

How Would You Manage This Patient With Chronic Insomnia?

Grand Rounds Discussion From Beth Israel Deaconess Medical Center

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Insomnia, which is characterized by persistent sleep difficulties in association with daytime dysfunction, is a common concern in clinical practice. Chronic insomnia disorder is defined as symptoms that occur at least 3 times per week and persist for at least 3 months. The American Academy of Sleep Medicine (AASM) published recent guidelines on behavioral and psychological treatment as well as pharmacologic therapy for chronic insomnia disorder. Regarding behavioral and psychological approaches, the only intervention strongly recommended was multicomponent cognitive behavioral therapy for insomnia. Regarding pharmacologic treatment, the AASM, based on weak evidence, suggested a limited number of medications that might be useful and others that probably are not. Here, 2 clinicians with expertise in sleep disorders—one a clinical psychologist and the other a physician—debate the management of a patient with chronic insomnia who has been treated with medications. They discuss the role of behavioral and psychological interventions and pharmacologic therapy for chronic insomnia and how the primary care practitioner should approach such a patient.

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ABOUT BEYOND THE GUIDELINES

Beyond the Guidelines is a multimedia feature based on selected clinical conferences at Beth Israel Deaconess Medical Center (BIDMC). Each educational feature focuses on the care of a patient who “falls between the cracks” in available evidence and for whom the optimal clinical management is unclear. Such situations include those in which a guideline finds evidence insufficient to make a recommendation, a patient does not fit criteria mapped out in recommendations, or different organizations provide conflicting recommendations. Clinical experts provide opinions and comment on how they would approach the patient's care. Videos of the patient and conference, the slide presentation, and a CME/MOC activity accompany each article. For more information, visit Annals.org/GrandRounds.

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Mr. F is a 64-year-old man who has experienced insomnia for decades. He reports difficulty getting to sleep and early morning awakening. He has tried traditional sleep hygiene measures as well as over-the-counter sleep aids, which were not helpful. He was prescribed zolpidem many years ago, which was initially taken as needed but now is a daily necessity to get to sleep. More recently, trazodone was added to his regimen. He does not report feeling groggy on awakening or any other side effects.

Mr. F was diagnosed 10 years ago with obstructive sleep apnea (OSA) on a home sleep study, with an apnea-hypopnea index of 9.2 (mild severity). A trial of auto-continuous positive airway pressure (CPAP) was advised but was never implemented by the patient. He does not currently describe snoring or abnormal breathing during sleep. His medical history is also noteworthy for anemia, benign prostatic hyperplasia, chronic renal insufficiency, diabetes mellitus, erectile dysfunction, gout, hypercholesterolemia, and hypertension. His medications include allopurinol, amlodipine, hydrochlorothiazide, oxybutynin, tamsulosin, trazodone (50 mg at bedtime), and zolpidem (10 mg at bedtime, as needed). He developed renal dysfunction while taking lisinopril but does not have any history of other adverse reactions to drugs.

Mr. F consumes alcohol (2 to 3 drinks) daily, but he reports no other substance use. He has a remote history of cigarette smoking. He has mild anxiety much of the time related to life issues but has not been diagnosed with an anxiety or depressive disorder.

Mr. F worked for many years as a firefighter, and his hours were irregular, including some overnight shifts. He more recently retired but works occasionally for a ride-sharing company.

Physical examination is noteworthy for blood pressure of 128/82 mm Hg, pulse of 72 beats/min and regular, unlabored respirations, and weight of 189.7 pounds with body mass index of 29.7 kg/m². Findings on examination of his head and neck, heart, lungs, abdomen, and extremities are within normal limits.

Laboratory studies show a complete blood count with hematocrit of 38.7%, glucose level of 124 mg/dL (6.9 mmol/L), blood urea nitrogen/creatinine level of 16/1.4 mg/dL (5.7/123.3 mmol/L), normal liver function test results and normal uric acid level, hemoglobin A_{1c} of 6.5%, and cholesterol level of 247 mg/dL (6.4 mmol/L) with low-density lipoprotein level of 143 mg/dL (3.7 mmol/L).

MR. F'S STORY (VIDEO AT ANNALS.ORG)

See the patient video (Video 1, available at Annals.org) to view the patient telling his story.

I've experienced insomnia for the past couple of decades. It's not something that's going to happen every day, but I would say it happens 90% of the time. I do have a problem with getting up early in the morning. I could get 5 hours of straight sleep and then I wake up in the morning and then I can go back to sleep for 2 hours. Some of the strategies that I tried before I was on zolpidem included over-the-counter medications, but they didn't work very well because they just kept me groggy and would never put me to sleep. Other things that I would try to get myself to sleep would be not eating so late or just going to bed a little bit earlier. I wasn't taking zolpidem every night because my job entailed me handling heavy equipment, so the nights I had to work all night I wouldn't touch the zolpidem at all. Now that I am retired, I do use zolpidem every night.

