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Benzodiazepine Use in Older Adults: Dangers, Management, and Alternative Therapies

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Abstract

Several major medical and psychiatric organizations, including the American Geriatrics Society, advise against using benzodiazepines or nonbenzodiazepine hypnotics in older adults. Despite these recommendations, benzodiazepines continue to be massively prescribed to a group with the highest risk of serious adverse effects from these medications. This article summarizes legitimate reasons for prescribing benzodiazepines in the elderly, serious associated risks of prescribing them, particularly when not indicated, barriers physicians encounter in changing their prescription patterns, and evidence-based strategies on how to discontinue benzodiazepines in older patients. Although more research is needed, we propose several alternatives for treating insomnia and anxiety in older adults in primary care settings. These include nonpharmacological approaches such as sleep restriction—sleep compression therapy and cognitive behavioral therapy for anxiety or insomnia, and as well as alternative pharmacological agents.

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The American Geriatrics Society (AGS) placed benzodiazepines on a list of medications that should be avoided in patients over 65 years of age.[1] Several major psychiatric associations also advise against using benzodiazepines for generalized anxiety disorder and insomnia in the elderly.[2] Despite these recommendations, benzodiazepines

continue to be prescribed to a group with the highest risk of serious adverse effects from these medications.[3] In the United States, more than 10% of women and 6% of men aged 65 to 80 years filled at least one prescription for benzodiazepines in a 1-year period, approximately one-third of them receiving benzodiazepines for longer than 120 days in a year.[3] This widespread prescription of benzodiazepines in a population for which they are generally contraindicated has the potential for important public health consequences because benzodiazepine use is associated with risk of dependence, cognitive deficits, falls resulting in fractures, motor vehicle accidents, and overall mortality.[1]

Primary care physicians prescribe the largest absolute number of long-term benzodiazepines, likely because they see the greatest number of elderly patients.[3] However, in relative numbers, primary care physicians do not prescribe benzodiazepines at a higher rate than psychiatrists.[4] There are several interdependent reasons why doctors are unable to change their benzodiazepine prescription patterns. Some are intrinsic to physicians, including insufficient recognition of adverse effects, conviction that the risk to benefit ratio favors the latter, perceived lack of skills and training on how to respond to problems that occur during a taper, resource constraints such as limited time and a resultant decision to focus on other important medical issues in this population, fear of jeopardizing the doctor-patient relationship or fear of push-back leading to patients finding other doctors, unwillingness to question other colleagues' prescription rationales, and opinion that discontinuation could be too stressful for an elderly user with a limited life expectancy.[5] Other reasons are external to physicians, such as patients' resistance to change, health systems with insufficient reimbursement for the invested time and effort, limited availability of psychotherapists, absence of scheduled medication reviews, or inability to access support from psychiatrists in a timely fashion.[5] Importantly, older adults are a very heterogenous group because this population ranges from 65-year-olds to centenarians, and not all older adults are affected equally by the aforementioned factors. For example, elderly patients in residential care facilities are at a higher risk of being exposed to benzodiazepines, and pressure from the nursing staff to prescribe psychotropics seems to play an important role in that setting.[5] This and other factors have likely contributed to the prevalence of benzodiazepine use remaining unchanged in the elderly population over the past decade.[1,6]

This article reviews the literature on the risks of prescribing benzodiazepines to older adults, problems associated with benzodiazepine use in the elderly, ways to reduce their use, and alternatives to benzodiazepines for anxiety and insomnia.

