits, harms, and costs of short-term use of medications, to decide whether to add pharmacological therapy in adults with chronic insomnia disorder in whom cognitive behavioral therapy for insomnia (CBT-I) alone was unsuccessful.

*(Grade: **weak recommendation, low-quality evidence**)*

https://doi.org/10.7326/M15-2175

But, nonetheless, we prescribe…

Poll Question #2

Which of the following do you prescribe most frequently for management of insomnia?

- Benzodiazepines
- Sedating antidepressants
- Melatonin or Ramelteon
- CBT-i

PHARMACOTHERAPY: Four General Categories

Benzodiazepine Receptor Agonists	Dual Orexin Receptor Antagonists	Histamine Receptor Antagonists	Melatonin Receptor Agonists
Non-benzodiazepine Eszopiclone (**Lunesta**) – long half-life, about 6 hours. Zaleplon (**Sonata**) – short half-life, about 1 hour. Zolpidem (**Ambien**) – intermediate half-life, about 1.5 – 4.5 hours. Benzodiazepine hypnotics Estazolam, flurazepam, quazepam, triazolam, etc *** ***virtually no reason to start with these due to dependence, habituation, daytime sedation, falls, confusion, etc.***	Lemborexant Suvorexant (**Belsomra**) Daridorexant	Doxepin (**Silenor**) is a TCA approved for sleep-maintenance insomnia at low doses (3mg – 6mg)	**Ramelteon** 8 mg – promotes circadian rhythm, used for sleep onset but not maintenance.

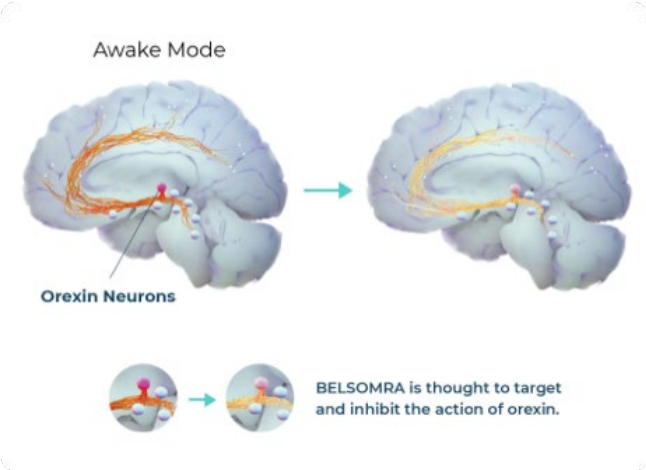


Table 1

Suvorexant: Fast facts

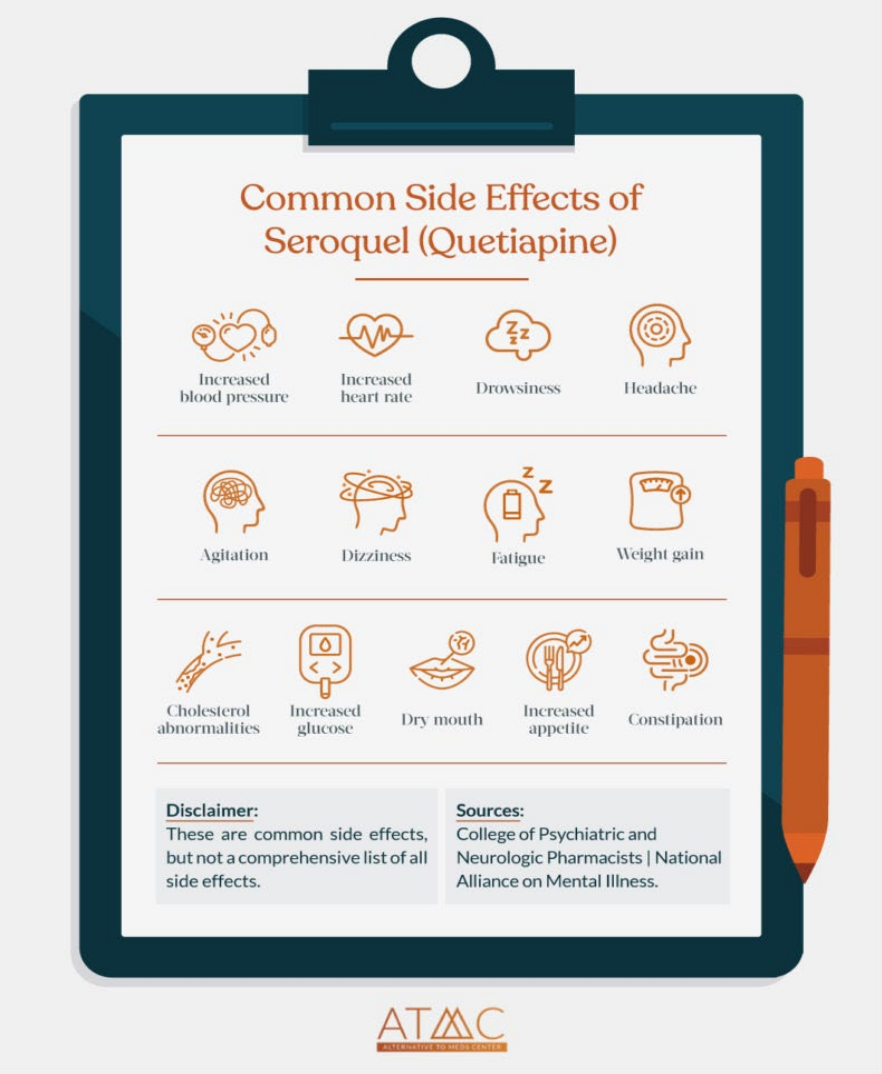
Brand name: Belsomra
Class: Dual orexin-receptor antagonist
Indication: Insomnia characterized by difficulty with sleep onset or sleep maintenance, or both
FDA approval date: August 13, 2014
Availability date: Early 2015
Manufacturer: Merck
Dosage forms: 5 mg, 10 mg, 15 mg, and 20 mg tablets
Recommended dosage: 10 mg taken only once within 30 minutes of going to bed, with at least 7 hours remaining before the planned time of awakening
Source: Reference 1