What I do feel is a lot of anxiety. And that is generally what I think is keeping me awake at night. I don't know if it's called restless leg syndrome or I just can't position myself in the right way, but I end up twisting and turning until the medication kicks in and I am done and I am okay after that. It's a lot of things that you get bombarded by, which is causing this anxiety, which would be the COVID-19 pandemic, Black Lives Matter, the economy, everything is running through my head, and it's hard for me to just shut it off.

I do use alcohol, and I use it for recreation. I have about 2 to 3 drinks per day.

I started working as a firefighter back in 1985. I couldn't sleep on a regular basis because every day would be different.

I look at a lot of programs on TV and they tell you to get 8 hours of rest. I am 64 years old, I have been hearing that the whole time, and I am wondering if something is wrong with me because I am only getting 5 hours and I need the help from the zolpidem just to get the 5 hours,

so to me, when other people would refer to it as "normal," this is normal for me, 5 to 6 hours.

CONTEXT, EVIDENCE, AND GUIDELINES

Insomnia is a common concern in clinical practice. Chronic insomnia disorder is defined as difficulty falling asleep and/or staying asleep occurring at least 3 times per week and persisting for at least 3 months (1). Insomnia can result in compromised daytime function, which may include sleepiness, fatigue or malaise, poor attention or concentration, mood disturbance or irritability, reduced motivation or energy, increased errors or accidents, and ongoing worry about sleep.

The American Academy of Sleep Medicine (AASM) published recent guidelines on behavioral and psychological treatment as well as pharmacologic therapy for chronic insomnia (2, 3). The AASM conducted a systematic review to identify randomized controlled trials and used the Grading of Recommendations Assessment, Development and Evaluation process to assess evidence. The task forces developed recommendations and assigned strengths based on the quality of evidence, the balance of benefits and harms, and patient values and preferences.

Regarding behavioral and psychological approaches (Table 1), the only intervention that the AASM *strongly recommended* was multicomponent cognitive behavioral therapy for insomnia (CBT-I) for the treatment of chronic insomnia disorder in adults. The authors assessed whether CBT-I improved patient-reported critical outcomes: insomnia remission rate, treatment responder rate, sleep quality, sleep latency, and wake after sleep onset (2). The authors identified 66 randomized controlled trials in adult patients diagnosed with chronic insomnia disorder that compared CBT-I to wait-list, minimal interventions, or placebo therapies. Forty-nine of the studies provided data suitable for meta-analyses for at least 1 critical outcome. Meta-analyses demonstrated clinically significant improvements in remission and responder rates with CBT-I compared with control conditions. Of these 49 studies, 11 included patients with insomnia and no comorbid conditions, 6 included patients with insomnia and comorbid psychiatric conditions, and 12 included patients with insomnia and comorbid medical conditions. Each of these patient groups was analyzed separately. Twenty studies included a mix of patients with and without comorbid conditions and were not separately analyzed.

Cognitive behavioral therapy for insomnia combines behavioral strategies, including stimulus control instructions and sleep restriction therapy, with cognitive therapy strategies, sleep hygiene education, and relaxation training and other counter-arousal methods. Treatment progresses using information typically gathered with sleep diaries completed by the patient throughout the course of treatment (typically 4 to 6 sessions). The authors conditionally suggested that clinicians *not* use sleep hygiene by itself, given lack of supporting efficacy data and the likelihood that this commonly used treatment would delay the initiation of an evidence-based approach (2).

Table 1. Cognitive Behavioral Therapy for Chronic Insomnia

Strategy	Description
Sleep restriction	Placing an initial limit on the amount of time permitted in bed, with the goal of helping patients reduce sleep onset latency and wake after sleep onset by increasing their homeostatic drive for sleep. Commonly guided by sleep efficiency, which is the ratio of total sleep time compared to time spent in bed, with a target of $\geq 85\%$ -90%.
Stimulus control	The patient's bed is no longer an effective discriminative stimulus for sleep because it has consistently been associated with other activities in bed, especially extended periods of non-sleep. This requires patients to limit the use of their bed to sleep (and sexual activity), and they must leave the bed if they cannot sleep for a predetermined duration (e.g., 15 minutes).
Cognitive therapy	Challenging and restructuring maladaptive and dysfunctional beliefs and attitudes that maintain insomnia. This includes modifying unrealistic expectations about sleep need, misattributions about the causes of insomnia, catastrophizing the effects of the consequences of insomnia, and dysfunctional beliefs about ways to improve sleep.
Sleep hygiene	There is no consensus as to what specifically comprises sleep hygiene, though these rules are generally guided by the overarching principles to avoid sleep interfering behaviors and to increase the practice of sleep promotion behaviors. Examples include avoiding caffeine consumption close to bedtime, reducing electronics use in the evening, and making the bedroom environment as dark, quiet, and comfortable as possible.
Relaxation exercises	Relaxation approaches can include a range of activities, including progressive muscle relaxation, autogenic training, and imagery.

Regarding pharmacologic treatment (Table 2) (4-11), the AASM, based on weak evidence, suggested that the following medications might be used for chronic insomnia disorder in adults: doxepin (sleep maintenance), eszopiclone (sleep onset or sleep maintenance), ramelteon (sleep onset), suvorexant (sleep maintenance), temazepam (sleep onset or sleep maintenance), triazolam (sleep onset), zaleplon (sleep onset), and zolpidem (sleep onset or sleep maintenance) (3). They also suggested based on weak evidence that the following medications *not* be used: diphenhydramine, melatonin, tiagabine, trazodone, tryptophan, and valerian (3).