PRESCRIBING BENZODIAZEPINES

AGS Guidelines and Clinical Practice

In 2015, the AGS published the fourth update of the so-called Beers criteria. These criteria are meant to be evidence-based recommendations by the AGS to guide decision making for prescribing to elderly patients by listing medications that have an unfavorable risk to benefit ratio. The criteria should be used to support clinical judgment and not to prohibit the use of the listed medications.[1] The AGS recommendations are intended for use in all clinical settings for people older than 65 years in the United States, outside of palliative or hospice care.[1] The 2015 update was authored by an interdisciplinary panel of 13 experts in geriatric care.[1] Each published recommendation was labeled as either "strong" or "weak" depending on the quality of available evidence, potential for harm, and availability of safer alternatives.[1] Most of the recommendations regarding benzodiazepine use are based on evidence of "moderate" quality and are given with a "strong" recommendation.[1] Two notable exceptions are (1) use of benzodiazepines in elderly patients with a history of falls and (2) use in elderly patients who are already receiving 2 or more drugs that act on the central nervous system.[1] The recommendation to avoid benzodiazepines in these 2 situations is based on "high" quality of evidence.[1] An important update in the new criteria is that nonbenzodiazepine receptor agonists (such as eszopiclone, zalpelon, and zolpidem) are unambiguously to be avoided regardless of duration of use, whereas the 2012 recommendations were more permissive of their use.[1] These drugs possess minimal efficacy in treating insomnia beyond acute periods measured

in days and considerably increase the risk of adverse effects, including delirium, falls, fractures, and motor vehicle accidents.[1]

In clinical practice, insomnia and anxiety are the most common reasons for physicians to prescribe benzodiazepines to older adults.[3,7,8] Most studies on benzodiazepine effects for these 2 indications were conducted in nonelderly patients, and long-term follow-up evaluating long-term efficacy is lacking.[9] In young adults, a short course of benzodiazepine use may be safe. In the elderly, however, even short-term use of benzodiazepines can have dangerous adverse effects, as discussed in the "Complications From Benzodiazepines in the Elderly" section. With regard to long-term benzodiazepine use, the lack of efficacy studies is complicated by the fact that the clinical presentation of withdrawal from benzodiazepines is associated with worsening insomnia and exacerbated anxiety in already anxious patients.[10] This situation is often erroneously interpreted as evidence that benzodiazepines are having beneficial effects.[10] This assumption would be analogous to interpreting withdrawal symptoms of alcohol, a substance that acts on the same receptors as benzodiazepines, as evidence of the long-term benefits of alcohol for sleep and anxiety.

Short-Acting vs Long-Acting Benzodiazepines

The rationale used by the AGS for listing benzodiazepines as inappropriate medications for elderly patients is that "older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults."[1] The panel strongly recommends that short- and intermediate-acting benzodiazepines be avoided in this population.[1] When benzodiazepines need to be used, such as for "seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and peri-procedural anesthesia," long-acting agents, such as clonazepam and diazepam, may be appropriate.[1] When it comes to a choice between long- vs short-acting benzodiazepines for other indications, the patient and clinician find themselves walking a tightrope. It seems that short-acting agents are more dangerous for falls and fractures, but because of the decreased metabolism of long-acting benzodiazepines, the use of the latter will leave an elderly patient with residual daytime sleepiness and cognitive impairment.[1,8,11]

COMPLICATIONS FROM BENZODIAZEPINES IN THE ELDERLY

Dependence

"Red flags" for an elderly patient becoming dependent on benzodiazepines are long-term use; rebound anxiety and insomnia on withdrawal of the drug; strong desire to use benzodiazepines; driving while under the influence of benzodiazepines; use of benzodiazepines despite falls; use of benzodiazepines in addition to other hypnotics; and continuing use of benzodiazepines despite physicians' recommendations to discontinue. Although these issues are often encountered in clinical practice, the 12-month prevalence of diagnosed sedative, hypnotic, or anxiolytic use disorder is as low as 0.04% in this age group.[12] There are several possible explanations for such low rates of diagnosed anxiolytic use disorder in this population. For example, anxiolytic use disorder may be preferentially diagnosed in young, often antisocial, polysubstance users, rather than elderly iatrogenic consumers.[12] Failure to diagnose, however, likely reduces the chances that physicians will recognize the problem and address it by initiating discontinuation protocols in their patients or that their efforts will be reflected in reimbursement.[5]

