

Vania Modesto-Lowe, MD, MPH

Department of Psychiatry, University of Connecticut, Farmington, CT; Medical Director, Hartford Behavioral Health, Hartford, CT

Margaret M. Chaplin, MD

Department of Psychiatry, University of Connecticut, Farmington, CT; Farrell Treatment Center, New Britain, CT

Roberto León-Barriera, MD

Assistant Professor, Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA

Lakshit Jain, MD

Assistant Clinical Professor, Department of Psychiatry, University of Connecticut, Farmington, CT; Connecticut Valley Hospital, Middletown, CT

Reducing the risks when using benzodiazepines to treat insomnia: A public health approach

ABSTRACT

Benzodiazepines are widely used but can cause considerable harm, including sedation, addiction, falls, fractures, and cognitive impairment, especially with long-term use and in elderly patients. The authors propose a public health approach to reduce the potential for harm when using benzodiazepines to treat insomnia. Primary prevention involves judicious patient selection and patient education. Secondary prevention requires keeping the duration of use as short as possible according to guidelines. Tertiary prevention, for patients who have been taking a benzodiazepine for a long time, uses shared decision-making to introduce a gradual and carefully monitored taper.

KEY POINTS

Be judicious about starting benzodiazepines, and avoid prescribing them to treat insomnia for longer than 4 weeks.

Provide ongoing education to patients currently on benzodiazepines about the risks and benefits and offer alternative treatment options.

Discuss deprescribing with patients on long-term therapy, and use shared decision-making to come to an agreement about when and how to initiate a gradual taper.

BENZODIAZEPINES are not inherently bad medications and can be safe and effective when used judiciously. With their anxiolytic, hypnotic, muscle-relaxant, and anticonvulsant properties, they are widely used, and primary care doctors often use them for rapid, short-term relief of insomnia, for which their efficacy is well established.¹⁻⁵

But these medications carry serious risks, including falls, fractures, overdose, misuse, and dependence, all of which increase with patient age and length of use.⁵ Neutel et al⁶ estimated the population risk of serious falls attributable to long-term benzodiazepine use at 3%. A South Korean study found a twofold higher risk of falls in patients taking benzodiazepines.⁷ Additional data suggest that the risk of fracture is increased by 50% to 110% in patients taking benzodiazepines.⁸ In the United States, benzodiazepine-related emergency room visits have been increasing substantially, as have cases of fatal opioid overdose in people also taking benzodiazepines.⁹ More than a few people are taking both types of drugs concurrently: Gerlach et al¹⁰ reported that 56.8% of long-term benzodiazepine users had also been prescribed an opioid.

Tolerance to the hypnotic effects of benzodiazepines (loss of efficacy) can develop in days.^{7,9} Likewise, physiologic dependence on benzodiazepines develops after 3 to 6 weeks at therapeutic doses,^{5,9} meaning that stopping abruptly will lead to rebound (worsening of original symptoms) or withdrawal.¹¹

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Consequently, in most instances, the use of a benzodiazepine should be temporary.^{5,6} Cross-national guidelines recommend limiting their use for anxiety or insomnia to 2 to 4 weeks in adults.^{5,12,13} This recommendation is based on data that suggest that these drugs start to lose their efficacy for insomnia after 4 weeks, while the risk of side effects and addiction remains.^{4,5,8} In the elderly, clinical guidelines are stricter: benzodiazepine use for anxiety is restricted to low doses and for less than a month, and using them as hypnotics is discouraged altogether.^{5,11–14}

However, for many patients and their doctors, the short-term benefits of benzodiazepines overshadow their long-term risks, and these drugs continue to be widely used.¹¹ Moreover, clinicians may unintentionally discount the risks and fail to adhere to prescribing guidelines.^{3,6}

A PUBLIC HEALTH APPROACH

Below, we outline a “public health” approach to decreasing long-term complications of benzodiazepines prescribed for insomnia. We frame the discussion in terms of the following:

- **Primary prevention**, ie, measures aimed at preventing harm before benzodiazepines are prescribed¹⁵
- **Secondary prevention**, ie, efforts to decrease any harm of benzodiazepines within 4 weeks after the initial prescription^{3,16}
- **Tertiary prevention**, ie, attempts to limit the harmful effects of long-term prescribing.^{5,10,11}