An algorithmic approach to chronic insomnia developed by the discussants is presented in the Figure.

CLINICAL QUESTIONS

To structure a debate between our 2 discussants, we mutually agreed on the following key questions to consider when applying this guideline to clinical practice and to Mr. F in particular:

Question 1: How effective and practical to implement are the behavioral and psychological interventions for chronic insomnia?

Question 2: What are the risks and benefits of pharmacologic treatment for chronic insomnia?

Question 3: How should a primary care clinician prioritize these management options?

DISCUSSION

Viewpoint: Eric S. Zhou, PhD

Question 1: How effective and practical to implement are the behavioral and psychological interventions for chronic insomnia?

Cognitive behavioral therapy for insomnia is highly effective at treating the root causes of chronic insomnia, rather than masking symptoms like pharmacotherapy. When patients complete CBT-I, it is expected that the improvement will be durable because they have made the decision to change their overall approach to sleep. Treatment with CBT-I results in excellent long-term insomnia remission rates (12).

Practically speaking, CBT-I requires that patients with chronic insomnia challenge themselves to behave and think about sleep in ways that are often the opposite of what has been ingrained in them over many years. Combined with the reality that insomnia may not start to improve until several weeks into treatment, some patients may not be amenable to this approach if they are seeking immediate relief, or if their life circumstances make behavioral modifications difficult (for example, a young child at home).

Furthermore, finding capable CBT-I clinicians can be difficult. Behavioral sleep medicine experts are often located in or near major cities (13). Because of poor reimbursement rates, some do not accept health insurance. The COVID-19 pandemic has resulted in changes that may help improve access. Some states have passed telehealth parity laws, requiring health insurance companies to reimburse for telemedicine care as they would for in-person care. Cognitive behavioral therapy for insomnia has been shown to be as effective when delivered remotely as when delivered in person (14). Recent efforts have been made to study and disseminate digital health CBT-I programs, including those tailored for minority populations (15). Organizations such as the Society of Behavioral Sleep Medicine offer CBT-I practitioner listings (16), which can be a good resource to begin a search within your state.

Like many patients, Mr. F has tried an ineffective monotherapy (sleep hygiene), which the AASM advises against but is commonly recommended by practitioners (17). As part of CBT-I, the clinician would teach Mr. F that one of his primary concerns is not accurate: Older adults do not *all* need 8 hours of sleep. This is a population-based norm being applied to 1 individual, resulting in Mr. F likely spending too much time in bed. This has resulted in fragmented sleep. The clinician would help him see that he has been functioning well with 5 to 6 hours of sleep and that he likely was spending more time in bed than needed on the "non-zolpidem" nights, chasing an unrealistic sleep duration target. I would be concerned whether Mr. F would be willing to give CBT-I a fair try. He has a history of nonadherence when it comes to his sleep as he did not implement CPAP when advised

to do so by his medical team. Would Mr. F be willing to initiate an intervention that requires far more engagement?

Question 2: What are the risks and benefits of pharmacologic treatment for chronic insomnia?

There are 2 distinct advantages to pharmacologic treatment. First, it works immediately. When a patient with chronic insomnia needs to sleep now, the delay to symptom relief is measured in minutes not weeks. Second, in the short-term, pharmacotherapy is inexpensive. Even without prescription benefits, a 30-day supply of zolpidem is likely to be within the budget of many Americans.

On the other hand, the risks associated with pharmacologic treatment are numerous. Some considerations:

1. A hypnotic or sedating antidepressant will only work if a patient is taking the medication. How well do you think they will sleep if they forget to pack it into the carry-on bag for vacation?

2. Medications such as zolpidem are indicated by the U.S. Food and Drug Administration for the “short-term treatment of insomnia.” However, patients are often fearful of what will happen if they discontinue it. Some may try to go “cold turkey” without medical guidance, only to end up panicking after a few bad nights of sleep. This psychological dependency is a significant issue that makes sense given how much the patient’s frame of mind matters when it comes to sleep. One meta-analysis suggested that more than 60% of drug responses for insomnia are the result of placebo effect (18).

3. The side effects of medications prescribed for insomnia are well known, including cognitive impairment and an increased risk for falls (3). There are additional concerns in some subpopulations, such as older adults (19) and pregnant women (20).

Despite evidence of limited efficacy for the treatment of insomnia, use of over-the-counter supplements for sleep is skyrocketing. Between 1999 to 2017, use of melatonin in the United States more than quadrupled (21). Cannabis use for the purpose of improving sleep is common in some populations (22), with limited data supporting its effectiveness and legal concerns in some states.

For Mr. F, a CBT-I clinician would explain that a behavioral and psychological approach to chronic insomnia would provide him with the knowledge to take control of his situation instead of relying on a prescription. For example, CBT-I is designed to help him understand that the timing of his anxiety (specifically his “insomnia legs” while waiting for the zolpidem to take effect) is likely sleep-related and not a generalized concern.