Falls and Fractures

Observational studies consistently report that benzodiazepine use is associated with a statistically and clinically significant increase in risk of falls and fractures.[7-11] Benzodiazepines are associated with falls through a number of mechanisms, including increased reaction time, disrupted balance and gait, sedation, and impaired vision.[7,8,11] It seems that the risk of fractures is dose dependent and starts at 20% of an average prescribed daily dose (ie, at approximately 0.3 mg/d of lorazepam or 3 mg/d of diazepam).[8,9] It was estimated that exposure to benzodiazepines increases the risk of falling by 50%, and annual costs of treatment for benzodiazepine-associated

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fall injuries in the European Union amount to €1.8 billion.[7,11] Benzodiazepines are particularly strongly associated with hip fractures, which is concerning because up to one-third of patients with hip fracture die within a year.[7,11] Even when falls do not result in fractures, they are associated with fear of further falls and consequent limitation of daily activities.[7]

Importantly, tapering benzodiazepines decreases the risk of falls in older patients, although larger controlled trials are needed.[11]

With regard to older adults with particularly high risk of falls and fractures, those with osteoporosis, sensory loss (eg, decreased vision, peripheral neuropathies), muscle weakness, Parkinson disease, arthritis, polypharmacy, and orthostasis, patients who frequently use the restroom at night, and those with a history of falls are particularly vulnerable.[1,7,11] A number of clinical tools have been designed to help identify those with a particularly high risk of falling in the community and in the hospital.[7] Future studies should address more rigorously the effect of comorbidities and the effect of duration of use on the risk of falls/fractures.[11]

Dementia and Cognitive Decline

Benzodiazepines cause short-term cognitive deficits, particularly in memory, learning, attention, and visuospatial ability, and they are also associated with the development of lasting cognitive deficits and dementia.[13-15] Several studies have indicated that even after benzodiazepines are discontinued, the cognitive function of long-term users continues to be impaired in most cognitive domains, suggesting lasting and possibly irreversible cognitive deficits associated with benzodiazepine use.[13,14] The overall effect sizes of such potentially irreversible deficits are in the medium range (Cohen d, −0.48) but range from large in verbal memory (Cohen d, −1.5) to no changes in sensory processing.[14] Furthermore, observational studies have revealed a consistent association between benzodiazepine use and dementia.[15] However, it is still not entirely clear if the association between benzodiazepines and dementia is causal or if benzodiazepines are more frequently given to patients experiencing prodromal symptoms of dementia, which can include anxiety. It is clear that those with established cognitive deficits or dementia are at a particularly high risk of major cognitive decline with the introduction of benzodiazepines.[1] Finally, although benzodiazepines may be associated with some irreversible cognitive deficits, cognitive function after tapering nevertheless improves substantially in long-term users.[14]

Mortality

Benzodiazepine use is associated with a considerable increase in all-cause mortality, with exposed patients dying at a 1.2- to 3.7-times higher rate per year compared with unexposed individuals.[16] However, as with dementia, it remains unclear whether this connection is causal or whether these drugs are being prescribed more frequently to patients at higher risk of dying. Although suicide attempts by benzodiazepine overdose are frequently seen in clinical practice, it is currently unclear whether prescribing benzodiazepines increases the risk of suicide.

DISCONTINUATION OF LONG-TERM BENZODIAZEPINE USE

Education

Educating patients about the potential risks of long-term benzodiazepine use is the most effective first step in tapering. A common misperception among primary care physicians is that convincing a patient to begin tapering benzodiazepines takes too much time and is unlikely to succeed.[5] However, studies have consistently found that minimal interventions are needed to initiate a successful tapering protocol in a large proportion of elderly long-term benzodiazepine users. Simply giving patients written educational materials with a tapering plan, which requires no time on the part of the physician, is one of the most effective strategies in discontinuing benzodiazepines and is more effective—at least as a first step—than time-consuming motivational interviewing.[17,18]

Tannenbaum et al[17] recently developed an 8-page booklet, available online, that educates patients on the risks of benzodiazepine use, presents peer success stories and alternative treatment options, describes the tapering protocol, and encourages patients to discuss tapering with their physician (Table 1). These investigators mailed the booklet to long-term

