Better Ways to Fall Asleep: The Danger of Benzodiazepines

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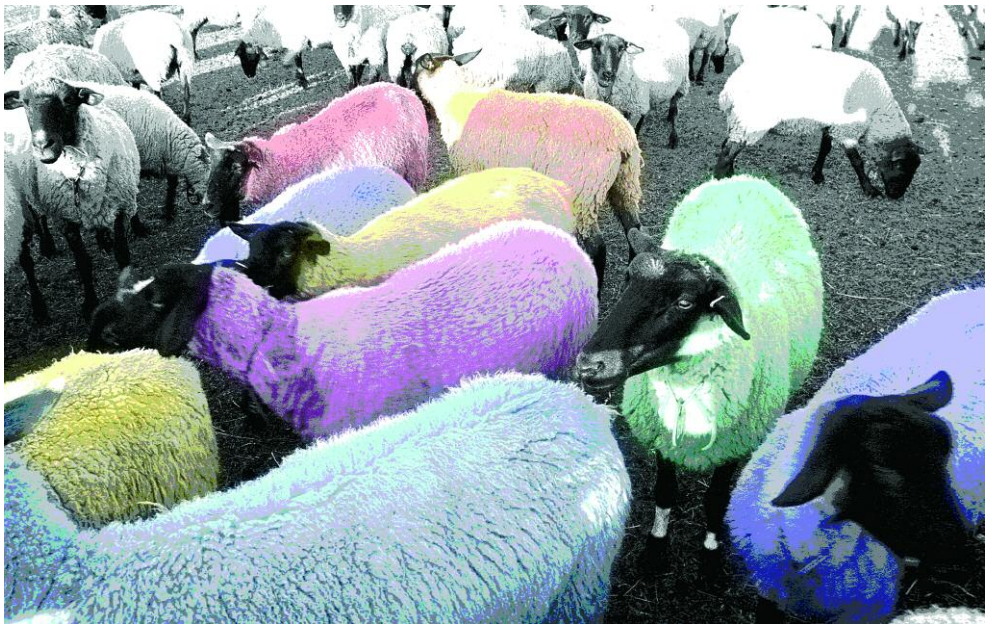
For better or worse, Medicare patients now have a more difficult time filling prescriptions for benzodiazepines. While it is indirectly the result of the danger inherent in the use of these medications, it is in fact the direct result of the Medicare Modernization Act (MMA)—specifically how Medicare Part D medications are defined. These medications have been associated with increased risks for seniors, but there are several better options, especially for the treatment of insomnia. The prevalence of sleep complaints in the elderly is significant (Figures 1 & 2). They are due, in part, to the physiological changes that affect sleep patterns as people age. These include increased time to fall asleep; a greater likelihood of being awakened by noise, light and other environmental disturbances; and an increased likelihood to waken during the night, perhaps because they experience less deep sleep and less REM (rapid eye movement) sleep.



Consequences of Insomnia for LTC Residents

Apart from needing to nap during the day, residents who suffer from insomnia have been shown to have a reduced quality of life,[1] including the inability to enjoy socializing. Even more importantly, insomnia is associated with increased risk of falls.[2] A recently published study by Avidan et al, looking at residents in long-term care settings, has raised questions about the long-held perception that hypnotic use is associated with the risk of falling. Avidan found that it was insomnia, not the use of hypnotics, that increased the risk of falls. Further studies are needed to confirm these findings, but the data suggest that current hypnotics may not make a major contribution to falls and to the hip fractures the elderly fear. In addition, insomnia may complicate treatment for and recovery from existing medical conditions.[3]

An Excluded Medicare Part D Medication

The writers of MMA needed a definition for what would be a Medicare Part D-covered medication, so they went back to some historic legislation. The legislation that started the Medicaid program defined covered medications as all medications with only a few exceptions. These medications were included on the list at the time because of questions about the potential for abuse and about their efficacy. Over time, despite the fact that states were not required to cover these medications, all but a very few chose to cover them for their Medicaid beneficiaries, thus receiving federal matching dollars for their effort.

The legislation excludes from coverage the following drugs or classes

of drugs, or their medical uses:

- Agents when used for anorexia, weight loss, or weight gain
- Agents when used to promote fertility
- Agents when used for cosmetic purposes or hair growth
- Agents when used for the symptomatic relief of cough and colds
- Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations
- Non-prescription drugs
- Outpatient drugs for which the manufacturer seeks to require associated tests or monitoring services be purchased exclusively from the manufacturer or its designee as a condition of sale
- Barbiturates
- Benzodiazepines[4]

Now, as a result of the movement of the dual eligibility of those with Medicare and Medicaid, the coverage for Medicare Part D-covered medications has shifted from each state's Medicaid program to the Medicare program—that is, all except the specifically excluded Medicare Part D medications, for which the individual states remain responsible for deciding whether or not to cover.