Question 3: How should a primary care clinician prioritize these management options?

A great starting point is to understand the patient’s priorities and current situation:

- Are they fully aware of the potential short- and long-term consequences of taking a sleep medication?
- What is going on in their life (medical, psychological, and social) that may affect their ability to engage with a CBT plan?
- Are they motivated to implement lifestyle modifications?

This will allow the primary care clinician to develop a patient-centered plan, which may involve more nuanced approaches such as combination or sequenced CBT-I and pharmacotherapy (23).

Patients may be initially reluctant to discontinue pharmacotherapy. As such, it would be entirely feasible to implement CBT-I while Mr. F concurrently takes his zolpidem or trazodone. Rather than wait until Mr. F has discontinued

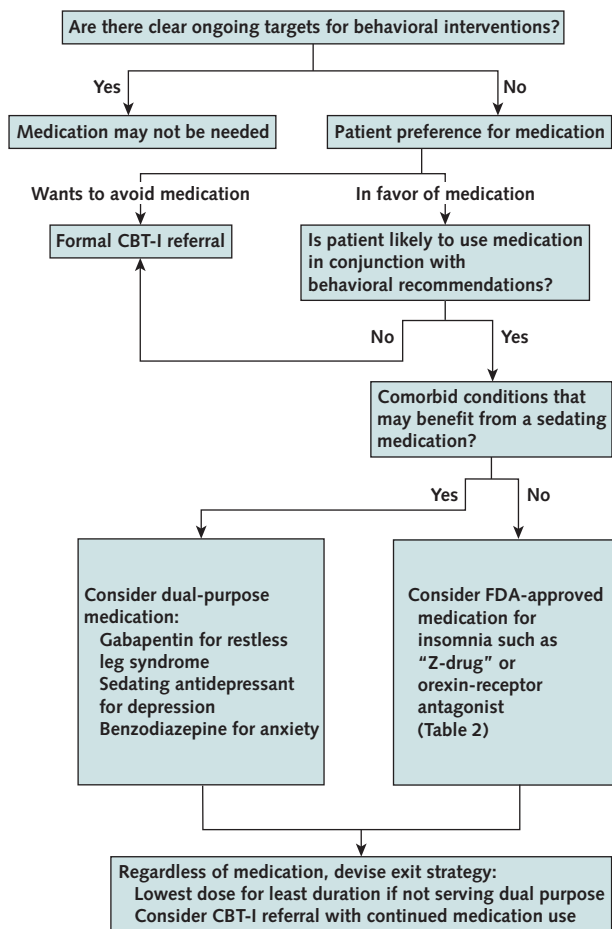
Table 2. Pharmacologic Treatment of Chronic Insomnia*

Treatment (Drug Class)	Bedtime Dose Recommendation	AASM Recommended and Insomnia Type	Evidence Strength	Evidence Quality	Notable Adverse Events† (Reference)
Suvorexant (orexin receptor agonist)	10-20 mg	Yes, maintenance	Weak	Low	Sleep paralysis Cataplexy REM behavior disorder (38)
Eszopiclone (benzodiazepine receptor agonist)	2-3 mg	Yes, onset and maintenance	Weak	Very low	Unpleasant taste (39) Parasomnias
Zaleplon (benzodiazepine receptor agonist)	10 mg	Yes, onset	Weak	Low	Parasomnias (40)
Zolpidem (benzodiazepine receptor agonist)	10 mg	Yes, onset and maintenance	Weak	Very low	Parasomnias
Triazolam (benzodiazepine)	0.25 mg	Yes, onset	Weak	High	Higher misuse and withdrawal potential (23)
Temazepam (benzodiazepine)	15 mg	Yes, onset and maintenance	Weak	Moderate	Higher misuse and withdrawal potential
Ramelteon (melatonin agonist)	8 mg	Yes, onset	Weak	Very low	-
Melatonin (melatonin agonist)	2 mg	No	Weak	Very low	Vivid dreams (41)
Doxepin (heterocyclic)	3-6 mg	Yes, maintenance	Weak	Low	Suicidality (42) Orthostasis Anticholinergic effects (43)
Trazodone (heterocyclic)	50 mg	No	Weak	Moderate	Suicidality Orthostasis Priapism (44)

AASM = American Academy of Sleep Medicine; REM = rapid eye movement [sleep].

* Modified from reference 3.

† In addition to residual daytime sedation.

Figure. Algorithmic approach to chronic insomnia.

sleep-related medications, it would be advisable to connect Mr. F with a trained behavioral sleep medicine expert to help him make an informed decision about his medication use moving forward. Primary care clinicians should familiarize themselves with providers in their state with CBT-I expertise. A recommendation from a trusted medical provider goes a long way toward the likelihood that a patient will ultimately seek CBT-I. Often, patients believe that they have “tried everything,” when all they have done is sleep hygiene. When making the referral, a primary care clinician should communicate that CBT-I goes well beyond sleep hygiene. They should also explain that it is not like CBT for other disorders such as depression. Although it has been shown that patients with comorbid insomnia and depression who complete CBT-I experience significant mood improvements (24), CBT-I focuses on insomnia and does not provide patients with specific strategies to deal with their emotional health.

