

CURRENT APPROACHES TO MANAGING

Insomnia *in the Elderly*



ACTIVITY OVERVIEW

This supplement consists of four sections on the diagnosis and management of older patients with chronic insomnia.

Intended Audience

This activity is intended for PAs and NPs treating elderly patients with chronic insomnia.

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Understand underlying mechanisms of systems that drive and maintain sleep.
2. Recognize, medical, psychiatric, pharmacologic, and environmental factors that contribute to chronic insomnia.
3. Identify the most appropriate first-line chronic insomnia therapies for individual elderly patients and second- and third-line treatments along with adjunctive measures, based on clinical recommendations.

How to Receive CME/CE Credit

There are no fees for participating and receiving CME/CE credit for this activity. Participants must:

1. Read the learning objectives.
2. Read each article in the supplement.
3. For AAPA CME go to www.aapa.org/InsomniaCME to complete the online post-test and evaluation in Learning Central (Post-test questions cover all articles in the supplement.) To obtain credit, participants must complete the post-test and evaluation. A minimum score of 70% is required on the post-test. Your certificate will be available under “My transcript” for your records.
4. For AANP CE go to <https://aanp.inreachce.com>
NPs go to <http://aanp.inreachce.com> in CE Center > browse by keyword “insomnia”. To obtain credit, participants must complete the post-test and evaluation. A minimum score of 70% is required on the post-test. Your certificate will be available under >My account > Portfolio.

Accreditation Statement

This activity has been reviewed by the AAPA/AANP Review Panel and is compliant with AAPA CME and AANP CE criteria. This activity is designated for 1 AAPA CME Category 1 credit and AANP 1.0 CE and 0.5RX contact hours of credit. PAs and NPs should only claim credit commensurate with the extent of their participation. Approval is valid until April 30, 2020.

Faculty

Daniel J. Buysse, MD

UPMC Professor of Sleep Medicine

Professor of Psychiatry and Clinical and Translational Science

University of Pittsburgh School of Medicine

Sharon M. O’Brien MPAS, PA-C

Practicing PA and Contributing Medical Editor, Clinical Advisor

Teresa D. Valerio, DNP, MSA, APRN, FNP-BC, DBSM

Family Nurse Practitioner, Essentia Health

DNP Leader and Assistant Instructional Professor,

Mennonite College of Nursing at Illinois State University

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Disclosure Policy Statement

It is the policy of both AAPA and AANP to require the disclosure of the existence of any significant financial interest or any other relationship a faculty member has with the commercial interest of any commercial product discussed in an educational presentation. Please review disclosures associated with authors on original articles.

Daniel J. Buysse, MD - *Consultant for BeHealth and Consultant and CME Content Development for CME Institute*

Sharon M. O’Brien MPAS, PA-C - *Nothing to disclose*

Linda Peckel - *Nothing to disclose*

Teresa D. Valerio, D.N.P., M.S.A., APRN, FNP-BC, DBSM - *Nothing to disclose*

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SECTION I: OVERVIEW OF INSOMNIA IN THE ELDERLY

Insomnia is defined as dissatisfaction with the quality or quantity of sleep, indicated by difficulty falling asleep, or difficulty returning to sleep after an awakening, and clinically significant daytime impairment or distress, despite adequate opportunities for sleep.^{1,2} Prevalence estimates of insomnia in very healthy older adults have indicated that they are similar to younger people of very good health—and yet, nearly half of all older individuals report some form of sleep disturbance.^{3,4} The high prevalence of insomnia among the elderly is often attributed to other factors associated with aging, particularly the onset of one or more comorbid conditions.

THE 4 STAGES OF SLEEP

The human sleep cycle is made up of 4 stages.^{5,6} The first 3 are non-rapid eye movement (NREM) stages, which take up an average of 18%, 48%, and 16% of sleep time in adults over 60. The last cycle of rapid eye movement (REM) sleep occupies about 18% of sleep time.

Stage N1 – *Light sleep.*

Stage N2 – *Deeper sleep, characterized by slowing of brain waves, drop in body temperature and heart rate*

Stage N3 “Delta” Sleep – *The deepest state, characterized by very slow brain waves and the highest arousal threshold.*

REM Sleep – *Sometimes called “paradoxical sleep” because it mimics the brain activity level of the awake state, although voluntary muscles remain atonic (except eye movement). REM is accompanied by variability in heart rate and blood pressure. Dreaming occurs predominantly during REM sleep, although some dreaming can also occur during NREM.*

These 4 stages typically cycle 4-5 times in a single night of sleep, punctuated by brief awakenings that typically occur during lighter NREM or REM stages.⁶

Circadian Rhythms and Sleep

Like all animals, humans have an endogenous circadian clock that has a period of about 24 hours. Circadian rhythms are an expression of self-regulating transcription-translation feedback pathways (a molecular “clock”) in every cell of our bodies.

The suprachiasmatic nucleus (SCN) functions as a sort of “conductor” to synchronize the circadian rhythms in all of our cells and tissues to control a range of body functions, including metabolism, hormonal balances, cardiac rhythms, and most notably, sleep/wake cycles.^{7,8}

Circadian rhythms represent the balance of multiple clocks driven by clock genes in all cells as they provide feedback to the main clock controlled by the SCN.⁸ These multiple rhythms operate in a delicate balance that becomes entrained to the environmental light-dark cycle, which varies by location and day of the year, and they are modified by the physiologic needs of the body, which can be altered on a daily basis.

Circadian rhythms govern all physical and mental functions; and that behavior, in turn, exerts feedback control over circadian timing. Sleep-wake cycles are the most obvious expression of circadian rhythmicity. Circadian rhythms and sleep-wake patterns can be disrupted by environmental factors such as shift work, jet lag, noisy environments, changes in meal or activity patterns, and the use of light-emitting electronic devices. Endogenous factors can also affect circadian rhythms and sleep; common examples include anxiety or depression, pain, neurological disorders (such as Alzheimer’s disease), and various medications.^{7,8}

Features of Sleep Affected by Aging

In general, older adults fall asleep earlier and wake earlier than they did when they were younger. These changes may result from advancing of circadian phase (ie, earlier timing), and a reduced homeostatic sleep drive (ie, sleep drive that increases as a function of prior wakefulness). The timing (phase) of core body temperature, melatonin, and cortisol levels have all been shown to shift to earlier times in middle-aged and older adults as compared to people in their twenties.⁷

Sleep is characterized by a number of different parameters of both timing and structure that are affected by aging to varying degrees:⁹

- **Total sleep time** ranges decrease from 10-14 hours in childhood to 6.5-8.5 in young adulthood, and further to 5-7 hours in middle age, plateauing in the sixth decade. TST decreases by about 10-12 minutes per decade of life, starting in the twenties.
- **Sleep efficiency** declines slowly throughout life, continuing past age 60.
- **Sleep maintenance** refers to the ability to stay asleep. After childhood, this decreases as the number of nighttime arousals and time to sleep onset both increase, plateauing at about age 60.

