Late-Life Comorbid Insomnia: Diagnosis and Treatment

Christina S. McCrae, PhD

Abstract

Changing sleep architecture in the elderly may increase their vulnerability to comorbid insomnia. Common comorbid conditions include chronic pain, depression, nocturia, and neurologic conditions such as Parkinson's and Alzheimer's disease. Diagnosing and treating comorbid insomnia in an older population poses special challenges for clinicians given the variety of coexisting medical and psychological conditions, polypharmacy, and the potential adverse effects of the most commonly used medications for insomnia in this population. Thus, the use of nonpharmacologic treatments, such as cognitive behavior therapy and relaxation techniques, is recommended before any medical approaches.

(Am J Manag Care. 2009;15:S14-S23)

For author information and disclosures see end of text.

Although sleep disorders such as insomnia, daytime sleepiness, and frequent awakenings become more common and chronic with age,[1,2] they are not an inevitable result of aging and should not be treated as such.[3]

Instead of linking insomnia in elderly patients to age, clinicians should consider the impact of coexisting physical and mental conditions on sleep. Foley et al, whose review of sleep complaints in nearly 7000 community-dwelling older adults forms the basis for most epidemiologic estimates of sleep disorders in the elderly, found that the prevalence of insomnia in this population increased in conjunction with depressed mood, respiratory symptoms, fair to poor health, or physical disability.[1] Reid et al showed that respondents with only 1 sleep complaint were still 40% more likely to have a poorer physical health summary score and 23% were more likely to have a higher mental health summary score (**Figure 1**).[4] In fact, sleep disorders in the elderly are strongly associated with significant limitations in activities of daily living, declining quality of life, and morbidity and mortality.[2,4,5] For instance, disrupted or lack of sleep may lead to falls and subsequent nursing home placement and affect cognitive functioning.[6] There is also evidence that sleep disturbances may produce physiologic abnormalities and dysfunction in the elderly that can cause physical[7] and mental disorders,[8] and may increase the severity of chronic conditions such as diabetes.[9]

Although current rates of insomnia in the elderly are significant, ranging from 23% to 57% and appearing more frequently in women,[1] practitioners can expect to see these numbers grow given that adults 65 and older make up the fastest growing segment of the US population.[10] Current estimates call for this sector to grow from 13% of the overall 2010 population in the United States to 19.6% in 2030. Thus, understanding the implications and repercussions of insomnia in older adults, as well as treatment issues specific to this population, is important.

Sleep Architecture and Comorbid Insomnia

Differentiating true sleep-related problems from age-related changes in sleep architecture in an elderly population can be challenging. Changes in sleep architecture are generally accepted as a normal part of aging, but, in reality, only a subset develop clinically significant changes in sleep architecture or complain of the subjective symptoms

of insomnia. After about age 50, older adults tend to have more awakenings and reduced sleep efficiency. They sleep less (an average of 6-6.5 hours vs 7 hours in middle age); experience more frequent brief arousals; spend more time in the light sleeping stage 1; and have more frequent shifts between sleeping stages. There is also evidence that older adults spend less time in the deeper, slow-wave sleep and rapid-eye movement (REM) sleep, with REM latency also declining with age. By age 60, however, these changes have become fairly constant and do not continue to worsen.[11] Thus, they should not be considered as sleep disorders or insomnia, but as a natural occurrence of aging.[12]

However, the lighter sleep older adults experience makes them more vulnerable to sleep-related interruptions from medical and psychiatric conditions, contributing to the high rates of comorbid insomnia in this population.[13]

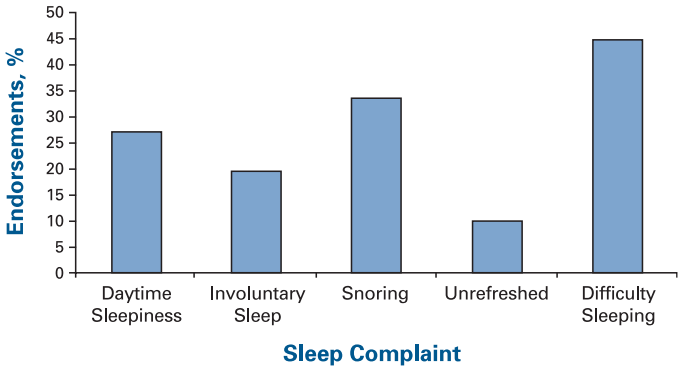
The 2003 National Sleep Foundation's Sleep in America Survey, which involved telephone interviews of 1506 participants aged 55 to 84 years of age about their sleep habits and mental and physical health conditions, found that 69% of respondents with 1 or more sleep problems also had 4 or more medical conditions, whereas just 36% of those with no major medical conditions reported sleep problems.[14] Table 1 shows the odds ratio for insomnia symptoms according to major medical condition.

Other works have found associations between insomnia and arthritis, hypertension, coronary heart disease (CHD), and diabetes.[1,4,14,15] Conversely, improved physical health or even the perception of improved health results in reduced reporting of insomnia.[1] Thus, insomnia in the elderly may be considered a marker for overall mental and physical health.