Regardless of the approach that Mr. F chooses, the primary care clinician should help him understand that his chronic insomnia is more complicated than at first glance. As a firefighter, he was subjected to a highly irregular sleep-wake pattern for 35 years. This probably set the stage for his erratic sleep patterns in retirement.

Although the stage may have been set for his insomnia decades ago, CBT-I could empower Mr. F to take control over his sleep within a matter of months.

Viewpoint: Eric Heckman, MD

Question 1: How effective and practical to implement are the behavioral and psychological interventions for chronic insomnia?

There is strong evidence that CBT-I is effective for the management of chronic insomnia, and it is recommended as first-line therapy by the American College of Physicians and AASM (2, 25). It helps improve symptoms of insomnia and overall perceptions of sleep (26). The real question is when to embark on a formal CBT-I course as part of the treatment regimen.

There are several logistic challenges: CBT-I is a structured program with multiple visits over months led by trained practitioners who are in high demand. Health insurance coverage may be an issue, and options can be limited for the non-English speaker. Patients also need to be willing to examine their approach to sleep and put in the work required to make progress. A pill may be viewed as a quicker fix, and coupling this with the common misconception that sleep hygiene counseling is the same as CBT-I may make patients skeptical of its usefulness.

Thankfully, more streamlined behavioral interventions are helpful. For example, the brief behavioral treatment of insomnia is a 4-session program meant to be given by a nonpsychologist (27), but its administration may be difficult with the limited time available in a primary care or sleep medicine clinic. However, a similar approach focusing on sleep restriction and stimulus control can be deployed in a more informal way during clinic sessions, and this approach is supported by small studies and AASM guidelines (2, 28, 29).

Before referral for CBT-I, the patient should be screened for comorbid sleep disorders (see later discussion). While this process is ongoing, I would recommend behavioral interventions without immediate CBT-I referral. I would explore whether he has daytime symptoms from the amount of sleep he gets. The normal sleep requirement decreases in later decades of life, and hence 6 hours may be adequate (30). His attempts to go to bed earlier to compensate for sleep onset difficulty is counterproductive, and I would advise sleep restriction, pushing back his bedtime targeting 6 to 7 hours in bed to match the actual sleep obtained. I would review stimulus control—the idea that he should get out of bed and clear his head with a calming activity that minimizes light exposure if he has a prolonged period of insomnia to avoid escalating frustration in bed. If there is hesitation to try behavioral changes, I would emphasize that he has tried multiple medications over a long period of time and that these have not remedied his insomnia, suggesting an alternative approach may be necessary.

Question 2: What are the risks and benefits of pharmacologic treatment for chronic insomnia?

One risk of sedatives is that they may worsen a comorbid sleep disorder. For instance, hypnotics may worsen severe OSA, and sedating antidepressants or antihistamines

worsen restless leg syndrome (RLS) (7, 31). Also, giving a medication for sleep may undercut the patient's motivation to focus on behavioral interventions that can have a long-term impact on their symptoms.

Tolerance, dependence, misuse, and withdrawal can develop with medications used to treat chronic insomnia. This is most likely to occur with benzodiazepines, particularly with higher doses and daily use (32). However, non-benzodiazepine receptor agonists like zaleplon, zolpidem, and eszopiclone ("Z-drugs") are not without risk for dependence and misuse (33). Rebound insomnia with future attempts to stop the medication can become a point of frustration.

Medications can have side effects, including over-sedation, or "hangover," or parasomnias with Z-drugs (34). Questions remain about the long-term effects of hypnotic agents, including their association with an increased risk for dementia (35, 36). However, it is uncertain whether this observed outcome is the result of chronic poor sleep or is an effect of the medication used to treat insomnia (37). Polypharmacy can be an issue for patients taking multiple medications or mixing them with other substances such as alcohol.

Despite their risks, hypnotics do show efficacy for improving sleep measures including total sleep time and sleep latency. However, most studies for these medications are short-term (38).

It is also possible that correct use of a medication could make it easier to adjust to behavioral interventions. For example, studies looking at CBT-I alone versus CBT-I and zolpidem showed the best outcomes with initial combination therapy and long-term CBT-I (39, 40). With this approach, it is key to have an exit strategy to make the medication an adjunct that is used with decreasing frequency.

Guidelines for insomnia pharmacotherapy do not compare medications head-to-head, making it difficult to pick the right medication for the right patient. They also often do not address cost. For instance, the AASM guideline recommends the melatonin agonist ramelteon but not the much cheaper melatonin despite the same average improvements in sleep onset (3). The analysis of melatonin used a dose of 2 mg, which is a smaller dose than often used for sedative effect (3). Melatonin has efficacy in persons with circadian rhythm disorders, which makes it attractive when these overlap with insomnia (41). The AASM recommends against trazodone given lack of numerous high-quality studies (3). Its risks may seem more palatable than the misuse potential of benzodiazepines, and hence off-label use of these medications for insomnia can make sense for some individuals. The use of Z-drugs or orexin receptor antagonists may be attractive in some patients, but orexin receptor antagonists are often nonformulary.