Insomnia in the Elderly

Some older patients may report falling asleep and waking earlier, awakening more frequently during the night, and taking daily naps. These sleep characteristics may be experienced as normal, acceptable patterns, which are not reported as problems. On the other hand, the most common sleep complaints of people in their sixties and older are difficulties with sleep maintenance, reported by 50-70% of individuals, while 35-60% have trouble falling asleep and 20-25% complain of non-restorative sleep.⁵ These symptoms may indicate specific sleep disorders, which can be associated with significant morbidity and mortality in older adults.^{5,10}

ABBREVIATIONS: Sleep Parameters

SE = Sleep Efficiency: *The ratio of time asleep to time in bed (X100)*

SOL = Sleep Onset Latency: *Amount of time to initially fall asleep*

TST = Total Sleep Time

WASO = Wake After Sleep Onset: *Total amount of wakefulness across all awakenings*

VARIATIONS IN DEFINITIONS OF INSOMNIA⁵

Clinical definitions of insomnia vary, depending upon the guidelines used:

The Diagnostic and Statistical Manual for Mental Disorders-5 (DSM-525): defines insomnia as a pattern of sleep disturbance occurring at least 3 nights weekly over 3 months, despite adequate opportunities for sleep, causing significant distress or functional impairment. The DSM-5 definition removed the criteria for "nonrestorative sleep."

The International Statistical Classification of Diseases and Related Health Problems-10 (ICD-10):^{5,11} specifies symptoms of nonrestorative sleep lasting at least 1 month not triggered by another sleep-wake cycle disorder, medical or psychiatric disorder, or substance abuse.

The International Classification of Sleep Disorders-3 (ICSD-3):¹² defines insomnia as difficulty initiating or maintaining sleep occurring at least 3 nights weekly over 3 months, producing daytime consequences and not caused by environmental disturbances or insufficient opportunities for sleep.

3 MAIN TYPES OF INSOMNIA COMPLAINTS

The majority of older adults have multiple sleep complaints. Up to 50% of older adults experience insomnia involving one or more symptoms:^{5,9}

- 1) Sleep onset insomnia (Difficulty falling asleep)
- 2) Sleep maintenance insomnia (Frequent awakenings and difficulty returning to sleep)
- 3) Early awakening with inability to return to sleep

Consequences of Insomnia in the Elderly

Insomnia in young and mid-life adults may have consequences including adverse effects (AEs) on memory and concentration, mood, and energy. Older adults may be less affected by and more tolerant of sleep disruptions than younger people, and they may be less likely to complain of sleep problems, even when symptoms are present.¹³ In general, older people with insomnia tend to complain of fatigue (tiredness) much more often than sleepiness (falling asleep during the day), as classic chronic insomnia is associated with reduced physiological sleepiness during the day and hyperarousal increases wakefulness at all times of day.

This was exemplified by a study of driving performance that found less impact of sleep deprivation on older adults as compared with those who were younger.¹⁴

On the other hand, insomnia contributes to poorer health outcomes in patients of all ages, including higher risks of depression, cancer, heart disease, and cognitive impairment.^{6,8,15} Higher mortality rates among older adults have been associated with longer sleep latency (>30 minutes) and a reduced sleep efficiency of <80%.¹⁰

SECTION II: Screening for Insomnia in the Elderly

Due to frequent contact with elderly patients, nurse practitioners (NPs) and physician assistants (PAs) have significant opportunities to identify and treat insomnia. No objective tests for insomnia exist, however, and so a clinical diagnosis is based primarily on history provided by the patient and/or caregiver. Several screening tools for general use are also available to evaluate the presence of insomnia in older adults. They are easy to use and take just a few minutes to administer during a clinical visit.

Assessing Sleep Quality

- The Patient-Reported Outcomes Measurement Information System (PROMIS) is a 27-item self-reporting questionnaire that assesses quality and depth of sleep and sleep satisfaction over the past week. The 7- or 8-item short form is more expedient for the patient and clinician and should serve just as well. Although many study samples included older adults, it has not been specifically evaluated in this population.^{16,17}
- The Pittsburgh Sleep Quality Index (PSQI) is an 18-item self-reported questionnaire that measures sleep across 7 domains (sleep quality, latency, duration, efficiency, daytime dysfunction, sleep disturbance, and use of sleep medications) during the prior month. Although the PSQI has produced variable results in adults over 80, it is considered a reliable tool for the measurement of subjective sleep quality in older adults.^{16,18}
- The Epworth Sleepiness Scale (ESS) is a validated self-reporting tool that assesses the likelihood of dozing in specific situations. Although it is widely used in people of all ages, it has also been specifically studied in older men. It was found to be reliable in men over 70 years of age¹⁹ and showed a particular sensitivity in men and women who were cognitively impaired.^{18,20} Scores of >10 are interpreted as reflecting excessive daytime sleepiness

- The Functional Outcomes of Sleep Questionnaire 30 (FOSQ-30) includes 30 questions designed to assess the impact of sleep disorders on daytime function in all individuals with insomnia. Questions cover 5 domains, including activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcomes, with 4-point scores for each, which are then totaled. In specific studies in older people, the FOSQ-30 and a shorter version, the FOSQ-10, both demonstrated good sensitivity to differences in daytime function between people over 65 with insomnias compared to those without.^{21,22}

Assessing Sleep Apnea

Obstructive sleep apnea (OSA) is typically associated with snoring and daytime sleepiness, and may be comorbid with insomnia. However, the presentation of OSA in older adults may differ from that seen in middle-aged patients. Specifically, older adults with OSA are less likely to have witnessed apneas and daytime sleepiness, and are more likely to have insomnia. Many instruments are used in adults of all ages to screen for possible obstructive sleep apnea (OSA), using a combination of self-reporting and objective features, and have been deemed useful in the older population as well.¹⁶

- The Berlin Questionnaire consists of 10 questions that cover 3 areas: witnessed episodes of snoring and/or apnea, daytime fatigue and sleepiness, and history of hypertension or BMI < 30 kg/m².¹⁶
- The OSA50 is a modified version of the Berlin Questionnaire that focuses on 4 features, including waist circumference, witnessed apneas, snoring, and age over 50. The first 2 areas are worth 3 points and the last 2 are worth 2 points each. A total of 5 points or greater out of 10 suggests a high probability of OSA.¹⁶
- The STOP-BANG questionnaire for sleep apnea has not been specifically studied in older populations, but is generally considered a good tool overall for assessment of risk of sleep apnea in all ages. Individual risk is measured by positive answers to 4 or more of 8 questions.¹⁶

Sleep Diary

The sleep diary is a particularly useful tool for assessing sleep disturbances in older adults. In 2008, an expert panel created a standardized consensus sleep diary designed to provide a basis for comparative research when assessing sleep disorders.²³

Sleep diaries are daily records of sleep and sleep-related behaviors, often completed in the morning and at bedtime. The morning portion collects information on the previous night's sleep, including bedtime and wake time, while the evening portion usually collects information on daytime activities. A sleep diary can capture information about sleep timing, regularity, quantity, and quality of sleep over a period of time (typically 1-2 weeks), as well as other behaviors and habits that may affect sleep:

Evening completion

- Time and content of
 - ◊ Meals
 - ◊ Caffeine consumption
 - ◊ Alcohol consumption
 - ◊ Use of tobacco or marijuana products
- Physical activity (including walking, workouts, and physical tasks at work or at home)
- Stress levels, emotional events, and moods
- Activities before bed time

Morning completion

- Bedtime
- Sleep onset latency
- Number and times of nocturnal awakenings
- Wakefulness after sleep onset
- Total sleep time
- Final awakening time
- Out of bed time
- Sleep efficiency

SECTION III: Assessment of Insomnia and Contributing Factors in the Elderly

Clinicians should review all potential factors that may cause or contribute to insomnia for each patient. The 3P Model of Insomnia proposed by Spielman et al²⁵ describes 3 categories of contributing factors—perpetuating, precipitating, or predisposing—which can be useful in assessing insomnia, educating patients about insomnia, and designing a treatment plan.