When assessing older adults for sleep issues, clinicians should consider the severity of the sleep problem; changes in psychosocial, occupational, or physical functioning; and daytime impairment. The latter may manifest as daytime fatigue, irritability, anxiety, feelings of restlessness or other negative effects, cognitive inefficiency, somatic symptoms, errors or accidents while driving, and excessive concerns or worries about sleep.[12]

It is also important that clinicians evaluate patients' overall mental and physical health and

Figure 1. Sleep Complaint Endorsement Rates[a]



[a]Percentage of patients who positively endorsed each complaint on the Five-Item Sleep Questionnaire. Among those reporting complaints with snoring, 29.5% reported feeling unrefreshed as a consequence (ie, 9.8% of the full sample).
Reprinted with permission from Reid KJ, et al. *Am J Geriatr Psychiatry*. 2006;14(10):860-866.

Table 1. Odds Ratio (OR) for Insomnia Symptoms by Major Medical Condition[14]

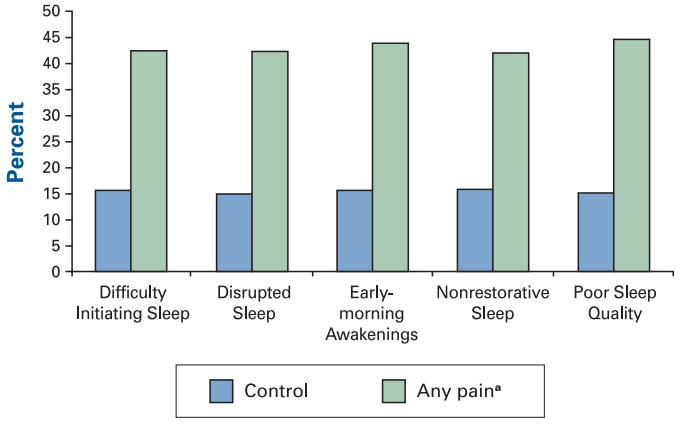
	Insomnia Symptom, %			
Medical Condition	**Difficulty Falling Asleep (9%), OR (95% CI)**	**Awake a Lot During the Night (22%), OR (95% CI)**	**Wake Too Early (11%), OR (95% CI)**	**Wake Unrefreshed (14%), OR (95% CI)**
Obesity	NS	1.36 (1.02-1.82)	NS	1.45 (1.04-2.01)
Bodily pain	1.89 (1.28-2.78)	2.68 (2.06-3.49)	1.88 (1.32-2.66)	2.11 (1.54-2.90)
Depression	2.44 (1.59-3.73)	1.59 (1.14-2.22)	2.21 (1.49-3.29)	NS
Heart disease	1.99 (1.29-3.07)	1.67 (1.23-2.31)	1.87 (1.27-2.78)	NS
Lung disease	NS	NS	NS	1.50 (1.01-2.24)
Memory problems	1.76 (1.08-2.87)	1.56 (1.07-2.27)	NS	NS

CI indicates confidence interval; NS, not significant.
Reprinted with permission from Foley D, et al. *J Psychosom Res*. 2004;56(5):497-502.

Table 2. Medications Associated With Insomnia[18,19]

Central nervous system stimulants
Dextroamphetamine
Methylphenidate
Mixed amphetamine salts
Pemoline
Antihypertensives
Alpha-blockers
Beta-blockers
Methyldopa
Reserpine
Respiratory medications
Albuterol
Theophylline
Chemotherapy
Decongestants
Phenylpropanolamine
Phenylephrine
Pseudoephedrine
Hormones
Corticosteroids
Thyroid medications
Psychotropics
Atypical antidepressants
Monoamine oxidase inhibitors
Selective serotonin reuptake inhibitors
Anticholinesterase inhibitors
Carbidopa, levodopa
Phenytoin
Alcohol
Caffeine
Nicotine

Figure 2. Insomnia Comorbid With Pain



N = 18,980; *P* <.001. Based on survey data.

[a]Pain categories included limb pain, backaches, joint pain, gastrointestinal pain, and headaches.

Reprinted with permission from Ohayon MM. *J Psychiatr Res.* 2005;39(2):151-159.

functioning, as well as all medications, given the high rates of polypharmacy in the elderly[16,17] and the impact of many medications on sleep (Table 2).[18,19]

It is also important to recognize that treating the comorbid medical condition does not necessarily improve the insomnia. This issue is discussed more in depth in the article by Dr Thomas Roth elsewhere in this supplement.[20]

Pain, Depression, and Comorbid Insomnia

One of the most common comorbid conditions affecting sleep quality is chronic pain, which is particularly prevalent in the elderly (Figure 2).[21] Between 50% and 88% of patients attending chronic pain clinics (albeit a self-selecting population) complain of impaired sleep.[22]

Medical conditions associated with chronic pain include rheumatoid arthritis, fibromyalgia, and osteoarthritis. In one of the largest community-based studies to explore the link, Power et al analyzed a cross-sectional nationally representative sample of 118,336 participants ≥18 years of age with arthritis pain, insomnia symptoms, and other sleep-related conditions.[23] They found significantly greater numbers of individuals with arthritis reported pain (45.8%), insomnia (24.8%), and unrefreshing sleep (11.9%) than those without arthritis (11.7%, 10.6%, and 6.1%, respectively [all P <.001]). The greater the level of pain, the greater the prevalence of insomnia symptoms and unrefreshing sleep, even in those without arthritis. Adjusting for pain reduced the effect of arthritis on unrefreshing sleep and insomnia symptoms by 64% and 53%, respectively.