For Mr. F, pharmacotherapy has not been perceived to be entirely successful. I would try to understand the relative importance he places on zolpidem and trazodone. I would not demand he immediately stop medications but would stress avoidance of alcohol while using them. I would attempt to stop trazodone in conjunction with the behavioral interventions, particularly if RLS is confirmed, because antidepressants can worsen this condition (31). Many patients do continue to take hypnotics long-term, despite the limited data on prolonged

use, but I would attempt to taper the zolpidem dose once other disorders have been addressed, to determine whether the effect of the medication remains critical to symptom control. If RLS is confirmed, one might consider tapering the zolpidem dose while introducing gabapentin, which may offer both sedating effects and benefit for RLS.

Question 3: How should a primary care clinician prioritize these management options?

Behavioral interventions, either a brief in-clinic approach or referral for CBT-I, should be considered as first-line therapy for the management of chronic insomnia. With relatively little practice, the primary care clinician can deploy the basics of behavioral therapy, such as sleep restriction and stimulus control, that are discussed earlier.

If you are thinking of recommending medication for chronic insomnia, ask yourself, is it going to help your patient embrace the behavioral changes or undercut their willingness to try them? If you think medication will be a helpful adjunct, can you identify a type that may help with another contributing factor for sleep disturbance? If you are going to use a medication, particularly if not serving a dual purpose, can you set expectations with the patient for its limited use?

Mr. F has known OSA that could have worsened over time and could be contributing to his hypertension (42). This condition can also cause symptoms experienced as sleep maintenance insomnia (43). I would recommend Mr. F repeat a sleep study to quantify his OSA and encourage therapy, most likely CPAP or a dental appliance. He himself describes taking hypnotics to help what he calls "restless legs." Further history is needed to determine if this is actually RLS, but this condition often causes difficulty with "sleep onset insomnia" (1). If RLS is confirmed, Mr. F could be screened for the need for iron repletion (44). He did night shift work for many years, and circadian rhythm disorders often present with insomnia symptoms. Sleep logs could help shed light on this possible issue.

SUMMARY

The AASM published recent guidelines on behavioral and psychological treatment as well as pharmacologic therapy for chronic insomnia disorder (2, 3). The only behavioral intervention strongly recommended was multicomponent CBT-I. Based on weak evidence, the AASM suggested several medications, including doxepin, eszopiclone, ramelteon, suvorexant, temazepam, triazolam, zaleplon, and zolpidem, that might be useful for the management of chronic insomnia.

Mr. F is a 64-year-old man who experienced insomnia for decades. He reported difficulty getting to sleep and early morning awakening. He tried traditional sleep hygiene measures as well as over-the-counter sleep aids, which were not helpful. He was prescribed zolpidem many years ago, which was initially taken as needed but now is a daily necessity to get to sleep. More recently, trazodone was added to his regimen. He had been diagnosed 10 years ago with OSA. A trial of auto-CPAP was advised but never implemented.

Dr. Zhou would advise CBT-I, emphasizing its ability to help the patient take control of his situation, instead of his current dependence on taking daily sleep medications. As part of the treatment, he would dispel the commonly held belief that all patients require 8 hours of sleep

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Dr. Libman is a Professor of Medicine, Emeritus at Harvard Medical School and a member of the Division of General Medicine at BIDMC.

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Dr. Heckman is an Instructor at Harvard Medical School and pulmonologist at BIDMC. He is the program director of the combined BIDMC and Boston Children's Hospital sleep medicine fellowship.

Dr. Smetana is a Professor of Medicine at Harvard Medical School and a member of the Division of General Medicine at BIDMC.

per night. As part of CBT-I, Dr. Zhou and Mr. F would collaborate on identifying his individual sleep need through a structured process involving sleep restriction and, subsequently, expansion. However, Dr. Zhou wonders, given the patient's history, whether he would be committed to the time and personal effort necessary for the successful implementation of CBT-I strategies.

Dr. Heckman agrees that CBT-I is the preferred intervention in this situation but would first evaluate and treat the patient for OSA and other comorbid conditions, such as RLS, that might affect his sleep. He would consider a streamlined, clinic-based behavioral intervention focusing on sleep restriction and stimulus control if CBT-I was not accessible or acceptable to the patient. He would not insist on discontinuation of medications immediately but would attempt to stop trazodone followed by reducing the dose of zolpidem over time as tolerated.

GRAND ROUNDS CONFERENCE (VIDEO AT ANNALS.ORG)

A transcript of the audience question-and-answer period is available in the **Appendix** (available at [Annals.org](https://www.annals.org)). To view the conference video (**Video 2**), including the question-and-answer session, go to [Annals.org](https://www.annals.org).