3P MODEL OF INSOMNIA IN THE ELDERLY: Perpetuating/Precipitating/Predisposing Factors^{5,6,25}

Predisposing factors: Patient characteristics that increase or decrease the likelihood of having insomnia. Common predisposing factors include comorbid physical and mental conditions, a family history of insomnia, or socioeconomic or financial stress.

Precipitating factors: Events or factors that initiate insomnia. Precipitating factors may include physical, emotional, or environmental changes, and can involve both positive life events—such as moving, planning a wedding, new pets or young children around the house—or negative life events, including loss of a loved one, hospitalization, recovery from surgery, recent trauma, or use of medications.

Perpetuating factors: External factors or behaviors that contribute to poor sleep, including poor sleep habits, patterns of emotional and behavioral responses to daily life, and use of medications and caffeine.

REFERRAL FOR OVERNIGHT SLEEP STUDY/POLYSOMNOGRAPHY²⁴

Polysomnography (PSG) involves an overnight stay at a sleep laboratory to monitor sleep stages and identify sleep disorders. This multi-dimensional type of study is used to detect primary sleep disorders, including OSA, periodic limb disorder, and REM sleep behavior disorder.

Multiple channels of electrophysiological data are collected simultaneously. At minimum, PSG includes:

- **Electroencephalography (EEG)** – 2 or more channels may be used, with 10-20 electrodes placed for monitoring of sleep onset latency and nocturnal arousals.
- **Electrooculography (EOG)** – 2 EOG channels are used to monitor vertical and horizontal eye movements to capture slow-rolling eye movements that signal sleep onset and later periods of REM sleep.
- **Surface electromyography (EMG)** – Used to measure muscle tone and periodic limb movements.

Additionally, sensors may be applied to measure sleep-disordered breathing (sleep apnea). These sensors typically include oral/nasal airflow, thoracic and abdominal respiratory effort, pulse oximetry, and EKG.

Video and audio recordings may also be conducted continuously to monitor changes to sleep positions and snoring.

TABLE 1: Factors Contributing to Insomnia in the Elderly^{2,4,26-30}

PRIMARY SLEEP DISORDERS	
<ul style="list-style-type: none"> • Sleep apnea • Periodic limb movements • Restless leg syndrome (RLS) • REM behavior disorder (RBD) 	<p>Several primary sleep disorders increase in prevalence in older adults compared to younger people,^{14,15} and may be comorbid with insomnia disorder. The secondary effects of RBD can cause interrupted sleep. RBD is seen in the older population.^{4,31}</p>
COMORBID MEDICAL CONDITIONS	
<ul style="list-style-type: none"> • Diabetes • Pain syndromes (arthritis, cancer) • Cardiac or pulmonary disease • Gastroesophageal reflux disorder (GERD) • Dementia 	<p>More than two-thirds of older adults have multiple comorbid conditions that may affect sleep.^{8,16}</p>
COMORBID PSYCHIATRIC CONDITIONS	
<ul style="list-style-type: none"> • Anxiety • Depression • Bipolar disorder • Psychotic disorders • Post-traumatic stress disorder (PTSD) 	<p>Insomnia is frequently comorbid with psychiatric disorders.¹⁷ Depression and anxiety are particularly common in older adults. Psychiatric conditions and insomnia may reinforce each other; insomnia is associated with both greater severity of psychiatric illness and greater risk of new psychiatric illness.¹⁸</p>
BEHAVIORAL FACTORS	
<ul style="list-style-type: none"> • Use of alcohol, nicotine, or caffeine • Daytime napping • Poor sleep habits 	<p>Sleep-interfering behaviors may both contribute to, and be exacerbated by, insomnia.</p>
MEDICATIONS	
<ul style="list-style-type: none"> • Angiotensin converting enzyme inhibitors • Alpha blockers • Antidepressants • Antihistamines • Antipsychotics • Beta blockers • Corticosteroids • Decongestants • Diuretics • Nicotine replacement patches and pills • Sedatives • Selective serotonin reuptake inhibitors (SSRIs) • Sympathomimetic stimulants • Theophylline • Thyroid hormone • Weight loss medications and diet pills 	<p>At least one-third of older adults are regularly taking 5 or more medications for chronic disorders.⁸ Many of these medications have significant effects on sleep parameters. Any medication that passes the blood-brain barrier can affect sleep.</p>
ENVIRONMENTAL FACTORS	
<ul style="list-style-type: none"> • Retirement/change of job status • Death of spouse or cohabiting partners • Moving to a new location • Financial stress • Hospitalization or nursing home residency 	<p>Environmental stressors of various types can contribute to insomnia.</p>
PHYSIOLOGIC CHANGES	
<ul style="list-style-type: none"> • Circadian rhythms • Reduced homeostatic sleep drive • Sleep related hormones (melatonin, cortisol, growth hormone, prolactin, TSH) 	<p>Physiologic changes directly associated with aging result in advanced sleep/wake phase timing, shorter TST, reduced sleep efficiency, and increased nocturnal awakenings.⁸</p>

^aTable adapted from Vitiello et al, 2012,⁴ Li et al 2018,¹³ Dean et al 2017,²⁸ Brewster et al 2018.³⁰

PRIMARY SLEEP DISORDERS

Impaired sleep is not a normal condition of aging, and when it appears, it may be multifaceted. It is important to differentiate between primary sleep disorders and chronic insomnia, and the comorbid presence of both in order to determine the best treatment options.

Sleep-Disordered Breathing

Sleep apnea is defined as a reduction (hypopnea) or absence (apnea) of airflow during sleep and lasting for at least 10 seconds. There are two major types of sleep apnea: obstructive sleep apnea (OSA) and central sleep apnea (CSA). OSA can be caused by anatomic factors (eg, obesity, long soft palate, large uvula, macroglossia, retrognathia), increased airway collapsibility (eg, medication effects), altered chemosensitivity, or an increased arousal threshold. Physical findings may include a crowded oral pharynx and/or hypertension. Sleep partners may complain about the snoring and the patient may be aware of daytime sleepiness, irritability, or fatigue. In CSA, apnea results from reduced central respiratory drive, often secondary to stroke, heart failure, or the use of opioids or other drugs.³² Both OSA and CSA increase in prevalence with age.

The consequences of OSA can include higher mortality, hypertension, coronary artery disease (CAD), depression, cognitive impairment, and increased risk of motor vehicle collisions, home-or work-related injuries.^{10,32} The STOP-BANG and other questionnaires³³ can be useful to screen for OSA, but a high level of suspicion (particularly in the presence of heart disease or cognitive impairment) should prompt referral for a home sleep test, (HST) or in-laboratory polysomnography.³²

Chronic insomnia and OSA can be comorbid, and for some patients, frequent arousals from apneic events at sleep onset may mimic an insomnia disorder. Additionally, an apneic event may trigger a full arousal from sleep and some patients have difficulty returning to sleep.