Antidepressants for Insomnia

- **Doxepin, amitriptyline, trazodone, mirtazapine**
- Sedation due to serotonergic (5-HT2A), muscarinic, and histaminic receptor blockade
- Risk-benefit ratio? *Serotonin syndrome, arrhythmia, orthostatic hypotension and syncope, increased bleeding risk, priapism (trazodone), mania/hypomania, hyponatremia, glaucoma, urinary retention, etc*.

Other "Off-Label" Prescriptions

- Antiepileptics: *gabapentin* – limited evidence, may be helpful in alcohol use disorders
- Antihypertensives: *clonidine* – especially in children, adolescents
- Antipsychotics: *quetiapine* (Seroquel) 25 – 100 mg; do **NOT** use when there is no comorbid psychiatric disorder (psychotic or bipolar illness)
- Anxiolytics: limited evidence for *alprazolam, clonazepam, lorazepam*; may be used as bridge in patients with insomnia 2/2 anxiety



Medication Selection

- Highly individualized

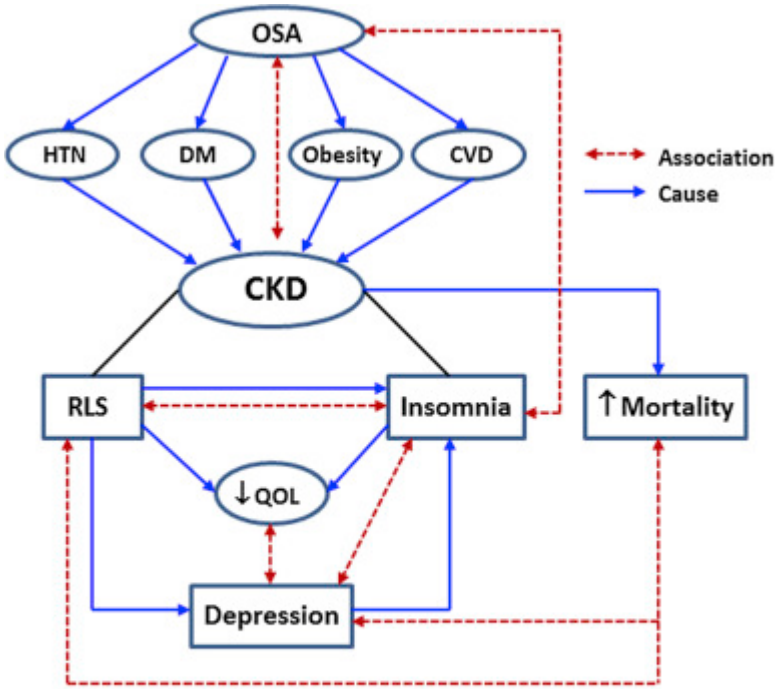
- Consider comorbid conditions – medical and psychiatric!
  - Avoid benzodiazepines in elderly, comorbid substance use disorders
  - Consider sedating antidepressant in patients with depression/anxiety

- Keep in mind that most patients do not experience full remission of symptoms with medications alone, and most medications (especially benzodiazepines) are intended for short-term use.