TABLE 1. Example of a Benzodiazepine Tapering Protocol[a]

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1 and 2	Full	Full	Full	Full	Full	Half	Full
3 and 4	Full	Half	Full	Half	Full	Half	Full
5 and 6	Half	Half	Half	Half	Half	Half	Half
7 and 8	Half	Half	Half	Half	Half	Quarter	Half
9 and 10	Half	Quarter	Half	Quarter	Half	Quarter	Half
11 and 12	Quarter	Quarter	Quarter	Quarter	Quarter	Quarter	Quarter
13 and 14	Quarter	Quarter	Quarter	Quarter	Quarter	0	Quarter
15 and 16	Quarter	0	Quarter	0	Quarter	0	Quarter
17 and 18	Quarter	0	0	Quarter	0	0	Quarter
19	0	0	0	Quarter	0	0	0
20	0	0	0	0	0	Quarter	0
21	0	0	0	0	0	0	Quarter
22	0	0	0	0	0	0	0

[a]Cells represent proportions of the initial daily dose. Full = full daily dose before tapering; Half = 50% of the initial dose; Quarter = 25% of the initial dose; 0 = a benzodiazepine-free day.
Modified from *JAMA Intern Med.*[17]

users and reported that 27% of the recipients discontinued benzodiazepine use within 6 months compared with only 5% in the control group, and an additional 11% of patients receiving the booklets reduced their use of benzodiazepines.[17] Drawing on freely available, evidence-based protocols such as that developed by Tannenbaum et al may help clinicians overcome the common opinion that they lack relevant skills or that their practice is too busy to take the time to initiate a taper.

Rate of Discontinuation

Abrupt discontinuation of benzodiazepines can induce seizures, and excessively rapid tapers can cause rebound anxiety (ie, anxiety levels higher than those preceding the initiation of treatment), making successful tapering unlikely. Few studies have tested the optimal rate of discontinuation of benzodiazepines in elderly long-term users. Anecdotal evidence suggests that slower tapers are more successful because they do not cause the increased anxiety associated with benzodiazepine withdrawal. A recent review of the literature found that approximately 60% of patients can become benzodiazepine free with 4-week protocols that decrease the benzodiazepine dose by 25% every 1 to 2 weeks.[19] This rate, however, may be too rapid for many patients. Tannenbaum et al[17] used a 22-week tapering protocol, with minimal intervention necessary. This protocol was developed for outpatient settings in primary care, but it is reasonable to consider applying it in other situations, such as initiating a taper in a newly identified long-term user before hospital dismissal.

Changing and Adding Medications During a Taper

A Cochrane review by Denis et al[20] in 2006 found that evidence does not support a strategy that switches patients to longer-acting benzodiazepines at the beginning of the taper. In 2013, this review was withdrawn because it was deemed out-of-date, but we are unaware of any new large randomized controlled studies or systematic reviews that either support or refute the 2006 conclusions.

Duloxetine, sertraline, citalopram, escitalopram, mirtazapine, and doxepin are antidepressants frequently used to treat anxiety and/or insomnia. However, no randomized controlled trials have addressed whether substituting one of these agents increases taper success rates. Randomized controlled studies documenting clear benefits for initiating antiepileptic medications during benzodiazepine tapering are also lacking. Using trazodone or valproic acid to treat anxiety or insomnia during a taper does not decrease withdrawal symptoms or improve long-term success of benzodiazepine discontinuation.[21] Nonbenzodiazepine sedatives, such as zolpidem and zaleplon, are associated with risks similar to those of benzodiazepines and should not be

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used in elderly patients as an alternative sleep agent.[1] A recent meta-analysis found no effects of melatonin on the odds of successful benzodiazepine discontinuation, and no published data are available on the role of the melatonin receptor agonist ramelteon.[22]

Cognitive behavioral therapy (CBT) should be considered during a taper because it has been reported to be effective in the first 3 months after initiating a benzodiazepine taper, although this effect is less obvious 6 months after initiating a taper.[18] Where CBT is available, patients having difficulties in the initial stages of a taper may benefit from referral (Table 2).