PRIMARY PREVENTION: PRESCRIBE BENZODIAZEPINES JUDICIOUSLY

Of concern, one of the most salient correlates of benzodiazepine misuse is the receipt of a prescription for one.⁹ Primary prevention efforts can include educational public campaigns as well as judicious prescribing.^{8,12–14} Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or causing extreme distress.⁸ Patients should be screened for risk of misuse and informed of the risks of long-term use.^{5,8}

Cognitive behavioral therapy is the first-line treatment

Clinical guidelines for insomnia recommend cognitive behavioral therapy as the first-line treatment and pharmacotherapy as the second line.^{10,12–14} This treatment aims to identify and target modifiable variables that influence sleep such as hyperarousal, as well as maladaptive thoughts and behaviors.^{10,12–14}

Unfortunately, despite empirical validation, cognitive behavioral therapy is not readily available, does not offer immediate results, and is time-consuming, making this a difficult mandate to follow in practice.¹⁷ Up to half of primary care patients say they have trouble sleeping, and they often present with a sense of urgency,² whereas the benefits of cognitive behavioral therapy are not seen for several weeks. Furthermore, cognitive behavioral therapy is time-consuming for the busy primary care physician to administer, and experts are scarce. While some primary care–friendly versions of this therapy look promising,¹⁷ they remain underutilized. For these reasons, both patients and practitioners prefer the simpler and more immediate effects of a sleeping pill.

Alternatives to formal cognitive behavioral therapy include online resources and apps based on its principles.¹⁸ For example, Dalhousie University’s initiative Sleepwell has a website (<https://mysleepwell.ca/insomnia/>) with links to self-help options for patients, such as books, other websites, and apps.⁵ Several commercially available apps have been studied and found to be effective in delivering self-guided cognitive behavioral therapy.¹⁸ These incorporate modules on sleep hygiene, challenging negative thoughts, sleep diaries, and sleep restriction. While these apps can be helpful, a drawback is that users must be familiar with technology and be self-motivated to use the app daily. Other alternatives to formal cognitive behavioral therapy are presented in **Table 1**.^{5,12,18}

Other drugs are approved

If cognitive behavioral therapy is not available or not acceptable to the patient, benzodiazepines are just 1 of several types of medication that have been approved for short-term treatment of insomnia.¹⁴ The so-called Z drugs—zopiclone, eszopiclone, zaleplon, and zolpidem—have also been approved by the US Food and Drug Administration.^{12,14} Other approved options include dual orexin receptor antagonists such as suvorexant, lemborexant, and daridorexant; melatonin receptor agonists (ramelteon); and the antidepressant doxepin in low doses.^{12,14} Clinicians can also prescribe other drugs such as sedating antidepressants and antipsychotics off-label to treat insomnia.^{12,14}

Persons taking opioids are at higher risk

Benzodiazepine use disorder refers to a strong desire to take the drug (cravings), difficulty in controlling its use, using more than intended, and using it despite adverse consequences in various domains of functioning.⁸ Fortunately, it is uncommon. Data from 102,000 participants in the 2015–2016 National Surveys on

Drug Use and Health¹⁹ revealed that although 12.5% of adults in the United States used benzodiazepines, only 17.1% of users misused them, and less than 2% of users met the criteria for benzodiazepine use disorder.¹⁹

People who have an opioid use disorder are at higher risk of developing benzodiazepine use disorder.¹⁹ Many states require that physicians check the state prescription monitoring program before issuing a prescription for a benzodiazepine.²⁰ These programs allow the clinician to see other undisclosed prescriptions for benzodiazepines or opioids. An existing prescription for opioids is a relative contraindication for beginning a benzodiazepine. A frank, individualized discussion of these risks, including any red flags found on the prescription monitoring program search, can lead to alternative approaches, a critical goal of primary prevention.²¹

A shared decision

Shared decision-making involves discussing the pros and cons of these options and noting patient characteristics that may influence medication choice.^{12,14} As discussed, risks of benzodiazepines include falls, fractures, overdose, and misuse and are greater for the elderly, frail individuals, and people with a history of personal or familial addiction.^{11,13}