Figure 1. Prevalence of Sleep Complaints in the Elderly

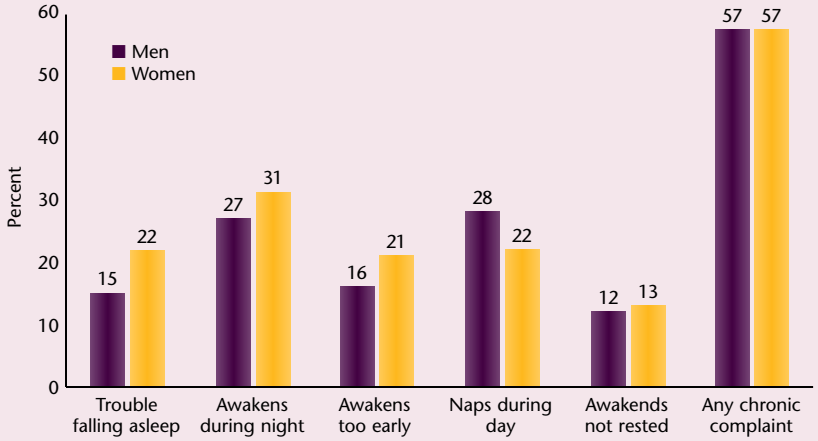
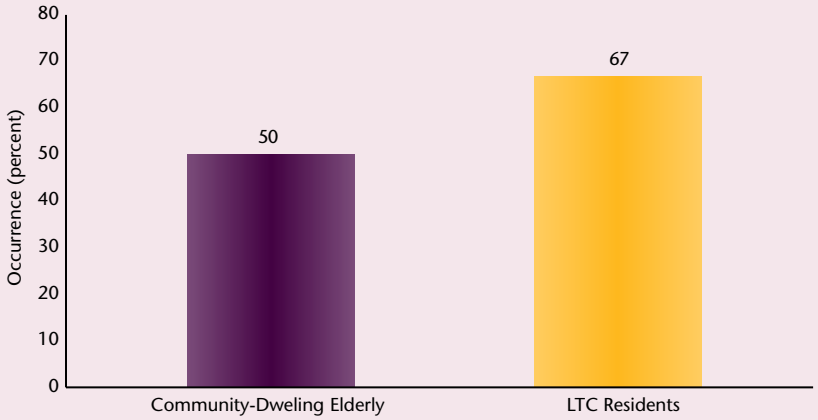


Figure 2. Prevalence of Sleep Disorders by Setting



The Clinical Case

Benzodiazepines have historically been used widely for management of acute anxiety, panic attacks, seizure disorders, and muscle spasms in those with cerebral palsy or other disorders. Examples include lorazepam (Ativan), alprazolam (Xanax), clonazepam (Klonopin), and diazepam (Valium).

The exclusion of benzodiazepines and barbiturates is of particular concern because these medications are significant in elderly populations. In 2000 alone, one study found that approximately 10% of nursing home residents receive anxiolytics, most commonly benzodiazepines.[1] Overall, benzodiazepines are the 13th leading class of medications in the United States, with 71 million prescriptions dispensed in 2002. It is estimated that 1.7 million of the 6.4 million dually eligible individuals (27%) take a benzodiazepine medication.

It is worth noting here that long-acting benzodiazepines such as flurazepem (Dalamane) are among the medications listed as potentially inappropriate for those aged 65 and older by the Beers' Criteria,[5] which were adopted into the CMS Guidelines for Potentially Inappropriate Medications in the Elderly. This warning is based in part on data suggesting an association between benzodiazepine use and hip fractures in the elderly. Most recently, a study published in the *Archives of Internal Medicine* showed that, contrary to several previous studies, short half-life benzodiazepines are not safer than those with longer half-life.[6]

Nonetheless, while there are other classes of anxiolytic-hynotic medications available for residents with primary anxiety or sleep disorders, only benzodiazepines can be used to arrest acute seizure disorders in residents with status epilepticus.[7] With the prevalence of epilepsy increasing with age, this is a real issue for nursing facility residents.[8]

Discontinuation of Benzodiazepines

Since many of these individuals have taken benzodiazepines for

years—or even decades—abrupt discontinuation can lead to relapse, rebound, and/or withdrawal symptoms. Relapse, defined as the gradual return of original symptoms of anxiety or sleep disorder, occurs in 63% to 81% of residents abruptly withdrawn from therapeutic doses of benzodiazepines.[9]

Some of the severe withdrawal symptoms relating to these medications can include seizures and other acute emergencies. So when these benzodiasepines are discontinued after long-term therapy, dosage tapering with close medical supervision over several months is the appropriate strategy. Abrupt discontinuation is likely to result in increased expenses for Medicare Part A and Part B because of the rise in hospitalizations, emergency room visits, and physician office visits that might result. Increased medication costs also are likely, as practitioners turn to more expensive and less desirable alternatives to benzodiazepines.[10]

The value of gradual and careful tapering is scientifically documented. For example, Valerie Curran, MD, at the University College in London, has studied seniors taking benzodiazepines for a prolonged period of time and compared the symptoms and cognitive performance of those who tapered off their medication slowly with a control group that did not taper off. The tapers occurred over a six-month period and showed significant improvements in cognitive function, including memory and reaction speed, and no adverse effects on sleep or increased anxiety. Additionally, there were no reported withdrawal symptoms.