Circadian Rhythm Sleep-Wake Disorders

These disorders are characterized by abnormal circadian timing, and abnormal timing of the sleep-wake cycle. Advanced sleep phase disorder, in which individuals fall asleep and awaken at very early hours, is more common in older adults. Other circadian rhythm sleep-wake disorders include delayed sleep phase disorder, most common in adolescents and young adults and characterized by very late sleep and

wake times; and non-24-hour sleep-wake disorder, which may occur in blind individuals, and is characterized by a sleep-wake cycle longer than 24 hours.^{29, 34-36} People with circadian rhythm sleep-wake disorders may complain of difficulty falling asleep, difficulty awakening, and excessive sleepiness during waking hours, which reflects a mismatch between timing of their endogenous circadian rhythm and timing of their desired sleep-wake cycle. Treatments may include behavioral sleep interventions, appropriately timed exposure of symptoms to bright light and darkness, and appropriately-timed use of melatonin or melatonin-receptor agonists.

Restless Leg Syndrome (RLS)

An estimated 10-35% of adults over age 65 may experience RLS, a condition which often causes difficulty falling asleep, awakenings and fragmented sleep.^{6,29,37} The hallmark of RLS is an urge to move the legs that: 1) is accompanied by discomforting sensations; 2) increases during rest or inactivity; 3) is temporarily relieved by movement; 4) becomes more severe during nighttime; and, 5) cannot be explained by other medical conditions.³⁷ Treatment may include pharmacologic agents such as gabapentin or dopamine receptor agonists, in addition to treating an underlying low serum ferritin level and sleep apnea.

REM Behavior Disorder (RBD)

REM sleep is usually characterized by atonia of the skeletal muscles. In REM sleep behavior disorder, this normal atonia is absent, resulting in dream enactment behavior including shouting, kicking, punching, and falling or jumping out of bed. These behaviors may lead to injury of the patient or bed partner. In clinical practice, REM sleep behavior disorder is most often seen in adults over the age of 60. Common medications, most notably selective serotonin or serotonin-norepinephrine reuptake inhibitor antidepressants, may cause or exacerbate REM behavior disorder. REM behavior disorder is associated with the development of neurological disorders such as Parkinson's disease, Lewy body dementia, Alzheimer's disease, and multiple system atrophy.^{29,38} Treatment involves the elimination of exacerbating medications (if possible), general sleep safety measures (such as moving the mattress to the floor), and use of higher-dose melatonin (up to 12 mg) or benzodiazepines. This condition may be comorbid with chronic insomnia.

AGE-RELATED CHANGES TO SLEEP HORMONES

Melatonin

Melatonin is a pineal hormone secreted during the dark period (corresponding to “biological night”) and suppressed by light. Melatonin secretion is strongly circadian, and regulated by the biological clock; secretion begins in the evening hours, peaks during the middle of the dark period at night, and is absent during the usual light period in the day. Light suppresses melatonin secretion at night, but has no effect during the daytime when levels are normally low.³⁹ Exogenous melatonin can also shift circadian rhythms in a time-dependent fashion, as evening melatonin advances rhythms and morning melatonin delays them. Secretion of endogenous melatonin decreases with age and is also suppressed by use of drugs such as beta blockers and non-steroidal anti-inflammatory drugs (NSAIDs). Although these factors may constitute a rationale for melatonin in older adults with insomnia, clinical trials have demonstrated small effects at best.

COMORBID MEDICAL CONDITIONS

Sleep disruptions are commonly observed in conjunction with a wide range of medical conditions and the medications used to treat them.^{4,40,41} The risk for sleep disorders comorbid with medical conditions increases as with age as people accumulate multiple chronic medical conditions. A 2013 evaluation of the presence of 15 prevalent chronic medical conditions from a database of 31 million Medicare fee-for-service beneficiaries revealed that 67% had multiple morbidities accumulated from diseases like osteoarthritis, cardiovascular disease, gastroesophageal reflux disorder (GERD), diabetes, lung disease, and cancer.⁴¹ The trends toward multimorbidities increased steadily with age, from a risk of 50% for people under age 65 years to 62% from ages 65-74 years and 81.5% after the age of 85 years.⁴¹

Pain and Insomnia

Pain syndromes and conditions that cause chronic pain, such as arthritis and cancer, are often associated with sleep disorders. Up to 50% of the general population with insomnia also report chronic pain, which is more common in older individuals. At the same time, older people often have a higher tolerance for pain and are less likely to complain about it, so it may not even be treated, although it may contribute to insomnia.²⁹

Nocturia

Nocturia, or urination at night, occurs in association with many medical conditions and frequently co-occurs with insomnia. Approximately 60% of older adults get up to void at least 2 or more times per night, with higher prevalence in women than men.⁴² Nocturia can contribute to fragmented sleep and difficulty falling back to sleep. Conditions that may promote nocturia include obstructive sleep apnea,⁴³ as well as hypertension, diabetes, arthritis, asthma, heart disease, anxiety, depression, inflammatory bowel disease, and benign prostatic hyperplasia in men.^{42,44}

COMORBID PSYCHIATRIC CONDITIONS

Insomnia is frequently comorbid with psychiatric disorders at all ages, including in older adults.^{17,41} Depression and anxiety are particularly common in older adults, contributing to ongoing insomnia symptoms including reduced sleep efficiency, poor sleep quality, greater sleep latency, and daytime sleepiness.^{40,45,46} Conversely, the presence of insomnia has been shown to exacerbate the severity of psychiatric illness and increase risks of new psychiatric illness.^{18,45,47}

MEDICATIONS

Older adults use medications on a regular basis. According to a recent study, 88% of community-dwelling adults aged 62-85 years reported using at least 1 prescription medication, while 38% used over-the-counter medications, and 64% used dietary supplements.⁴⁸ Many commonly used medications can cause or exacerbate symptoms of insomnia, including antidepressants, blood pressure medications, allergy medications, and weight loss and thyroid medications, among others (See Table 1).

Lifestyle/Recreational Substances

Frequent consumption of alcohol or caffeine, or use of nicotine products, can have detrimental effects on sleep.²⁹ Alcohol may cause drowsiness, reduced sleep onset latency, and increased delta sleep in the first part of the night; however, the quality of subsequent sleep is poor, with increased REM sleep, increased awakenings, and reduced sleep efficiency. Caffeine and nicotine can interfere with initiation, continuity, and depth of sleep, depending on the time of consumption/use.

Polypharmacy

Polypharmacy is often defined as the use of 5 or more drugs, or alternatively, as the use of more drugs than are medically necessary.⁴¹ As people age and develop chronic illnesses, the likelihood for polypharmacy increases. A 2008 study by Qato et al⁴⁹ found that over half of the 3005 community-based residents (ages 57-85) surveyed were taking 5 or more medications. Polypharmacy can result in drug-drug interactions and cumulative AEs, many of which can adversely impact sleep or alertness.⁴¹

SETTINGS THAT CAUSE SLEEP DISTURBANCES

Hospitals and nursing homes are settings that frequently cause acute sleep problems. Although hospitalized patients need substantial amounts of sleep for health recovery from an acute illness, injury, or surgery, the hospital environment may interfere with this recuperative process.