Roehrs et al reported that sleep loss increased pain sensation, likely as a result of REM sleep deprivation, which is associated with hyperalgesia.[24] Other studies reported insomnia causing headaches and headaches causing insomnia,[25] and sleep deprivation increasing next-day pain receptivity in patients with fibromyalgia and arthritis.[26,27]

Pain often manifests in conjunction with depression. Wilson et al reported that patients with major depression and insomnia were more likely to score higher on severity (P = .005), interference (P = .041), life control (P <.001), and affective distress (P = .005) on the Multidimensional Pain Inventory (MPI) than those with insomnia but without major depression, or with neither

insomnia nor major depression.[28] One potential reason for the link could be that patients reporting depression and pain are more likely to exhibit sympathetic nervous system arousal, a factor in insomnia.[29-31]

In addition, patients with insomnia who did not have major depression still showed higher scores on the Beck Depression Inventory, less life control on the MPI, and higher scores on the sensory-discriminative dimension of the McGill Pain Questionnaire than participants without either major depression or insomnia.[28] There is also evidence that insomnia perpetuates depression in elderly adults, even after treatment.[32]

In older adults, Taylor et al showed that elderly patients with insomnia exhibited more severe symptoms of depression and anxiety than those without, and were 9.82 and 17.35 times more likely to have clinically significant depression and anxiety, respectively.[33]

Comorbid Insomnia in Parkinson's and Alzheimer's Diseases

Sleep disturbances are particularly prevalent in patients with neurologic diseases related to aging, such as Parkinson's and Alzheimer's disease. Up to two thirds of patients with Parkinson's disease experience sleep-related disorders, including problems falling asleep, and nighttime and early-morning awakenings.[34]

Meanwhile, Tractenberg et al compared sleep quality in 399 healthy elderly individuals without dementia and 263 persons with a diagnosis of possible or probable Alzheimer's disease. They found a lower prevalence of sleep problems in those without Alzheimer's (18.3%) than in those with Alzheimer's (27.6%) (P <.01). Specifically, patients with Alzheimer's had greater prevalence and frequency of waking after sleep onset (WASO), sleep latency (>30 minutes to fall asleep), waking too early, and waking at night with pain.[35]

Other Comorbid Conditions

Other conditions that may occur comorbidly with insomnia symptoms include nocturia, a common complaint in the elderly. Nocturia is associated with increased mortality, related in part to the consequences of falls resulting from elderly persons awakening in the night to urinate.[36] In one survey of 100 older adults, 59% attributed their sleep disruption to nocturia.[37]

Insomnia and other sleep complaints may be present with CHD. A review of articles on the association between CHD events and sleep complaints exclusive of sleep apnea found risk ratios of 1.47 to 3.90 between "trouble falling asleep" and coronary events after adjusting for age and various coronary risk factors (combined effect, 1.7; P <.0001).[38]

Hypnotic-Dependent Insomnia

Hypnotic-dependent insomnia (HDI) results from chronic use of hypnotics and sedatives as sleep medication. The disorder is particularly prevalent in the elderly, who are most likely to be prescribed hypnotics for sleep-related disturbances and to use them nearly twice as long as younger users.[39,40] It is characterized by a pattern of tolerance and dependence, and marked by rebound insomnia or excessive sleepiness, anxiety, and depression when the medication is stopped.[41] Older adults with HDI are also at risk for seizures and hallucinations.[42]

The condition should be treated with gradual tapered withdrawal from the medication (10%-25% every 1-2 weeks) over 8 to 12 weeks.[43,44] At the lowest possible dose, medication-free nights should be gradually introduced before the medication is completely stopped. Behavioral interventions may also help facilitate medication withdrawal.[45] If tapered withdrawal fails, switching to a longer-acting, cross-tolerant medication such as clonazepam and/or using medication to suppress withdrawal symptoms such as carbamazepine is an option.[44]

Treating Comorbid Insomnia in the Elderly

When determining the appropriate treatment for older adults with comorbid insomnia, it is important to consider the consequences of any treatment on the patient's overall health and interactions with other medications given the high rate of polypharmacy in older adults.[16]

The most commonly used treatments for insomnia in the elderly are medications, primarily benzodiazepine sedative-hypnotics (estazolam, flurazepam, quazepam, temazepam, and triazolam), the nonbenzodiazepine sedative-hypnotics (eszopiclone, zaleplon, and zolpidem), sedating antidepressants (trazodone, nefazodone) used off label, and over-the-counter antihistamines.[46] More recently,

the first nonsedating sleep medication, ramelteon, a selective MT1/MT2 melatonin receptor agonist was approved for the long-term treatment of insomnia characterized by sleep-onset difficulty in the United States.[47] In addition, eszopiclone, zolpidem extended-release, and ramelteon no longer have any implied limitation on the duration of their use. For some patients, long-term use may be successful in improving nighttime sleep and daytime functioning. However, patients taking any of these medications should be regularly observed and evaluated.[48]