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APPENDIX: COMMENTS AND QUESTIONS

Dr. Gerald W. Smetana: I want to thank you both for the rebuttal discussion today. We will next move to the Q&A section. So, I am going to take the liberty of asking the first question: A number of medicines were suggested as options by the American Academy of Sleep Medicine, what is your process in terms of the sequence of a medication trial? So, for example, are certain medications more likely to cause tolerance or addiction? It's my sense that many internists try not to be the first one to prescribe benzos [benzodiazepines] for chronic insomnia for the risk that they're never going to be able to come off them, and I wonder if you have some guidance about in which order you would think about these medicines? And particularly how this might vary a bit based on patient characteristics? And we'll start with Dr. Zhou, please.

Dr. Eric S. Zhou: Yes, if that question came up in my clinic, I would say, "There is this Dr. Heckman, that is really great, and you should go and see and talk to him."

Dr. Eric Heckman: Yeah, that's why I try to go for that algorithm as a starting point. I try to think, is there a 2-for-1 deal? Can I give them medication that may be beneficial in multiple ways? Benzodiazepines are probably not my first choice often because they probably have at least somewhat more risk for tolerance and misuse than some of the alternatives—but if I have someone who is so anxious that when I walk in the room they make me feel anxious too, then perhaps that means that this could be a 2-for-1 deal for them, and there are times where I do consider doing that. I think this is where you really have to dive into what the patient has tried in the past, and acknowledge what has worked and what hasn't worked, and why it hasn't worked for them. Sometimes this is where you might find yourself diving away from the onset versus maintenance label. So, for instance, if I have someone who has tried zolpidem in the past and they had severe grogginess in the morning, then looking for a shorter half-life medication probably makes sense, and I might use that to whittle down what ones I am choosing from rather than sticking strictly to the onset versus maintenance insomnia category.

Dr. Smetana: Okay. Next we're going to move to the questions from the audience. I'll allow either of you to provide your comments, and feel free to engage in a dialogue if you have comments you'd like to share with each other. Our first question is from Dr. Gloria Yeh in our Division of General Medicine at Beth Israel Deaconess Medical Center who asked, "What about virtual or online CBT-I options or mobile-app-based options if local providers are not available?" And I know you did make some comments about that; perhaps you can amplify that a bit? That may actually be relevant for a large number of people who are watching and who don't have access to the type of providers we are discussing.

Dr. Zhou: Absolutely. I have 2 thoughts on that, Dr. Smetana. First is that there are excellent evidence-based online programs for insomnia that deliver CBT-I. Perhaps the best studied is a program called SHUTi,

which stands for "Sleep Healthy Using the Internet" that was developed at the University of Virginia. This program is being delivered now in an FDA [Food and Drug Administration]-approved format in a program called the Somryst, and providers can prescribe this to patients and hopefully their insurance will reimburse for this service. The one caveat I will say is that this is the equivalent of an internist in their practice seeing an obese patient and giving them a link to Weight Watchers online programming; while it is evidence-based and it's effective, engagement in that process is really difficult. This is where I want to emphasize what Dr. Heckman has brought up: that the internist has such a great opportunity to be a champion of something other than pharmacotherapy, and giving them some tools in their clinic would be really valuable rather than saying, "Here is a script for Somryst, good luck!" And the second comment related to this is, perhaps thanks to COVID-19, the silver lining for behavioral sleep medicine providers is there is much better insurance parity for paying for online or telehealth sessions, and as a result, there are better options in terms of access to providers that might be able to see our patients, even if the providers are not local within your city.

Dr. Heckman: Yes, I agree with that. If you have someone who is motivated enough to really do this independently, then they probably are also motivated enough to do a CBT-I session. However, this is probably going to be customized less for them than when seeing an in-person provider. So, I think that undercuts the utility just a tad. I think the other place where the online providers really made a mistake is that the cost of this is around \$800. I think they would have had the opportunity to really capture a much bigger market if they offered a much lower price. Maybe that will change over time.

Dr. Smetana: And my next question is from our editor, Dr. Libman, who asks, "If you were planning on stopping pharmacologic therapy in our particular patient today, how would you go about doing that? Because I think that can be challenging." Maybe we'll start with Dr. Heckman for that one.

Dr. Heckman: First of all, you don't want to make the patient hate you for taking something away without giving them a landing plan, right? So, I would try to get them started on the behavioral interventions or addressing other causes of fragmentation and then peeling off medications over time. I find that if you are able to address behavioral issues and get them on better sleep habits that it is not as challenging as when you try to actually peel them back because they're starting to see that they're making progress. So, you know, gradual—for this patient in particular. I would pick trazodone first; it probably has less evidence that it's effective, and as I mentioned, if indeed he does have restless leg syndrome on clinical history, which I think is an unanswered question, some antidepressants could augment that. So that is why I would probably try to come down, but I would try to do it gradually. I would probably halve it before stopping. And another thing to stress too is sometimes just changing when they are taking the

medicines. If someone is going to bed way too early, they're often trying to shoehorn themselves into that habit while taking the medication very early. By just pushing back their bedtime and then moving the medication time with it, it can often make it a lot easier to wean them, too.

Dr. Zhou: The only addition that I would make is that a sleep diary, in this case, is often a valuable part of the toolkit. Patients have a bias to believe, as we have talked about, that their medications may be effective, and being able to track that in terms of when they have taken medications and how they have slept over a period of time, like a matter of weeks. It is often eye-opening for patients to see just how poorly that medication is affecting their sleep.