Noise and nighttime light exposure in hospitals contribute to fragmented sleep and reduced sleep efficiency.²⁸ Hospital routines to check vitals, administer medications, or draw blood, as well as pain and discomfort from the patient's medical condition, cause frequent awakenings and reduce REM sleep, deep sleep, and TST. These stressors, along with daytime napping, frequently lead to disrupted sleep during hospitalization, which is often untreated.

In nursing homes, frequent medications, boredom, low levels of light exposure, and lack of routines may contribute to sleeping in or staying in bed during wake times and napping that can also distort normal circadian rhythms. These effects may compound the sleep disturbances associated with neurodegenerative and medical conditions.

SECTION IV: TREATMENT OF CHRONIC INSOMNIA IN THE ELDERLY

Guidelines from both the American College of Physicians (ACP)⁵⁰ and the Journal of Clinical Sleep Medicine (JCSM)⁵¹ agreed that initial treatment of chronic insomnia in the elderly should start with psychological and/or behavioral interventions when appropriate. The JCSM guidelines committee further spelled out conditions for the use of pharmacotherapy, based on the presence of comorbid conditions, contraindications, concurrent medication interactions, and side effects, which are all significant influencing factors in prescribing for the elderly, in addition to symptom pattern, treatment goals, past treatment responses, patient preference, cost, and availability of other treatments.⁵¹

Drug therapy for chronic insomnia should be prescribed in the elderly with extreme caution, starting at the lowest dose of the most effective, safest therapy. Patients should be followed every few weeks for regular evaluation of efficacy, tolerance, and side effects. When conditions allow, tapering of therapy is recommended. It is important to adequately treat comorbid conditions and modify behaviors that contribute to insomnia.⁵¹

Nonpharmacologic Treatment

Nonpharmacologic treatments are considered first-line therapy for chronic insomnia.^{50,51} These interventions are aimed at eliminating or reducing environmental and physical factors that may disrupt sleep, and altering behavioral and cognitive factors to promote sleep. Nonpharmacologic treatments address the predisposing, precipitating, and perpetuating factors that contribute to insomnia (See 3P Model on page 6).

Mitigating Comorbidities

A 2004 survey of older adults conducted by Foley et al⁵² found that nearly 1 in 4 people over age 65 who reported insomnia also had major comorbidity, defined as 4 or more medical and/or psychiatric conditions. This suggests that proper evaluation and treatment of individual comorbid causes should be an early approach to treating insomnia, after which more specific individual treatments can be added. In older patients at risk for insomnia, clinicians should consider drug therapies for primary conditions that have the fewest effects on sleep, particularly where polypharmacy is a potential issue.

Chronic insomnia in the presence of psychiatric disorders such as depression and anxiety should include optimal treatment of these comorbidities, which may also improve sleep symptoms. Psychologic and/or behavioral therapies are considered safe and effective for older adults and should be included in the treatment plan for all older patients with insomnia.⁵¹

Although many middle-aged individuals with OSA present with daytime sleepiness, insomnia is a common presentation with OSA in older adults. In older individuals, OSA is less likely to be caused by obesity and may be present even in those of normal weight. Central sleep apnea is more common in older than younger adults, given its association with conditions such as congestive heart failure and stroke.

Conservative management of OSA includes recommendations for weight loss and sleeping in the lateral position. In most cases, however, continuous positive airway pressure (CPAP) therapy is considered first-line therapy. These recommendations will usually be made by a sleep specialist following overnight sleep study, although all clinical practitioners should continue to monitor therapeutic efficacy and patient adherence to CPAP therapy.⁵³ Other treatment options for OSA include oral appliance therapy, upper airway stimulation, and surgical procedures.⁵⁴

Cognitive Behavioral Therapy for Insomnia (CBTi)

Cognitive behavioral therapy for insomnia (CBTi) is the most effective nonpharmacologic therapy for treatment of insomnia in adults of all ages. CBTi is a structured program administered by trained clinicians to help patients modify habits, behaviors, and beliefs that interfere with sleep. CBTi includes multiple components, which are typically presented as a treatment package tailored to each patient's specific complaints.

Sleep hygiene education involves evaluation of personal habits that may interfere with sleep, and introducing lifestyle modifications that help facilitate more regular, predictable, satisfying sleep patterns.⁵⁵ Aging often involves some changes in sleep habits related to biological, occupational, and social changes. However, voluntary behaviors and habits can compound these developmental sources of sleep problems. Identifying poor sleep hygiene practices can suggest changes to habits and routines that may help sleep, although sleep hygiene instruction alone has not been found to be efficacious as a therapy for insomnia.

Stimulus control (SC) is one of the most effective components of CBTi, intended to strengthen associations between the sleeping environment and sleep. Stimulus control instructions aim to reduce sleep-interfering stimuli from the environment (noise, light, mental activities such as reading or TV) and associate the bedroom with only sleep and sexual activity.^{55,57} One specific, widely-used stimulus control instruction addresses prolonged awakenings in the middle of the night. During such awakenings, patients are instructed to get out of bed, keep the lights low, and engage in some other low-stimulation activity, such as reading or crossword puzzles. They are further instructed to return to bed only when they start to fall asleep, thereby reinforcing the association of bed with sleep.

GOOD SLEEP HYGIENE HABITS

A Handout For Helping Older People Sleep Better

Sleep hygiene involves making lifestyle and environmental changes to facilitate better sleep.

1) Maintain the Right Sleep Temperature

Check the room temperature shortly before sleep to make sure it will be comfortable, as extremes of heat or cold are likely to interfere with sleep and cause unnecessary awakenings. It is best not to bathe directly before going to bed, as the basal body temperature needs to go down for sleep.

2) Create a Relaxing Sleeping Environment

You should always sleep in a bedroom when possible (rather than on a couch or chair), and keep it ready for sleep. The room should be dark, cool, quiet, and the bedding (including mattress and pillows) comfortable. Reduce outside distractions such as streetlights and noise by putting up curtains and using a small fan or white noise device if needed.

3) Don't Exercise Right Before Bedtime

Exercise can help you relax. In particular, low-exertion stretching exercises and gentle yoga may help with relaxation before bed. However, exercising too vigorously too close to bedtime can disrupt sleep for some people.

4) Avoid Stimulants at Night

Nicotine products and alcohol should be avoided for several hours before bedtime, as they have stimulating properties. Caffeinated products such as tea, coffee, and soft drinks, as well as chocolate, should be avoided for at least 6 hours prior to bedtime.

5) Light Snacking is Okay

Many people find it hard to fall asleep and stay asleep if they are hungry. A small snack about an hour before bedtime often prevents people from waking hungry. The choices should be healthy and easy to digest—fruit, vegetables, nuts, toast. Have only small amounts of liquids in the 90 minutes before sleep, to avoid frequent nocturnal awakenings to urinate.

Adapted from Morin & Espie, Insomnia, 2003.⁵⁶

Sleep restriction therapy is a highly effective therapy and often used with stimulus control. The aim is to improve the quality of sleep by reducing the awake time in bed. A sleep diary is critical to this approach, as the information is used to identify SOL, WASO, TST, and total time in bed, as reported by the patient.^{30,55,57} Initially, the bedtime is delayed to increase the success with falling asleep and to induce the homeostatic drive to consolidate sleep time for greater efficiency, while morning wake time is maintained.⁴⁷ Gradually, the bedtime is advanced to increase the TST to 7 hours or more per night.