MANAGEMENT OF INSOMNIA AND ANXIETY IN OLDER ADULTS

Insomnia

For older patients with insomnia, 2 nonpharmacological approaches—sleep restriction—sleep compression therapy and CBT—have strong evidence of efficacy.[23] Sleep restriction—sleep compression therapy focuses on restricting time in bed to actual time sleeping. The patient first keeps a 2-week log of time spent in bed and overall estimated sleeping time.[23] According to Bloom et al,[23] if a patient sleeps 5½ hours but spends 8½ hours in bed, the time in bed should first be restricted to 5½ to 6 hours. This period is then gradually extended by 15- to 20-minute intervals every 5 days until optimal sleep time is achieved.[23] Cognitive behavioral therapy for insomnia incorporates sleep education, cognitive therapy, and behavioral interventions relying on sleep hygiene and sleep restriction.

Of all the US Food and Drug Administration (FDA)—approved pharmacotherapeutic agents for insomnia, most are barbiturates, benzodiazepines, antihistamines (eg, diphenhydramine, doxylamine), or benzodiazepine receptor agonists (zolpidem, zaleplon, eszopiclone), all of which should be avoided in older adults per recommendations of the AGS.[1] Trazodone, a sedating antidepressant, can cause orthostasis and lacks evidence for sustained efficacy in treating insomnia.[23]

The antidepressants doxepin and mirtazapine may be good options for treating insomnia in elderly patients. Doxepin is an FDA-approved medication for insomnia, and the AGS criteria permit the use of doxepin at dosages of less than 6 mg/d in older patients.[1] At such ultralow doses, doxepin is purported to be highly selective for H_1 receptors, to lack anticholinergic effects, and to induce sleep effectively.[1,24] In our opinion, prescribers should continue to exert caution and monitor for anticholinergic effects even with ultralow doxepin doses, particularly when prescribed to fragile older patients. Other tertiary amines, including amitriptyline, clomipramine, and

TABLE 2. Summary of Recommendations for Discontinuation of Benzodiazepine and Management of Insomnia and Anxiety in Older Adults

Discontinuing benzodiazepines	• First inform patients about the risks of benzodiazepines. Use of freely available educational materials can be effective (Tannenbaum et al[17]) • Use slow tapering protocols[a] • Cognitive behavioral therapy should be considered during a taper (Darker et al[18]) • **Avoid** adding new psychopharmacological agents or switching to longer-acting benzodiazepines during a taper
Management of insomnia	• Nonpharmacological approaches, such as sleep restriction—sleep compression, cognitive behavioral therapy for insomnia, and/or sleep hygiene, should be the first line of treatment • Doxepin at <6 mg/d can be safe and effective (Bostwick[24]) • **Avoid** benzodiazepines, anticholinergics, benzodiazepine receptor agonists, trazodone, or barbiturates (American Geriatrics Society[1])
Management of anxiety	• Cognitive behavioral therapy is effective in older patients with anxiety (Stanley et al[25]) • Duloxetine can be used if creatinine clearance is >30 mL/min (American Geriatrics Society[1]) • Sertraline, escitalopram, and citalopram may be considered, but data is lacking • **Avoid** benzodiazepines, paroxetine, tricyclic antidepressants, antihistamines, anticholinergics, benzodiazepine receptor agonists, trazodone, or barbiturates (American Geriatrics Society[1])

[a]For example, Tannenbaum et al[17] developed a successful 22-week tapering schedule.

imipramine, and doxepin in the higher doses typically used for neuropathic pain, dermatologic conditions, and psychiatric disorders are listed as "avoid" by the AGS because of strong anticholinergic properties.[1] Mirtazapine is a sedating antidepressant, and the AGS criteria do not classify it as "avoid" but rather as "use with caution," although the reasoning behind this classification is not provided.[1] Ramelteon is an FDA-approved hypnotic for insomnia that is not mentioned in the AGS criteria. It is effective in treating initial insomnia in both the short and long term, is not sedating, has no abuse potential, and has a benign adverse effect profile.[23] However, although both melatonin and ramelteon certainly show promise, more robust randomized controlled trials in older adults are needed before their efficacy and safety profile are sufficiently understood in this age group (Table 2).