If, after carefully considering all options, a benzodiazepine is selected, it is essential to set realistic expectations.^{8,11} Clinicians must convey the message that this is a crisis-oriented, short-term strategy and set the stage for deprescribing. Patients need to know that benzodiazepines are reinforcing and have long-term risks. They should be informed that tolerance may develop and that increasing the dose at that point will only lead to further tolerance and dependence. Setting the stage in this way will help avoid long-term use, a critical goal of secondary prevention.³

■ SECONDARY PREVENTION: KEEP THE DURATION OF USE SHORT

Secondary prevention refers to efforts to decrease any harm of benzodiazepines after appropriate short-term use.^{3,16} The American College of Physicians guideline suggests slowly tapering the dose in adults who have been regularly using the drugs for more than 4 weeks, particularly the elderly.¹⁴ Similarly, Canadian guidelines recommend tapering benzodiazepines used for insomnia, irrespective of age.⁵

Arguably, it is easier to write guidelines than to implement them,⁶ and preventing short-term use from turning into long-term use may be difficult.^{7,11,22–24} In a British study,⁴ 35% of patients taking benzodiazepines

TABLE 1

Alternatives to formal cognitive behavioral therapy for insomnia

Online apps and self-help books

Online resources include books patients can read on their own and apps that guide patients through cognitive behavioral therapy for insomnia

Brief therapies for insomnia

Abridged versions of cognitive behavioral therapy that emphasize behavioral aspects of sleep regulation

Education is given on sleep hygiene, factors that affect sleep, and principles of sleep restriction (described below)

After examining a sleep diary, primary care clinicians can inquire about the patient's sleep habits and provide education on patient-specific factors that may be affecting sleep (eg, excess alcohol, using screens in bed, attempting to go to bed too early)

Sleep-restriction therapy

Aims to limit a patient's time in bed to when asleep

Patients are asked to limit their time in bed to their average sleep time, go to bed only when sleepy, get up if they cannot fall asleep, and return to bed only once sleepy: the idea is that most of the time spent in bed is sleeping

Gradually the time spent in bed is increased as sleep duration and quality improve

Stimulus control

The idea is to extinguish the association between the bed and wakefulness

Patients should be instructed to use the bed only for sleep and sex, establish a consistent bedtime and waking time, go to bed only when sleepy, get out of bed if unable to sleep, and refrain from daytime naps

Relaxation therapies

Includes exercises designed to decrease tension, eg, deep breathing, abdominal breathing, progressive muscle relaxation, and meditation

A variety of applications can be used for guided meditation and relaxation

Based on information in references 5, 12, and 18.

had been on them for more than 1 year, far longer than the recommended 2 to 4 weeks.⁵

Some physicians may not think that stopping is necessary, or know how to conduct the taper, or how to communicate the rationale to patients. Patients may not always accept that the effectiveness of benzodiazepines decreases with time, even when that has been explained to them. In fact, the advice to restrict benzodiazepine prescriptions to severely anxious and sleepless individuals may contribute to these

challenges, as patients with more severe symptoms may feel more attached to benzodiazepines because previous treatments have failed. Further, it is challenging to convince patients of decreased effectiveness if they have rebound symptoms on discontinuation.¹¹

Efforts to decrease the gap between theory and practice include strategic interventions targeting prescribers. An example is the Reducing Use of Sedatives program in Australia,¹⁶ in which interdisciplinary case reviews at 3 and 6 months led to reduced use of benzodiazepines in nursing homes.

Brief interventions

Additional examples of secondary prevention include patient education delivered in brief interventions.¹¹ In essence, a brief intervention consists of discussing risks of benzodiazepines with the patient and then advising the patient to decrease or discontinue use. Brief interventions can be done via letters, brochures, or face-to-face discussions.²³

In the Eliminating Medications Through Patient Ownership of End Results (EMPOWER) study, face-to-face discussions combined with informational pamphlets resulted in 27% of participants quitting benzodiazepines within 6 months, compared with 5% in the control group.²² Subsequently, Lynch et al³ conducted a systematic review of 8 studies assessing the effects of brief interventions in 2,071 patients in primary care. The main outcome was discontinuation of the benzodiazepine or reduction of use by at least 25%. Relative to usual care, individuals who received brief interventions were more likely to be off the drug at 6-month and 12-month follow-up. The authors concluded that brief interventions were more effective than usual care in reducing or discontinuing benzodiazepines.³

The results, while suggestive, do not provide clear evidence about which subset of benzodiazepine users benefits most from brief interventions.³ In practice, long-term users are a clinically heterogeneous population.^{1,7,10} Patients taking benzodiazepines a short time may respond better to brief interventions,³ while those who have been on them for a long time may have higher levels of physiologic and psychological dependence and thus be less responsive.^{4,25} While some users may respond to brief interventions, failure to do so contributes to persistent use.