Relaxation therapy is used to detach attention from intrusive and distracting thoughts while in bed. Relaxation techniques such as meditation, guided imaging, biofeedback, progressive muscle relaxation, and deep breathing can effectively help reduce arousal and allow for initiation of sleep.^{10,55,57}

Cognitive therapy is designed to identify any dysfunctional beliefs or emotional responses that may contribute to irregular sleep patterns and/or disturbances and restructure them.^{30,35} These may include general anxiety or emotional distress, persistent beliefs that falling asleep means “missing something,” or worry about how others perceive their bedtime. The provider can lead discussion through questioning to identify and challenge thinking behind misguided beliefs. It is important to then help the patient replace dysfunctional thinking with more appropriate thoughts and perceptions.⁵⁵

Online CBTi Programs

For many patients with insomnia who do not have access to in-person CBTi, online programs using the same components (sleep restriction, stimulus control, cognitive restructuring, sleep hygiene, and relapse prevention), have been found effective for treating insomnia, and for relieving comorbid symptoms of depression, anxiety, and fatigue as well.⁵⁸

A 2016 meta-analysis of 15 studies reported increases in TST and SE, as well as improvements in depression among adults being treated with online CBTi for insomnia.⁵⁹ Results of a large-scale study of 303 participants of all ages, reported in 2017, found a nearly 70% response rate to internet-delivered CBTi that was maintained at 1-year follow-up,⁶⁰ suggesting an important role for these programs in insomnia treatment, particularly for older or sicker patients who have less ability to participate in live programs.

Additional Therapies

A range of technologies are increasingly being used as adjunctive measures for treatment of insomnia.

Bright light therapy – Exposure to bright light in the evening shifts sleep to a later time, while bright light in the morning shifts sleep onset to an earlier time. Thus, individuals who struggle to remain awake in the evening and who awaken too early might consider evening light. Conversely, those who have difficulty falling asleep and awaken too late might consider morning light therapy.⁶¹

Blue light-blocking glasses – Reducing light, and especially blue light, in the evening hours can be helpful for individuals who have difficulty falling asleep. In particular, wearing blue-light blocking amber lenses from 9 pm to bedtime can advance sleep onset times and improve symptoms of delayed sleep phase disorder (DSPD) in elderly patients.⁶²

Ebb Insomnia Therapy is an FDA-cleared cooling device worn on the head that is a commercially available, with a benign safety profile that has been shown in independent studies to produce improvements in latencies to stage 1 and 2 sleep.⁶³

Alpha-Stim® is a cranial electric nerve stimulating device with FDA approval for use in insomnia. Results from a 2013 pilot study by Lande and Gagnani⁶⁴ indicated some mild effects but a benefit was not found for insomnia. The modality was well tolerated by most.

PHARMACOLOGIC TREATMENTS

A number of hypnotic medications, representing several pharmacologic classes, are FDA approved for treatment of insomnia. Although several of these medications have demonstrated efficacy for 6-12 months, most guidelines recommend the shortest feasible duration of treatment with hypnotic medications. All sleep medications can produce some adverse effects, including daytime sleepiness, tolerance, rebound insomnia, motor incoordination, cognitive impairment, and increased risk for falls. These risks are often magnified in the elderly, due to advancing age, comorbidities, polypharmacy, and changes in both pharmacokinetic and pharmacodynamic properties of drugs.

TABLE 2: Pharmacologic Treatment Recommendations for Insomnia in the Elderly^{6,61,65,66}

DRUG	BEDTIME DOSAGE	SLEEP EFFECTS*	HALF-LIFE (hours)	ADVERSE EFFECTS	COMMENTS
Benzodiazepine Receptor Agonists with Nonbenzodiazepine-Ring Structure					
Zaleplon	5 mg	Sleep onset latency	±1.0	Headache, dizziness, drowsiness, paresthesia, nausea, rhinitis, asthenia, abdominal pain, memory impairment	Not recommended for patients with severe hepatic impairment. <i>Do not</i> take directly after a high-fat meal.
Zolpidem	5 mg IR 10 mg IR 6.25 mg CR/ER 12.5 mg CR/ER 1.75 mg SL 3.5 mg SL	Sleep onset latency; Sleep maintenance	2.6	Headache, drowsiness, nausea, dizziness, diarrhea, vomiting, anterograde amnesia, hallucinations, delirium, unusual nighttime behaviors	Absorption may be delayed when taken with a meal. Dose not recommended to exceed 5 mg for older adults with impaired motor and or cognitive function.
Eszopiclone	1-3 mg 2 mg = max	Sleep onset latency; Sleep maintenance	6	Headache, somnolence, unpleasant taste, dry mouth, dyspepsia, dizziness	Elderly should not take more than 2 mg. Absorption may be reduced when taken with high-fat meal.
Benzodiazepine Receptor Agonists with Benzodiazepine-Ring Structure					
Estazolam	1-2 mg (adults) 0.5 = max recommended dose for elderly or debilitated patients	Sleep maintenance	10-24	Somnolence, dizziness, lightheadedness, dementia, hypokinesia, impaired coordination	Older patients are at increased risk for falls and hip fractures. Not recommended by American Academy of Sleep Medicine.
Flurazepam	15 mg	Sleep maintenance	47-100	Daytime sedation, confusion, dizziness, impaired motor coordination	Older patients are at increased risk for falls and motor vehicle accidents.
Temazepam	7.5-15mg 7.5 = initial dose for patients 65 or older	Sleep onset latency; Sleep maintenance	3.5-18.4	Drowsiness, dizziness, headache, fatigue, impaired motor coordination	Older patients are at higher risk for falls.
Triazolam	0.125 mg	Sleep onset latency; Sleep maintenance	1.5-5.5	Drowsiness, dizziness, lightheadedness, rebound insomnia, anterograde amnesia, dependence, anxiety	Short-acting, with higher plasma concentration and lower clearance in older adults. Not recommended by American Academy of Sleep Medicine.
Quazepam	7.5 mg	Sleep onset latency; Sleep maintenance	39-73	Drowsiness, dizziness, headache, fatigue, dry mouth, dyspepsia	Older patients are at risk for confusion and oversedation. Not recommended by American Academy of Sleep Medicine.

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TABLE 2: Pharmacologic Treatment Recommendations for Insomnia in the Elderly^{6,61,65,66}