Anxiety

With regard to nonpharmacological approaches, CBT used in primary care settings substantially reduces worry and depressive symptoms and improves the general mental health of older patients with generalized anxiety disorder.[25]

Use of antidepressants to treat anxiety disorders in older adults is an evolving topic. Duloxetine, a serotonin-norepinephrine reuptake inhibitor, can be used to treat anxiety in older adults but should be avoided if creatinine clearance is less than 30 mL/min.[1] Tricyclic antidepressants (eg, amitriptyline, clomipramine, imipramine) should be avoided.[1] Although doxepin doses of less than 6 mg are effective for sleep without causing anticholinergic adverse effects, such a low dose of this tricyclic antidepressant is unfortunately not effective for treating anxiety or depression.[24] Selective serotonin reuptake inhibitors (SSRIs) can be used with caution in older adults. Sodium levels should be closely monitored because SSRIs can cause hyponatremia or the syndrome of inappropriate antidiuretic hormone secretion.[1] In accordance with the AGS recommendations, clinicians should be lean prescribers of psychotropics, and SSRIs should not be combined with more than one centrally acting agent in an elderly patient with uncomplicated depressive or anxiety disorders.[1] As a group, SSRIs increase the risk of falls and fractures and may even decrease bone mineral density.[1,7] Importantly, the magnitude of the risk for falls and fractures differs between various SSRI agents, although large randomized controlled trials quantifying this risk difference are not available. The SSRIs with strong anticholinergic effects, such as paroxetine, have a higher risk for falls and fractures and should be avoided in elderly patients.[1] Sertraline, escitalopram, and citalopram, all FDA-approved and commonly used antidepressants for treating anxiety disorders, are not specifically mentioned in the updated AGS criteria, and we are not aware of randomized controlled trials confirming or refuting that these specific agents increase the risk of falls and fractures in older adults (Table 2).

CONCLUSION

Physicians prescribing benzodiazepines to their elderly patients should educate these patients about the risks of their benzodiazepine use and when advisable, offer them tapering protocols. There is increasing evidence that a substantial proportion of long-term users can discontinue benzodiazepines via interventions that require minimal investment of the physician's time. As long as benzodiazepines are tapered gradually, their discontinuation is safe and comfortable, and many patients can achieve benzodiazepine abstinence. Several alternative pharmacological and nonpharmacological options are available for treating insomnia and anxiety in older adults, obviating the need for benzodiazepines in this group.

Abbreviations and Acronyms: **AGS** = American Geriatrics Society; **CBT** = cognitive behavioral therapy; **FDA** = Food and Drug Administration; **SSRI** = selective serotonin reuptake inhibitor

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REFERENCES

1. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015;63(11):2227-2246.
2. College of Psychiatry of Ireland. A consensus paper on the use of benzodiazepines in specialist mental health services. College