In addition, age-related metabolic changes may extend the half-life of these drugs in older adults, leading to cognitive and motor impairment and sleep-related breathing disorders.[49] Sleep medications in the elderly are also associated with falls, fractures, and more days in the hospital (although these adverse effects may, however, be less frequent and severe with the newer benzodiazepine receptor agonists).[49,50] Because of these age-related issues, there is particular need to monitor drug doses and make any necessary adjustments in the elderly. The starting dose of eszopiclone in an elderly individual, for example, is 1 mg and should not exceed 2 mg (compared with 2-3 mg for nonelderly adults).[51]

In 2007 the US Food and Drug Administration requested that manufacturers of all sedative-hypnotic drug products include stronger language on product labeling concerning the potential for severe allergic reactions and complex sleep-related behaviors, which may include sleep-driving.

A meta-analysis of 24 randomized clinical trials in elderly populations (>60 years of age) who used any pharmacologic sleep aids for ≥5 nights for insomnia (over-the-counter medications, benzodiazepine and nonbenzodiazepine sedative-hypnotics) found similar efficacy and adverse effects between the benzodiazepines and nonbenzodiazepines eszopiclone, zaleplon, and zolpidem, but suggested that sedative-hypnotics may have less benefit for older than younger people with similar or greater risk for adverse effects.[52]

Cotroneo et al conducted one of the few, if not the only, published clinical trials to evaluate medical insomnia treatment on elderly patients with comorbid conditions.[53] Researchers evaluated insomnia treatment with zolpidem, triazolam, or oxazepam on 60 subjects aged ≥70 years. Fifteen had insomnia and dementia; 30 had insomnia and depression; and 15 had insomnia only.

After 6 months of treatment, patients with dementia, who were also treated with the anticholinesterase drugs donepezil, galantamine, or rivastigmine, and/or antipsychotic drugs, reported an optimal quality of sleep that positively impacted caregiver satisfaction and quality of life. Patients with depression and insomnia, who were also treated with sertraline, venlafaxine, or escitalopram, reported a sufficient quality of sleep. Finally, those with insomnia only, who were treated only with hypnotic drugs, reported "sufficient" sleep. There were no significant adverse effects with any treatment.[53]

No other trials examine the use of sleep medications in elderly adults with comorbid insomnia. However, it is worthwhile examining published trials of these agents in elderly patients with transient or chronic primary insomnia.

Two published trials examined the effects of eszopiclone 1- and 2-mg dosages compared with placebo on transient insomnia in elderly adults (ages 64-86) during a 2-week period.[54,55] All doses were superior to placebo in improving sleep latency; the 2-mg dose was superior in maintaining sleep. The most commonly reported adverse effect was unpleasant taste. One trial showed a trend toward morning-reported sleepiness.[55] There was no clinically significant evidence of withdrawal symptoms after up to 12 months of eszopiclone use.[56]

Zolpidem has been evaluated in the elderly in one published randomized, double-blind, placebo-controlled trial.[57] This trial evaluated the effect of extended-release zolpidem (6.25 mg) in 205 elderly adults (mean age, 70.2 years) with primary insomnia during a 3-week treatment period. Patient-reported sleep time and awakening after sleep onset were significantly improved with zolpidem over placebo. Polysomnography showed significantly reduced WASO in the zolpidem group compared with placebo with no residual sedation. However, abrupt withdrawal from zolpidem led to 1 night of rebound insomnia while none occurred after withdrawal from placebo. There did not appear to be any issues with tolerance, however. Although zolpidem is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or maintenance, it carries a warning that elderly or debilitated patients may be especially sensitive to its effects.[58] Zolpidem has also been associated with anxiety and subjective ratings suggestive of abuse potential.[59]

Zaleplon has been evaluated in 3 clinical trials in elderly patients. In the first, zaleplon 5 and 10 mg were evaluated during 2 weeks of active treatment against zolpidem 5 mg in 549 elderly patients (ages 65-92) based on morning questionnaires.[60] Zaleplon 10 mg reduced subjective sleep latency (P <.001) during both weeks; zaleplon 5 mg also reduced it during week 2 (P <.01). There was no clinically significant rebound insomnia after discontinuation with zaleplon, although there was some evidence of rebound effects with zolpidem discontinuation. Central nervous system adverse effects were similar among both agents and placebo.

Hedner et al evaluated 5- and 10-mg zaleplon for 2 weeks (among individuals ≥65 years of age) with results provided via postsleep questionnaires.[61] Although both doses significantly reduced subjective sleep latency during the treatment period, there was some evidence of rebound insomnia after discontinuation of treatment with the 10-mg dose.