■ TERTIARY PREVENTION: STOPPING AFTER LONG-TERM USE

Tertiary prevention includes strategies to decrease harm in patients who have been on benzodiazepines for more than 6 months and are likely to have sub-

stantial problems with stopping.^{4,10} In a study of long-term benzodiazepine users, only 13% had stopped after 1 year, and the number was lower in those who also used opioids, despite the serious risks of fatal overdose in this cohort.¹⁰

Such difficulties are further illustrated by a Canadian study examining clinical encounters for deprescribing long-term proton pump inhibitors and benzodiazepines in primary care.²³ Educational brochures were distributed to patients and conversations were recorded to explore to what extent the content reflected dose instructions, medication efficacy, risks, side effects, attitudes, emotions, and follow-up. Of interest, conversations of deprescribing for proton pump inhibitors focused on medication efficacy and the need for follow-up, while conversations about stopping benzodiazepines were more likely to center on the “if” rather than the “how.” The nuts and bolts of how to conduct the taper were not addressed, perhaps reflecting patient concerns about the consequences of stopping benzodiazepines.²³ Complementary data show that patients are more receptive to deprescribing if they understand the rationale (risk for harm), are engaged in the tapering process, and are offered behavioral advice.⁵

Stages of change

Patients who regularly use benzodiazepines focus mainly on the benefits rather than the risks.²⁶ Since many patients overestimate the benefits and don’t want to stop, clinicians must ascertain an individual’s readiness to change to optimally engage them in conversations about deprescribing, ie, the supervised discontinuation or dose reduction of a medication that may cause harm (or no benefit) to improve outcomes.^{5,23,27} According to motivation theory, people go through several stages when changing their behavior, including benzodiazepine use^{8,25}:

Precontemplation. Precontemplators do not see their benzodiazepine use as a problem. They may believe that the medication is utterly necessary to their life, functioning, and well-being.²⁵ Hence, the goal is to help them to develop ambivalence about long-term benzodiazepine use instead of ordering them to stop.^{25,26} Asking patients about balance problems, daytime sedation, or falls may help them recognize benzodiazepine-related problems.⁵ It is also important to appreciate the patient’s perception of benefits of benzodiazepines.²⁵ It is helpful to present a summary of the patient’s responses reflecting both sides of their experience. For example, “While Xanax helped you to fall asleep at first, you may also find that 1 tablet is no longer enough and that you need to take 2 now.”²⁵

TABLE 2
Strategies and tips for tapering benzodiazepines

Strategies

Taper by 25% every 2 weeks

If dosage forms do not allow for a 25% reduction, consider a 50% reduction

Consider slowing to 12.5% for the final 2 weeks of the taper

Consider alternate-day dosing for the final 2 weeks of the taper

Tips

Educate patients on what to expect and reassure them that symptoms will resolve

Consider switching to a medication formulation with lower dose options

Consider using a nonaddictive medication alternative

Some patients may require an extremely slow taper—over months, not weeks

Based on information in reference 5.

Contemplation. Contemplators recognize the harm of long-term benzodiazepine use, but they are ambivalent about change.²⁵ Getting a commitment from the patient to reduce benzodiazepine use is the appropriate goal for contemplators²⁵: “Mrs. A, you told me that clonazepam helps you sleep. But you had several falls that left you bruised and shaken. Have you considered alternatives to help you sleep?”