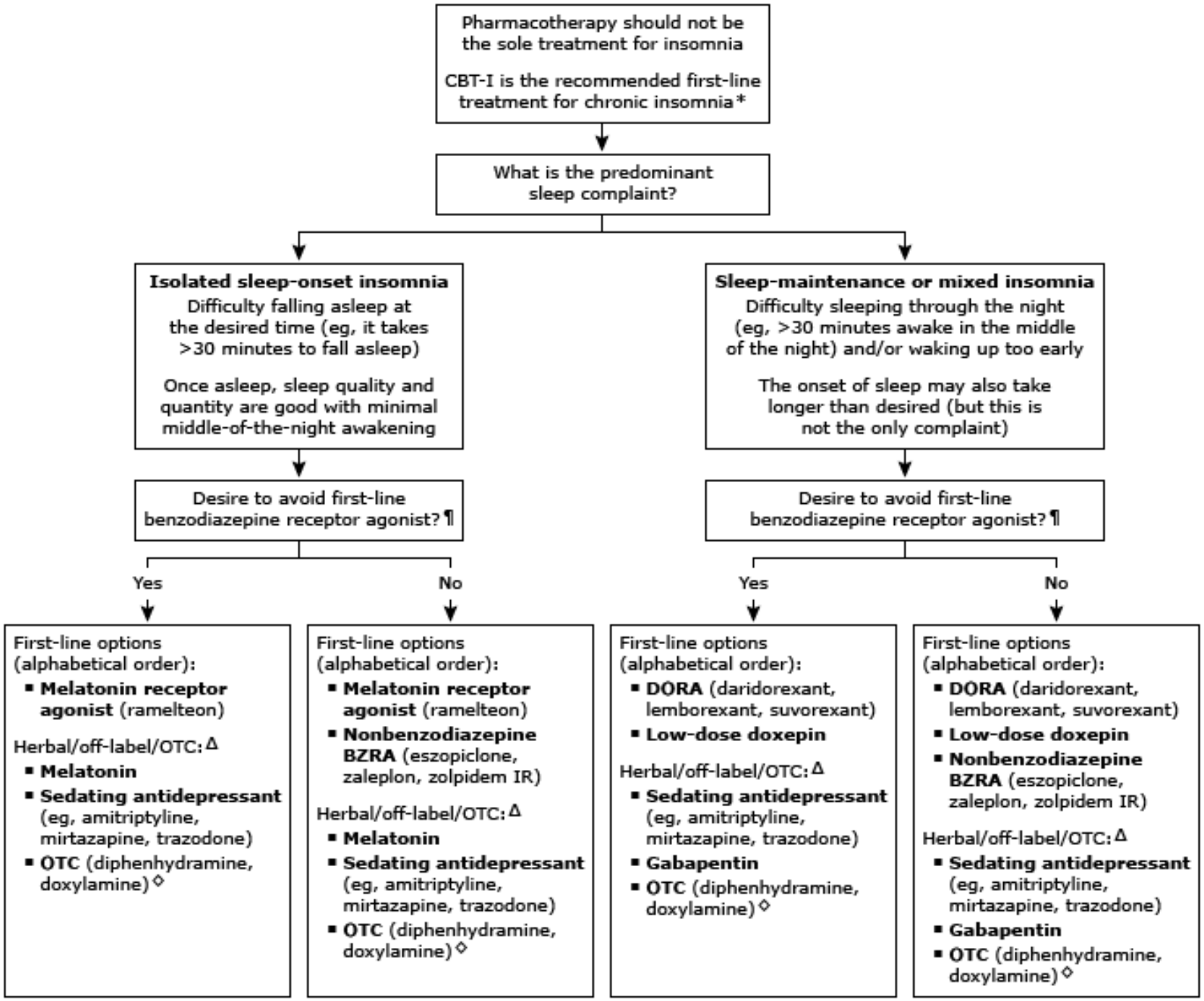
  Non-pharmacological interventions MUST be utilized (e.g., sleep hygiene tactics and cognitive behavioral therapy)!

Special Considerations

- **Older adults**: decreased hepatic metabolism, increased risk of adverse drug reactions → sedation, cognitive impairment, delirium, falls
- **Substance use disorders**: additive effects; consider contribution
- **Comorbid psychiatric disorders**: treat underlying depression, anxiety, bipolar disorder, etc.
- **Hepatic impairment and renal impairment**: consider reduced clearance of medications, increased risk of adverse effects
- **Neurocognitive disorders**: circadian rhythm disturbances, risk of delirium; **avoid benzos, anticholinergic agents**
- **Comorbid sleep disorders**:
  - OSA: CPAP adherence, short-term sedatives
  - Restless leg syndrome: treat with gabapentin/pregabalin, possibly dopamine agonists; serotonergic agents can exacerbate symptom
- **Pain, pregnancy, menopause**



Abbreviations: OSA= obstructive sleep apnea; HTN = hypertension; DM = diabetes; CVD = cardiovascular disease; CKD = chronic kidney disease; RLS = restless leg syndrome; QOL = quality of life



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So what happened to our sleepless case?

Plan:

- **Increase Lexapro** to 25 mg PO daily
- **Start melatonin** 3 mg PO bedtime for insomnia and circadian rhythm regulation
- **Education** regarding sleep hygiene provided
- **Referral** for cognitive behavioral therapy and behavioral activation with depression care management
- Will **coordinate with PCP** to address barriers to CPAP adherence


THANK
YOU