Finally, to evaluate the long-term use of zaleplon in elderly insomnia patients, Ancoli-Israel et al conducted a 1-year, open-label, extension phase of the 2 previously discussed trials. Patients self-administered zaleplon nightly from 6 to 12 months and were then followed through a 7-day, single-blind, placebo-controlled, run-out period. The study showed similar efficacy in terms of sleep latency and duration and reduced nocturnal awakenings (P <.001 for each) with no evidence of rebound insomnia after discontinuation.[62]

Two published trials evaluated ramelteon in elderly subjects (n = 1156) with primary chronic insomnia for 5 weeks. In the first trial, Roth et al compared ramelteon 4 or 8 mg versus placebo in 829 older adults (mean age, 72.4 years). Patient-reported data showed significantly reduced reports of sleep latency throughout the treatment period with no significant rebound insomnia or withdrawal effects.[63] The second trial was a post hoc analysis of the first trial and focused on 327 older adults (mean age, 72.3 years) with severe sleep-onset difficulty (subjective sleep latency ≥60 minutes).[64] Subjects received 8 mg or placebo. Ramelteon significantly reduced self-reported time to fall asleep during nights 1 through 7 of treatment, an improvement that was sustained through week 5.

Table 3 depicts the dosing recommendations and mean half-life elimination of the nonbenzodiazepine sedative-hypnotics and ramelteon for older adults.

Nonprescription Treatment

In contrast to the lack of published literature on medical treatments for comorbid insomnia in elderly populations, at least 5 published studies have evaluated the use of behavioral therapies for older adults with comorbid insomnia.

Lichstein et al exposed 44 participants (≥58 years of age) with comorbid insomnia to four 1-hour sessions of cognitive behavioral therapy (CBT) consisting of relaxation and stimulus control, or to a delayed-treatment control group. The CBT group

Table 3. Nonbenzodiazepine Sedative-Hypnotics in Older Adults

Medication	Indication	Dosing Patients	Mean Half-Life Elimination in Elderly, h
Eszopiclone[65]	Treatment of insomnia in patients who experienced difficulty falling and/or staying asleep	Sleep-onset difficulty: 1 mg immediately before bed Sleep-maintenance difficulty: 2 mg immediately before bed	~9
Ramelteon	Insomnia characterized by difficulty with sleep onset	8 mg	~1-2.6
Zaleplon	Short-term treatment of insomnia	5 mg	1
Zolpidem[58]	Treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance	6.25 mg once daily immediately before bedtime	2.9

self-reported increased sleep efficiency and sleep quality ratings, both of which were maintained at the 3-month follow-up regardless of the type of comorbidity (psychiatric or medical).[66]

Rybarczyk et al studied comorbid insomnia related to physical medical conditions, screening out patients with psychiatric disorders, in a sample of 38 older adults (mean age, 67.9 years).[67] Participants were randomized to either 8 sessions of group CBT, home-based audio relaxation treatment, or delayed treatment. Based on self-reported measures, the CBT group significantly improved on sleep efficiency, WASO, the Pittsburgh Sleep Quality Index (PSQI) global sleep score, and total score on the Dysfunctional Beliefs and Attitudes about Sleep scale at treatment end and follow-up compared with the control group. The relaxation group improved on sleep efficiency, WASO, and PSQI global score compared with controls. In addition, patients who experienced clinically significant sleep changes also exhibited reduced levels of anxiety.

A larger study in 92 participants with coronary artery disease, osteoarthritis, or chronic obstructive pulmonary disease showed a 78% treatment efficacy across a wide range of sleep-related parameters for participants undergoing CBT compared with a 24% treatment efficacy in the control group, which received stress management training. The results held regardless of the comorbid disease.[68]

Rybarczyk et al also conducted a pilot study in 12 older adults with comorbid insomnia who received a home-based video CBT program. They compared the 12 to 24 participants who received classroom CBT or no treatment and found improvements in the video CBT group similar to those who received the classroom CBT. Attrition in the video CBT group was, however, higher, and the number of participants who achieved clinically significant change was lower (50% vs 73%).[69]

Finally, McCurry et al evaluated a sleep education program in 36 dementia patients in which caregivers received either general dementia education (control) or recommendations about sleep hygiene and training in behavior management skills. Patients also took daily walks and increased their light exposure. Those participating in the education program showed greater reductions in nighttime awakenings and total time awake, and increases in weekly exercise days than control (P <.05). The treatment gains continued at the 6-month follow-up with continued improvement in night awakenings.[70]

In addition to studies of behavioral interventions in comorbid insomnia in the elderly, a meta-analysis of behavioral interventions for primary insomnia in adults aged 55 and older found these interventions (CBT, relaxation training, or behavioral intervention only) were all effective in reducing sleep latency and WASO, and improving sleep quality and efficiency (P <.001), and somewhat effective in improving total sleep time (P <.038).[71] Two studies compared CBT with pharmacologic study in older adults. In one study, 78 older adults with primary or chronic insomnia received either 8 weeks of CBT (stimulus control, sleep restriction, sleep hygiene, and cognitive therapy) (n = 18), temazepam (n = 20), temazepam with CBT (n = 20), or placebo (n = 20). The 3 active treatments were more effective than placebo, with those receiving the combined treatment showing a nonsignificant trend to a slightly higher improvement in sleep continuity measures. However, participants receiving CBT were most likely to show sustained improvement at 6 and 24 months of follow-up than those receiving other treatments.[72]

Sivertsen et al compared CBT to zopiclone or placebo in 46 older adults with chronic primary insomnia. After 6 weeks, participants receiving CBT improved on 3 of 4 outcome measures (sleep efficiency, slow-wave sleep, time awake during the night) than those receiving medication or placebo. Total sleep time was similar in all 3 groups. At 6 months, those who received CBT continued to show greater improvements in sleep efficiency than those who received zopiclone.[73]

Thus, it is recommended that clinicians begin any treatment for comorbid insomnia in the elderly with behavioral therapies, with an attempt at medications after these approaches have failed.