of Psychiatry of Ireland website. http://www.irishpsychiatry.ie/Home.aspx. Published June 2012. Accessed April 27, 2016.
3. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. *JAMA Psychiatry*. 2015;72(2):136-142.
4. Weisberg RB, Dyck I, Culpepper L, Keller MB. Psychiatric treatment in primary care patients with anxiety disorders: a comparison of care received from primary care providers and psychiatrists [published correction appears in *Am J Psychiatry*. 2007;164(5):833]. *Am J Psychiatry*. 2007;164(2):276-282.
5. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. *BMJ Open*. 2014;4(12):e006544.
6. Marra EM, Mazer-Amirshahi M, Brooks G, van den Anker J, May L, Pines JM. Benzodiazepine prescribing in older adults in U.S. ambulatory clinics and emergency departments (2001-10). *J Am Geriatr Soc*. 2015;63(10):2074-2081.
7. Hill KD, Wee R. Psychotropic drug-induced falls in older people: a review of interventions aimed at reducing the problem. *Drugs Aging*. 2012;29(1):15-30.
8. Bakken MS, Engeland A, Engesæter LB, Ranhoff AH, Hunskaar S, Ruths S. Risk of hip fracture among older people using anxiolytic and hypnotic drugs: a nationwide prospective cohort study. *Eur J Clin Pharmacol*. 2014;70(7):873-880.
9. Cumming RG, Le Couteur DG. Benzodiazepines and risk of hip fractures in older people: a review of the evidence. *CNS Drugs*. 2003;17(11):825-837.
10. Moore N, Pariente A, Bégaud B. Why are benzodiazepines not yet controlled substances [editorial]? *JAMA Psychiatry*. 2015;72(2):110-111.
11. Xing D, Ma XL, Ma JX, Wang J, Yang Y, Chen Y. Association between use of benzodiazepines and risk of fractures: a meta-analysis. *Osteoporos Int*. 2014;25(1):105-120.
12. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013:553.
13. Rummans TA, Davis LJ Jr, Morse RM, Ivnik RJ. Learning and memory impairment in older, detoxified, benzodiazepine-dependent patients. *Mayo Clin Proc*. 1993;68(8):731-737.
14. Barker MJ, Greenwood KM, Jackson M, Crowe SF. Persistence of cognitive effects after withdrawal from long-term benzodiazepine use: a meta-analysis. *Arch Clin Neuropsychol*. 2004;19(3):437-454.
15. Zhong G, Wang Y, Zhang Y, Zhao Y. Association between benzodiazepine use and dementia: a meta-analysis. *PLoS One*. 2015;10(5):e0127836.
16. Palmaro A, Dupouy J, Lapeyre-Mestre M. Benzodiazepines and risk of death: results from two large cohort studies in France and UK. *Eur Neuropsychopharmacol*. 2015;25(10):1566-1577.
17. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. *JAMA Intern Med*. 2014;174(6):890-898.
18. Darker CD, Sweeney BP, Barry JM, Farrell MF, Donnelly-Swift E. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. *Cochrane Database Syst Rev*. 2015;5:CD009652.
19. Paquin AM, Zimmerman K, Rudolph JL. Risk versus risk: a review of benzodiazepine reduction in older adults. *Expert Opin Drug Saf*. 2014;13(7):919-934.
20. Denis C, Fatséas M, Lavie E, Auriacombe M. Pharmacological interventions for benzodiazepine mono-dependence management in outpatient settings. *Cochrane Database Syst Rev*. 2006;(3):CD005194.
21. Rickels K, Schweizer E, Garcia España F, Case G, DeMartinis N, Greenblatt D. Trazodone and valproate in patients discontinuing long-term benzodiazepine therapy: effects on withdrawal symptoms and taper outcome. *Psychopharmacology (Berl)*. 1999;141(1):1-5.
22. Wright A, Diebold J, Otal J, et al. The effect of melatonin on benzodiazepine discontinuation and sleep quality in adults attempting to discontinue benzodiazepines: a systematic review and meta-analysis. *Drugs Aging*. 2015;32(12):1009-1018.
23. Bloom HG, Ahmed I, Alessi CA, et al. Evidence-based recommendations for the assessment and management of sleep disorders in older persons. *J Am Geriatr Soc*. 2009;57(5):761-789.
24. Bostwick JM. A generalist's guide to treating patients with depression with an emphasis on using side effects to tailor antidepressant therapy. *Mayo Clin Proc*. 2010;85(6):538-550.
25. Stanley MA, Wilson NL, Novy DM, et al. Cognitive behavior therapy for generalized anxiety disorder among older adults in primary care: a randomized clinical trial. *JAMA*. 2009;301(14):1460-1467.