Dr. Smetana: It strikes me as being very similar to what headache clinics do. When we refer patients for headache management, one of the first things they do is obtain a headache diary to help inform the patient and help them understand patterns that they may not have perceived on their own without going through that exercise.

Dr. Zhou: Exactly.

Dr. Smetana: Next question is, "How do you respond to a patient who says, 'I am really not willing to pursue behavioral therapy, I don't want to go down that road with you'? Do you just, in those patients, say we'll go with pharmacologic therapy alone? Or can you think of any ways of moving them along that spectrum a little bit?"

Dr. Heckman: I can take that one first. I would say, "Well, how well do you think things are controlled?" because if they are there complaining of insomnia, then I would point out that the medications don't seem to be working very well. I would point out that they often don't have a lot to lose by trying something that is a different modality, and I would point out that it has quite good evidence for it. When you spin it like that, people are often willing to give it a shot, and sometimes this is where digging into the other comorbid sleep problems can really be telling. If you have someone who is a chronic night owl with a late sleep phase and they're trying to take a medication at 8:00 in the evening, and they can list off 15 different meds that they have tried and they haven't worked, then you can use that to say, "Well, maybe no medication is really going to work here; we need to change your behavior on your sleep times to really get you to a good end point."

Dr. Smetana: Our next question, from Dr. Libman as well, is about the patient's alcohol use. What role do you think his alcohol use may play in his chronic insomnia, and should we be giving him some advice about perhaps modifying his drinking behavior?

Dr. Heckman: I am happy to start with that one, too. Could he be self-medicating a little bit for insomnia with this? Alcohol can be problematic here for a couple of reasons. One, although it may make you initially sleepy, when it wears off it definitely fragments your sleep, so it could have a compounding effect to your symptoms. I also worry about mixing it with hypnotics. If he is having 2 or 3 drinks per night, there are plenty of people who

are underestimating what you're actually taking per night, and could that actually be increasing your risk for bad outcomes by combining with hypnotics.

Dr. Zhou: What I might add to that is that, when I do work with patients, I want them to buy into the idea that as they're working with me for a period of a month or 2, they are really doing everything that they can right when it comes to their sleep. In this case, as Dr. Heckman has mentioned, it may be causing sleep disruption in the middle of the night as well (as we know that alcohol does). This is the time to limit their use of alcohol, not because I think that is a driver of their insomnia, but because we really want them living "clean," if you will, and they can choose to add these pieces back in the future when then they can make an informed decision as to how much this particular substance might affect their sleep.

Dr. Smetana: Next question, this is from me, and that is: Does his work as a rideshare driver change your thoughts about pharmacotherapy for insomnia? I thought that was very interesting in his social history and we haven't picked up on that yet.

Dr. Heckman: I think it's a good habit to counsel against drowsy driving for anyone with a sleep disorder, period, and that includes both if he has untreated insomnia or if it's someone who is a shift worker. Particularly for medications, I think you need to make sure that the person is giving enough time after taking a pill for it to wear off before trying to get behind the wheel. What I'll routinely do with any medication that has a sedating effect is say, "Take this for the first time when you don't have an important meeting in the morning or you don't have to get behind the wheel at a certain time, because there is definitely a huge variability in how people respond to any medication, and you need to be confident that the effects of the medication are completely out of your system before you get behind the wheel."

Dr. Zhou: I may even consider using that as a hook to get him to buy into the idea of perhaps considering alternatives to medication. He wants to be able to drive safely, for both his passengers as well as for himself, and that may be an important place to think about thoroughly with him.

Dr. Smetana: And I imagine that is probably something that you want to document very carefully too from a charting standpoint, that you have that conversation as sort of a safety evaluation?

Dr. Heckman: Definitely.

Dr. Smetana: So, let's do one more question, which will be our last question, and that is: "Has chronic insomnia worsened during the COVID-19 pandemic?" I am curious if you are seeing more patients who are reporting insomnia related to the stresses of life over the past 2 and a half years.

Dr. Zhou: I can say that some of my work has to do with adolescents and young adults, and this is an age group for which the pandemic—at least before schools reopened and in-person attendance was required again—that they were by and large doing better actually. We saw in study after study across the world that, by not forcing 17-, 18-, 19-year-olds to wake up at 6:00 AM to catch

a 7:15 AM bus to go to school, and instead having that extra time to sleep [was] ending up being good because it was better aligned with their circadian preferences. And for some adults, they found that this extra time not having to commute into work allowed more flexible sleep patterns that were better aligned with their lifestyle. So, I know the question that you asked, Dr. Smetana, was whether this was a negative event, and I would say that, for some, the pandemic might have been the best sleep they've gotten in a long time.

Dr. Heckman: Yeah, I would say it's a very divergent phenomenon. Some people definitely do better because it saves the commuting time that they turn into extra sleep, but there is also a group of people who have less structure to their day and then, with that lack of structure, their sleep habits got more erratic and things spiraled. So, there are definitely people in both camps.

Dr. Smetana: Thank you both for your wonderful discussions this morning.