Conclusion

Comorbid insomnia is a prevalent problem in the elderly population. However, misperceptions continue to exist that age-related changes in sleep architecture underlie sleep disturbances in this population. Instead, comorbid medical conditions

are likely to be the most common cause of sleep disturbances. Thus, it is important that clinicians consider patients' overall medical and psychological status when evaluating, diagnosing, and treating insomnia. Several effective medications exist for the treatment of primary insomnia in older adults. Although they have not been specifically studied for the treatment of comorbid insomnia in this population, studies in older adults with primary insomnia suggest they are safe for short-term use. However, because the use of hypnotics in this population may lead to falls, cognitive changes, and other morbidities, nonpharmacologic approaches should also be considered.

Acknowledgment

Thank you to Debra Gordon, medical writer, who assisted in the writing of this article.

Author Affiliation: From the Department of Clinical and Health Psychology, University of Florida, Gainesville.

Funding Source: Financial support for this work was provided by Sepracor.

Author Disclosure: The author reports 2 grants received and several pending grants from the National Institutes of Health.

Authorship Information: Concept and design; drafting of the manuscript; critical revision of the manuscript for important intellectual content.

Address correspondence to: Christina C. McCrae, PhD, Associate Professor, Department of Clinical and Health Psychology, University of Florida, PO Box 100165 (HSC), 101 S Newell Dr, Gainesville, FL 32610-0165. E-mail: csmccrae@phhp.ufl.edu.

REFERENCES

1. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep.* 1999;22(suppl 2):S366-S372.

2. Newman AB, Enright PL, Manolio TA, Haponik EF, Wahl PW. Sleep disturbance, psychosocial correlates, and cardiovascular disease in 5201 older adults: the Cardiovascular Health Study. *J Am Geriatr Soc.* 1997;45(1):1-7.

3. Maggi S, Langlois JA, Minicuci N, et al. Sleep complaints in community-dwelling older persons: prevalence, associated factors, and reported causes. *J Am Geriatr Soc.* 1998;46(2):161-168.

4. Reid KJ, Martinovich Z, Finkel S, et al. Sleep: a marker of physical and mental health in the elderly. *Am J Geriatr Psychiatry.* 2006;14(10):860-866.

5. Schubert CR, Cruickshanks KJ, Dalton DS, Klein BE, Klein R, Nondahl DM. Prevalence of sleep problems and quality of life in an older population. *Sleep.* 2002;25(8):889-893.

6. Cricco M, Simonsick EM, Foley DJ. The impact of insomnia on cognitive functioning in older adults. *J Am Geriatr Soc.* 2001;49(9):1185-1189.

7. Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter E. Sleep loss: a novel risk factor for insulin resistance and type 2 diabetes. *J Appl Physiol.* 2005;99(5):2008-2019.

8. Chang PP, Ford DE, Mead LA, Cooper-Patrick L, Klag MJ. Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study. *Am J Epidemiol.* 1997;146(2):105-114.

9. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet.* 1999;354(9188):1435-1439.

10. US Census Bureau. U.S. Interim Projections by Age, Sex, Race, and Hispanic Origin. March 18, 2004. www.census.gov/ipc/www/usinterimproj/. Accessed April 16, 2008.

11. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep.* 2004;27(7):1255-1273.

12. Nau SD, Cook KG, McCrae CS, Lichstein KL. Treatment of insomnia in older adults. *Clin Psych Rev.* 2005;25:645-672.

13. McCrae CS, Lichstein KL. Secondary insomnia: diagnostic challenges and intervention opportunities. *Sleep Med Rev.* 2001;5(1):47-61.

14. Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. *J Psychosom Res.* 2004;56(5):497-502.

15. Vitiello MV, Moe KE, Prinz PN. Sleep complaints cosegregate with illness in older adults: clinical research informed by and informing epidemiological studies of sleep. *J Psychosom Res.* 2002;53(1):555-559.

16. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J Geriatr Pharmacother.* 2007;5(4):345-351.

17. Hayes BD, Klein-Schwartz W, Barrueto F Jr. Polypharmacy and the geriatric patient. *Clin Geriatr Med.* 2007;23(2):371-390, vii.

18. Ancoli-Israel S. Sleep and aging: prevalence of disturbed sleep and treatment considerations in older adults. *J Clin Psychiatry.* 2005;66(suppl 9):24-30.

19. Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 1. Sleep disorders commonly found in older people. *CMAJ.* 2007;176(9):1299-1304.

20. Roth T. Comorbid insomnia: current directions and future challenges. *Am J Manag Care.* 2009;15:S6-S13.

21. AGS Panel on Persistent Pain in Older Persons. The management of persistent pain in older persons. *J Am Geriatr Soc.* 2002;50(6 suppl):S205-S224.

22. Pilowsky I, Crettenden I, Townley M. Sleep disturbance in pain clinic patients. *Pain.* 1985;23(1):27-33.

23. Power JD, Perruccio AV, Badley EM. Pain as a mediator of sleep problems in arthritis and other chronic conditions. *Arthritis Rheum.* 2005;53(6):911-919.

24. Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T. Sleep loss and REM sleep loss are hyperalgesic. *Sleep.* 2006;29(2):145-151.

25. Paiva T, Batista A, Martins P, Martins A. The relationship between headaches and sleep disturbances. *Headache.* 1995;35(10):590-596.

26. Moldofsky H, Scarisbrick P, England R, Smythe H. Musculoskeletal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. *Psychosom Med.* 1975;37(4):341-351.

27. Moldofsky H. Sleep influences on regional and diffuse pain syndromes associated with osteoarthritis. *Semin Arthritis Rheum.* 1989;18(4 suppl 2):18-21.

28. Wilson KG, Eriksson MY, D'Eon JL, Mikail SF, Emery PC. Major depression and insomnia in chronic pain. *Clin J Pain.* 2002;18(2):77-83.

29. Roehrs T, Roth T. Sleep and pain: interaction of two vital functions. *Semin Neurol.* 2005;25(1):106-116.

30. Husain MM, Rush AJ, Trivedi MH, et al. Pain in depression: STAR*D study findings. *J Psychosom Res.* 2007;63(2):113-122.

31. Roth T. A physiologic basis for the evolution of pharmacotherapy for insomnia. *J Clin Psychiatry.* 2007;68(suppl 5):13-18.

32. Pigeon WR, Hegel M, Unützer J, et al. Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep.* 2008;31(4):481-488.

33. Taylor DJ, Lichstein KL, Durrence HH, Reidel BW, Bush AJ. Epidemiology of insomnia, depression, and anxiety. *Sleep.* 2005;28(11):1457-1464.

34. Tandberg E, Larsen JP, Karlsen K. A community-based study of sleep disorders in patients with Parkinson's disease. *Mov Disord.* 1998;13(6):895-899.

35. Tractenberg RE, Singer CM, Kaye JA. Symptoms of sleep disturbance in persons with Alzheimer's disease and normal elderly. *J Sleep Res.* 2005;14(2):177-185.

36. Stewart RB, Moore MT, May FE, Marks RG, Hale WE. Nocturia: a risk factor for falls in the elderly. *J Am Geriatr Soc.* 1992;40(12):1217-1220.

37. Hoch CC, Bysse DJ, Monk TH, Reynolds CF III. Sleep disorders and aging. In: Birren JE, Sloane RB, Cohen GD, eds. *Handbook of Mental Health and Aging.* San Diego, CA: Academic Press; 1991.

38. Schwartz S, McDowell Anderson W, Cole SR, Cornoni-Huntley J, Hays JC, Blazer D. Insomnia and heart disease: a review of epidemiologic studies. *J Psychosom Res.* 1999;47(4):313-333.

39. Morgan K, Clarke D. Longitudinal trends in late-life insomnia: implications for prescribing. *Age Ageing.* 1997;26(3):179-184.

40. Stewart R, Besset A, Bebbington P, et al. Insomnia comorbidity and impact and hypnotic use by age group in a national survey population aged 16 to 74 years. *Sleep.* 2006;29(11):1391-1397.

41. American Academy of Sleep Medicine. *The International Classification of Sleep Disorders-2.* Westchester, IL: American Academy of Sleep Medicine; 2005.

42. Landry MJ, Smith DE, McDuff DR, Baughman OL 3rd. Benzodiazepine dependence and withdrawal: identification and medical management. *J Am Board Fam Pract.* 1992;5(2):167-175.

43. Morin CM, Baillargeon L, Bastien C. Discontinuation of sleep medications. In: Lichstein KL, Morin CM, eds. *Treatment of Late Life Insomnia.* Thousand Oaks, CA: Sage; 2000:271-296.

44. DuPont RL. A physician's guide to discontinuing benzodiazepine therapy. *West J Med.* 1990;152(5): 600-603.

45. Morin CM, Bastien C, Guay B, Radouco-Thomas M, Leblanc J, Vallieres A. Randomized clinical trial of supervised tapering and cognitive behavior therapy to facilitate benzodiazepine discontinuation in older adults with chronic insomnia. *Am J Psychiatry.* 2004;161(2):332-342.

46. Bain KT. Management of chronic insomnia in elderly persons. *Am J Geriatr Pharmacother.* 2006;4(2):168-192.

47. Rozerem [package insert]. Deerfield, IL: Takeda Pharmaceuticals; 2006.

48. Neubauer D. Optimizing the long-term treatment of insomnia. http://www.medscape.com/viewarticle/549102_1. Accessed November 10, 2008.