DRUG	BEDTIME DOSAGE	SLEEP EFFECTS*	HALF-LIFE (hours)	ADVERSE EFFECTS	COMMENTS
Orexin Receptor Agonist					
Suvorexant	5- 20 mg	Sleep onset latency; Sleep maintenance	10-22	Daytime somnolence, headache, dizziness, fatigue, dry mouth, sleep paralysis, increased risk of falls	5 mg recommended dose for older adults, to be taken 30 minutes before bedtime; not recommended for patients with severe hepatic impairment.
Melatonin Receptor Agonist					
Ramelteon	8 mg	Sleep onset latency	1.0-2.6	Somnolence, dizziness, fatigue, nausea, worsened insomnia, nasopharyngitis, headache	Does not cause CNS depression. Take within 30 minutes of bedtime; do not take with a high-fat meal.
Sedating Heterocyclic (Antidepressant) Drugs					
Doxepin	3-6 mg	Sleep maintenance	15.3	Headache, somnolence, sedation, mild anticholinergic effects, nausea, upper respiratory infection	3 mg is recommended initial dose for older adults, to be taken 30 minutes before bedtime and 3 hours after or before a meal.
Mirtazapine	7.5 mg	Sleep onset latency	20-40	Daytime sedation, anticholinergic effects, weight gain	May benefit patients with comorbid depression. Not FDA approved for insomnia.
Trazodone	25-50 mg	Sleep maintenance	5-13	Daytime sedation, orthostasis, headache, nausea, vomiting, xerostomia	Widely prescribed. Not FDA approved for insomnia. Not recommended by the American Academy of Sleep Medicine.
Other Therapies					
Gabapentin	100-1200 mg	Sleep maintenance	5-7	Drowsiness, somnolence	Used off-label. May help patients with restless leg syndrome. Not FDA approved for insomnia.
Diphenhydramine	12.5 mg	Sleep latency onset	8-17	Daytime sedation, anticholinergic effects	Development of tolerance. Not FDA approved for insomnia. Not recommended by American Academy of Sleep Medicine.
OTC/Herbal Supplements					
Melatonin	1-5 mg	Sleep latency onset	1.8-2.1 20-50 min ⁵	Daytime sedation	Some older adults may choose this over no treatment, although it is not recommended by American Academy of Sleep Medicine due to weak evidence of efficacy.
Valerian	Preparations have different ingredients and active components.	Sleep latency onset	1.1 ± 0.6	Drowsiness, headache, depression	Inconsistent results to studies. Not recommended by American Academy of Sleep Medicine.

 Adapted from Schroeck et al 2016,⁶¹ Lie et al 2015,⁶⁵ Sateia et al 2017,⁶³ Gooneratne 2014.⁶

 Additional Sources: Bloom et al¹⁰, DSM-5², www.drugs.com (accessed 12/18/18), www.accessdata.fda.gov (accessed 12/18/18)

Selecting Pharmacotherapies in Older Adults

The ACP guidelines relied upon clinical trials in adolescents and young adults for prescribing practices for insomnia, which are often extrapolated to older adults.⁵⁰ Few studies have looked at specific interventions in the elderly, and the ACP guidelines committee determined that current evidence is insufficient to determine the benefits of benzodiazepine therapy in this population, although they do make the following drug recommendations:^{50, 67, 68}

- Moderate-quality evidence indicated that suvorexant increased treatment response and improved sleep latency, TST, and WASO.⁶⁹
- Low-to-moderate quality evidence showed that doxepin improved mean scores, SOL, TST, and WASO.^{70, 71}
- Low-quality evidence demonstrated that eszopiclone improved reversion, TST, and WASO,⁶⁷ and zolpidem⁶⁸ and ramelteon⁷² reduced SOL.

Benzodiazepine Receptor Agonists

This class of agents includes two kinds of drugs—those that have a nonbenzodiazepine-ring structure and those that have the true benzodiazepine-ring structure. Both types bind to the same GABA receptor complex and both have sedative-hypnotic, anticonvulsant, and muscle-relaxing effects. Due to altered pharmacokinetics and pharmacodynamics, older patients are more susceptible to side effects, including next-day sedation.

Good efficacy in reducing SOL and nocturnal awakenings have caused benzodiazepine-receptor agonists to be most frequently prescribed for short-term insomnia in the elderly; however, nearly one-third of patients continue taking them on a long-term basis.⁶¹ Side effects, including daytime drowsiness, dizziness, falls, and cognitive dysfunction have been reported.⁵¹ Benzodiazepine receptor agonists can be associated with tolerance, dependence, and withdrawal symptoms upon abrupt discontinuation. For these reasons, benzodiazepine receptor agonists are discouraged in the elderly. When they are prescribed, they should be used at the lowest dose for the shortest duration of time, with tapering to discontinue treatment.⁶¹

Zolpidem is available as an immediate-release 5 mg and 10 mg tablet (IM) or spray dose for sleep initiation, as a controlled-release (CR) 6.25 and 12.5 mg tablet for sleep onset and sleep maintenance, and as a sublingual 1.75 and 3.5 mg tablet given as needed for middle-of-night awakening.⁶¹ All forms should be taken on an empty stomach for optimal absorption, with rapid onset of effects within 30 minutes to 1 hour.

Zaleplon is the shortest-acting of the “Z” drugs, with a rapid onset of about 30 minutes, but also the shortest duration of effects (2–4 hours). It is most suitable for SOL complaints and for sleep recovery after awakening early, if there are still at least 4 hours of sleep time left in the night. The effects may be significantly reduced by concurrent administration with CYP3A4-inducing drugs such as rifampin, phenytoin, carbamazepine, and phenobarbital. It should not be taken with alcohol or other CNS depressant medications. Recommended dosing for elderly patients is 5 mg (which can be increased to 10 mg) immediately before bedtime. For fastest onset, zaleplon should not be taken within a few hours of a high fat meal.⁶¹

Eszopiclone has less specificity for a particular subset of GABA-A receptors compared to zolpidem and is indicated for improving difficulty falling asleep and maintaining sleep. It has good efficacy in patients over 64 for shortened SOL, less WASO, higher sleep efficiency, and longer TST, as well as better patient-reported quality and depth of sleep. Recommended dosing is 1 mg at bedtime. For fastest onset, it should not be taken within a few hours of a high-fat meal. Eszopiclone should be used with caution in patients who have depression, or those who have hepatic or respiratory impairment.⁶¹

Orexin Receptor Agonists

Suvorexant is the only drug in this class used for insomnia, approved in wider doses than other drugs, ranging from 5–20 mg. It is recommended for the treatment of sleep maintenance complaints only, and as with other sedating agents, should be started at the lowest dose of 5 mg in the elderly, with slow increases to 10 mg maximum.⁵¹ Suvorexant appears to have a similar AE profile compared to benzodiazepines, with the exception of lower potential for abuse. Evidence compiled from 3 RCTs indicates it is well tolerated and suitable for patients over age 65⁷³ although it carries warnings against prescribing in cases of narcolepsy. For fastest onset, suvorexant should not be taken with a meal or shortly after food consumption.⁶¹

Melatonin Receptor Agonists

Ramelteon was the first melatonin receptor agonist to receive FDA approval for treatment of sleep-onset insomnia. With its short half-life of about 1.1 hours, it is mainly useful for insomnia with SOL difficulty. Ramelteon poses little risk of dependence, abuse, daytime sleepiness or other AEs. Because of this, and lack of CNS sedating effects associated with other insomnia drugs, ramelteon may be taken to

reduce SOL in older patients, although there are only minimal effects on sleep maintenance symptoms. It interacts with CYP1A2 inhibitors such as fluvoxamine, zileuton, ciprofloxacin, and mexiletine. Recommended dosing for elderly patients is 8 mg at bedtime. For fastest onset, it should not be taken within a few hours of a high-fat meal.⁶¹

Heterocyclic Drugs (Sedating Antidepressants)

Several heterocyclic drugs, originally approved for treatment of depression, are sedating even at very low doses, and have been used for treatment of insomnia. At hypnotic doses, these drugs often have far fewer side effects than they do at higher, antidepressant doses, since specific receptor effects differ according to dose.