Another study also involved a taper over six months and demonstrated similar results.[11] At the same time, other studies have shown that the symptoms associated with abrupt discontinuation can be controlled through a shortened taper over a 2 to 4 week period in an inpatient psychiatric setting. With coverage for these medications ending at the end of this year, tapering attempts for individuals currently taking benzodiazepines and barbiturates should have begun no later than July, 2006.

One approach to tapering benzodiazepines is a weekly taper rate that is determined by dividing the total daily dose in milligrams of benzodiazepines by 5 and rounding the number to a dose attainable with available dosage forms. Calculate the tapering dose that way each week. For example, a patient receiving diazepam 20mg/d would be tapered with 16mg/d during week one, 12mg/d during week two, 8mg/d during week three, and 4mg/d during week four. If necessary, the tapering schedule can be slowed toward the end of the protocol for symptom control. Tapering requires close medical supervision, which, while available to nursing-home residents is absent from seniors living in the community, therefore presenting increased risks. In addition, current nursing-home regulations already require periodic dose-reduction attempts, so many nursing-home residents taking benzodiazepines have already failed dosage-reduction efforts, leaving them with few good options.

Definitions

- **Insomnia**—experience of poor quality sleep, with difficulty in initiating or maintaining sleep, waking too early, or failing to feel refreshed.
- **Chronic Insomnia**—insomnia occurring for at least 3 nights a week for a month or more.
- **Primary Insomnia**—chronic insomnia without specific underlying medical or psychiatric disorders, such as sleep apnea, depression, or medication side effects.

Better Sleep Alternatives

Nonpharmacologic measures should be employed first when undertaking the management of insomnia. All patients reporting insomnia should avoid caffeine, nicotine, and alcohol; in the evening, fluids of all types should be avoided. As much as possible, each resident's room at night should be quiet, dark, and comfortable, with as much privacy as possible. Disturbances in the room, including TVs, telephones, and outside noises should be kept to a minimum. Bedtime rituals, including reading, listening to relaxing music, personal hygiene routines, or light snacks, should be encouraged because they all are healthy bedtime habits that promote healthy sleep.

To reduce or eliminate trips to the bathroom during the night, avoid administering diuretics in the evening. Conversely, medications with sedative side effects should be given close to bedtime. If it is determined that a pharmacologic sleep aid is called for, the lowest dose should be used for a limited time.

The latest generation of sleep aids is the non-benzodiazepines. These agents are being preferred over the benzodiazepines because of their more favorable side-effect profile. Until recently, 2 treatment options in this drug class were available—zolpidem (Ambien), and zaleplon (Sonata). These products have been found effective for sleep onset, although perhaps because of their short-acting nature, their sleep maintenance effects are inconsistent. Similarly, there is a lack of long-term controlled data related to their use.

Two additional agents eszopiclone (Lunesta) and ramelteon (Rozerem) have recently become available. These are unique in that they are the only agents approved for long-term use and ramelteon is the only hypnotic agent that is not a controlled substance. Both work somewhat differently so identification of the type of sleep disturbance is important. Differentiation between sleep onset problems versus sleep

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Meanwhile, new agents designed specifically for the treatment of IEED are needed and are, in fact, in development.[2] ALC

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maintenance is essential to determine if for example ramelteon or eszopiclone would be effective. Ramelteon is effective in the treatment of sleep onset problems while eszopiclone's benefit is in the treatment of sleep maintenance.

In the end there are safer alternatives to the benzodiazepines for the treatment of sleep and within the year additional agents are likely to be approved by the FDA. These newer agents may result in the demise of the use of benzodiazepines for sleep. These newer options promise to offer a safe and effective treatment of sleep disorders for seniors with the added advantage that they are covered under Medicare Part D. ALC

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Primary Insomnia—DSM-IV Diagnostic Criteria

A. The predominant complaint is difficulty initiating or maintaining sleep, or having nonrestorative sleep, for at least 1 month.
B. The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of function.
C. The sleep disturbance does not occur exclusively during the course of narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep disorder, or a parasomnia.
D. The disturbance does not occur exclusively during the course of another mental disorder (eg, major depressive disorder, generalized anxiety disorder, a delirium).
E. The disturbance is not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication), or a general medical condition.