49. NIH State-of-the-Science Conference Statement on manifestations and management of chronic insomnia in adults. *NIH Consens State Sci Statements.* 2005;22(2):1-30.

50. Ray WA, Griffin MR, Downey W. Benzodiazepines of long and short elimination half-life and the risk of hip fracture. *JAMA.* 1989;262(23):3303-3307.

51. Lunesta [package insert]. Marlborough, MA: Sepracor; 2008.

52. Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ.* 2005;331(7526):1169.

53. Cotroneo A, Gareri P, Nicoletti N, et al. Effectiveness and safety of hypnotic drugs in the treatment of insomnia in over 70-year-old people. *Arch Gerontol Geriatr.* 2007;44(suppl 1):121-124.

54. Scharf M, Erman M, Rosenberg R, et al. A 2-week efficacy and safety study of eszopiclone in elderly patients with primary insomnia. *Sleep.* 2005;28(6):720-727.

55. McCall WV, Erman M, Krystal AD, et al. A polysomnography study of eszopiclone in elderly patients with insomnia. *Curr Med Res Opin.* 2006;22(9):1633-1642.

56. Roth T, Walsh JK, Krystal A, Wessel T, Roehrs TA. An evaluation of the efficacy and safety of eszopiclone over 12 months in patients with chronic primary insomnia. *Sleep Med.* 2005;6(6):487-495.

57. Walsh JK, Soubrane C, Roth T. Efficacy and safety of zolpidem extended release in elderly primary insomnia patients. *Am J Geriatr Psychiatry.* 2008;16(1):44-57.

58. Ambien [package insert]. Bridgewater, NJ: Sanofi-Aventis; 2008.

59. Rush CR, Baker RW, Wright K. Acute behavioral effects and abuse potential of trazodone, zolpidem and triazolam in humans. *Psychopharmacology (Berl).* 1999;144(3):220-233.

60. Ancoli-Israel S, Walsh JK, Mangano RM, Fujimori M. Zaleplon, a novel nonbenzodiazepine hypnotic, effectively treats insomnia in elderly patients without causing rebound effects. *Prim Care Companion J Clin Psychiatry.* 1999;1(4):114-120.

61. Hedner J, Yaeche R, Emilien G, Farr I, Salinas E. Zaleplon shortens subjective sleep latency and improves subjective sleep quality in elderly patients with insomnia. The Zaleplon Clinical Investigator Study Group. *Int J Geriatr Psychiatry.* 2000;15(8):704-712.

62. Ancoli-Israel S, Richardson GS, Mangano RM, Jenkins L, Hall P, Jones WS. Long-term use of sedative hypnotics in older patients with insomnia. *Sleep Med.* 2005;6(2):107-113.

63. Roth T, Seiden D, Sainati S, Wang-Weigand S, Zhang J, Zee P. Effects of ramelteon on patient-reported sleep latency in older adults with chronic insomnia. *Sleep Med.* 2006;7(4):312-318.

64. Mini LJ, Wang-Weigand S, Zhang J. Self-reported efficacy and tolerability of ramelteon 8 mg in older adults experiencing severe sleep-onset difficulty. *Am J Geriatr Pharmacother.* 2007;5(3):177-184.

65. Lunesta [package insert]. Marlborough, MA: Sepracor; 2007.

66. Lichstein KL, Wilson NM, Johnson CT. Psychological treatment of secondary insomnia. *Psychol Aging.* 2000;15(2):232-240.

67. Rybarczyk B, Lopez M, Benson R, Alsten C, Stepanski E. Efficacy of two behavioral treatment programs for comorbid geriatric insomnia. *Psychol Aging.* 2002;17(2):288-298.

68. Rybarczyk B, Stepanski E, Fogg L, Lopez M, Barry P, Davis A. A placebo-controlled test of cognitive-behavioral therapy for comorbid insomnia in older adults. *J Consult Clin Psychol.* 2005;73(6):1164-1174.

69. Rybarczyk B, Lopez M, Schelble K, Stepanski E. Home-based video CBT for comorbid geriatric insomnia: a pilot study using secondary data analyses. *Behav Sleep Med.* 2005;3(3):158-175.

70. McCurry SM, Gibbons LE, Logsdon RG, Vitiello MV, Teri L. Nighttime insomnia treatment and education for Alzheimer's disease: a randomized, controlled trial. *J Am Geriatr Soc.* 2005;53(5):793-802.

71. Irwin MR, Cole JC, Nicassio PM. Comparative meta-analysis of behavioral interventions for insomnia and their efficacy in middle-aged adults and in older adults 55+ years of age. *Health Psychol.* 2006;25(1):3-14.

72. Morin CM, Colecchi C, Stone J, et al. Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. *JAMA.* 1999;281(11): 991-999.

73. Sivertsen B, Omvik S, Pallesen S, et al. Cognitive behavioral therapy vs zopiclone for treatment of chronic primary insomnia in older adults: a randomized controlled trial. *JAMA.* 2006;295(24):2851-2858.