Preparation. Patients in the preparation stage show curiosity about the process but may have doubts about their ability to manage without benzodiazepines.²⁵ It is important to enhance their confidence in tapering off the drug and to offer strategies to manage stress and insomnia by means other than benzodiazepines.²⁵

Action. Once patients reach the action stage, they show a willingness to discontinue benzodiazepine use.²⁵ This is the appropriate stage at which to begin deprescribing.⁵

Stopping is difficult but possible

While stopping benzodiazepines is often difficult,^{23,24} there is evidence that it is possible.²⁸ In a meta-analysis of 10 randomized controlled trials, Soni et al²⁸ evaluated benzodiazepine deprescribing in 1,431 outpatients. The primary measure was complete medication discontinuation. Studies were classified by the type of intervention, ie, pharmacologic or nonpharmacologic. Despite heterogeneity in these interventions, study design, and effects, a gradual taper supported by nonpharmacologic interventions was more successful than routine care.²⁸

TABLE 3
Preventing harm from benzodiazepines

Primary prevention¹⁵

Educate the public about benzodiazepine harms

Educate prescribers and patients about cognitive behavioral therapy for insomnia

Educate patients about risks of falls, fractures, and addictive potential

Limit use to a carefully selected population

Set the stage for limiting use to less than 4 weeks

Secondary prevention^{13,22}

Taper after 4 weeks

Use behavioral interventions, letters, brochures, or face-to-face interventions to encourage patients resistant to intervention

Educate prescribers about the need to discontinue benzodiazepines

Tertiary prevention^{5,11}

Use motivational interviewing to evaluate the stage of change

Use shared decision-making to discuss risks and benefits to help move the patient to the action level of change

Optimize deprescribing by addressing rebound (through education), withdrawal (through gradual tapering), and relapse (through addition of psychological support)

For the primary care clinician, the first step in deprescribing can be to discuss the risks and benefits of stopping.⁵ Benefits may include improved alertness and prevention of falls and accidents. From a patient’s perspective, addressing relapse and discontinuation syndromes is critical.^{5,8} In particular, patients must know what to expect and be reassured that the clinician will appropriately treat any symptoms that emerge.⁵

Rebound is a reemergence of symptoms with increased intensity after a period of recovery.^{8,11} It is self-limited and can last approximately 3 weeks.²⁹

Also, withdrawal symptoms can develop in people who have regularly been using benzodiazepines if the medication is stopped suddenly. Withdrawal is heralded by new autonomic symptoms such as sweating, increased heart rate, myoclonus, paresthesias, and tremors. In severe cases, seizures or delirium may occur. These symptoms generally begin a week or so after stopping treatment and last 2 to 4 weeks, but they can persist in an attenuated fashion for several months. There are case reports of individuals experiencing residual symptoms such as tinnitus for several years.²⁹

Relapse is the return of symptoms that were initially controlled with a benzodiazepine.²⁹ It can be prevented by initiating alternative treatments, particularly cognitive behavioral therapy.²

Tapering is essential to minimize these difficulties, along with the patient's apprehension and fear.⁸ Canadian guidelines recommend gradual decreases such as 25% every 2 weeks and, if possible, 12.5% reductions near the end of the taper. If symptoms return, the taper is paused for 1 or 2 weeks before proceeding slowly.⁵

Patients with high levels of medical or psychological stress may require an extra-slow taper that may take up to a year. Negotiating a flexible taper responsive to the patient's level of distress may increase its chance of success. If the first attempt is unsuccessful, patients should be encouraged to try again, as even dose reductions may be beneficial to decrease long-term harm. Some approaches to tapering can be found in Table 2.⁵

CONCLUSION

Prolonged benzodiazepine use can cause harm and remains a challenge for healthcare systems worldwide. Public health strategies to decrease benzodiazepine-related harm are a novel approach to this problem

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(Table 3).^{5,11,13,15,22} Primary prevention aims to decrease prescribing levels by employing judicious prescribing. Secondary prevention can be accomplished by improving adherence to existing guidelines. Tertiary prevention efforts recognize that in clinical practice we are likely to encounter patients who have been on benzodiazepines for a long time.

Clinicians must become comfortable with the principles of motivational interviewing and deprescribing guidelines to improve outcomes for these patients. With practice, patience, and support from their mental health colleagues, even busy clinicians can master these techniques and derive professional satisfaction from the knowledge that they have made a significant difference in their patient's health status and quality of life.

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- Address: Lakshit Jain, MD, Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, Farmington, CT 06457; lakshit.jain@ct.gov