Doxepin is currently the only sedating antidepressant medication that is FDA approved for the treatment of insomnia. Trazodone and amitriptyline are among the most frequently prescribed agents, despite a lack of formal evidence supporting their use for insomnia in the elderly.⁷⁴ At antidepressant doses, these drugs can be associated with serious cardiovascular AEs, and have significant potential for harm with overdoses.⁷⁴

- **Trazodone** – Often given off-label for insomnia in elderly patients at low doses of 25 mg at bedtime, with titration every 3-4 days to a maximum of 100 mg/day. For comorbid depression, higher doses ranging from 150-600 mg/day may be used, although significant sedation at these doses is likely. For fastest onset, it should not be taken within a few hours of a high-fat meal.⁶¹
- **Mirtazapine** – A noradrenergic/serotonergic antidepressant indicated for depression, it may have additional benefits for patients with comorbid insomnia. Mirtazapine may be more pre-sedating at lower doses, due to changing receptor effects at higher doses.⁶¹
- **Doxepin** – A tricyclic antidepressant that produces a histamine-mediated sedative effect. It has FDA approval for insomnia at doses of 3 mg and 6 mg in elderly patients, taken before bedtime. It should not be taken within a few hours of any food consumption, and a high-fat meal can delay peak concentrations by up to 3 hours.⁶¹
- **Amitriptyline** – A tricyclic antidepressant often prescribed off-label for insomnia. Use of antidepressant doses in older patients is discouraged by the American Geriatric Society (AGS) due to anticholinergic effects, impaired cognition, potential for delirium, and a high rate of drug-to-drug interactions.⁶¹

Other Off-Label Therapies

- **Gabapentin** – Often used for insomnia associated with neuropathic pain or restless leg syndrome. Doses of 250 mg and 500 mg were associated with polysomnographically measured increases in TST and decreases of WASO, although little data is available in older adults.⁷⁵ Gabapentin is lipid soluble, and so it can be taken with or without food, shortly before bedtime.

Hormone and Herbal Preparations

- **Melatonin** is a hormone that is normally secreted by the pineal gland at night. Exogenous melatonin may reduce sleep latency; however, efficacy trials have yielded inconsistent results.⁶¹ The American Academy of Sleep Medicine (AASM) does not recommend the use of melatonin for SOL or SM, although patients may choose to use it themselves.⁶⁶ If melatonin is used in older adults, the smallest doses of 1 mg to 2 mg are recommended, in immediate-release formulation, 1 hour before bedtime.⁷⁶
- **Valerian** is a root extract that may cause drowsiness through inhibition of GABA uptake and stimulation of GABA release, as well as through adenosine and serotonin agonist effects. Studies of valerian have yielded inconsistent findings, perhaps due to the wide variation in specific preparations tested. These limitations prevent recommending its use in the clinical setting.⁶¹

Clinical Approaches to the Management of Chronic Insomnia in the Elderly

Treatment for chronic insomnia is warranted when poor sleep quantity or quality lead to significant distress, or have a negative impact on general health, comorbid conditions, and/or daytime function.⁵¹

Treatment Goals

Goals of therapy for chronic insomnia are to improve sleep quality, reduce symptoms such as prolonged SOL or excessive WASO, and improve daytime function and distress.⁵¹ Before evaluating treatment choices, clinicians should discuss both general goals of improving sleep and secondary goals of improving specific symptoms with individual patients.⁵¹ Such evaluation should take into account the primary complaint and baseline measures of specific symptoms such as sleep onset and sleep maintenance difficulties.

Therapeutic Strategies

As chronic insomnia is a multifaceted diagnosis with a range of therapeutic options, it is important to narrow the focus of therapy for best efficacy. Both nonpharmacologic and pharmacologic therapies can be effectively employed for the treatment of insomnia.^{51,77,50} Psychological and CBTi treatments are recommended by the ACP⁵⁰ as first-line therapies, and have minimal risks of side effects. In selected patients, pharmacotherapies may serve well as adjunctive therapy, although many patients are not good candidates for available medications (particularly those with significant comorbidities and polypharmacy issues). Clinicians and older patients should discuss whether medication may be appropriate as an alternative, or adjunct, to CBTi.

The first steps in a comprehensive therapeutic plan for chronic insomnia should involve:⁵¹

1. Discussion of features of therapy important to the patient (cost, availability, personal preference).
2. Identifying and mitigating the effect of comorbid conditions that contribute to chronic insomnia with treatment of those conditions.
3. Identifying and modifying the impact of substance use, including alcohol, medications, caffeine, and nicotine on sleep.
4. Evaluation of current therapies for optimal timing of doses to reduce potential interference with sleep.

Choosing Therapies

Once these conditions have been considered, clinicians should work with patients to determine whether to initiate psychological/behavioral, or pharmacological therapy alone or in combination. The most effective psychological/behavioral therapy is CBTi, the components of which can be adapted to meet individual needs. There is little risk to such therapies, although efficacy varies significantly, depending upon the skill of the provider, access, and adherence to the modalities recommended. Based on patient preference and abilities, treatment availability, and cost, pharmacotherapy may be used in conjunction with, or as an alternative to, CBTi. The potential for AEs in older patients, however, needs to be carefully considered.

The most commonly prescribed agents for the treatment of primary and comorbid chronic insomnia are hypnotics, including benzodiazepine receptor agonist drugs, which are considered effective for short-term treatment of most complaints.⁷⁷ None of these drugs, including zaleplon, zolpidem, eszopiclone, triazolam, and temazepam, have

been identified as generally superior to the others, so the choice between them depends largely on factors such as past response, cost, and pharmacokinetic properties, especially half-life and duration of action.

Switching Therapies

When a first agent is not effective or well tolerated, it is appropriate to choose an alternative from the same drug class. Many undesired effects from the first agent can be modified by prescribing a second drug with a different half-life than the original choice.

If these agents fail or are not considered due to contraindications or patient preference, then other types of medications may be considered for specific symptoms (See Table 2 for doses and indications):

- Low-dose sedating antidepressants for management of WASO, SE, and TST
- Ramelteon, for management of SOL and SM (effects on WASO are inconsistent)
- Melatonin, for SOL

While many agents, such as trazodone, amitriptyline, and tiagabine are often used off-label for the treatment of insomnia, due to higher risk of AEs in older patients, their use in this population is not recommended.

Safety of Pharmacologic Therapies

All drug therapies are to be prescribed with caution in the elderly, who are at highest risk from associated side effects. The 2015 *Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults** released by the AGS specifically addressed safety concerns with a number of drug therapies used to treat insomnia in the elderly, particularly benzodiazepines and benzodiazepine receptor agonists.⁷⁸

Many clinicians prescribe benzodiazepine medications to elderly patients for indications of anxiety and insomnia.⁷⁸ The real-world effectiveness of these treatments in older people is less well established than it is in younger adults; the majority of studies have been conducted in nonelderly patient populations and do not examine long-term follow up.⁷⁹ The half-life of the agent selected is important to reducing the risk profile to their use in the elderly. Both short-acting and long-acting agents may contribute to falls and fractures, but longer-acting agents in older people leads to greater risks of daytime sleepiness and cognitive impairment.⁷⁸⁻⁸⁰ With all sedating therapies, it is best to start with lowest dose, and go slowly with any increases to evaluate therapeutic effects and side effects.

Falls and Fractures

Several observational studies have reported increased risks of falling in elderly adults taking benzodiazepines by as much as 50%, which is associated with daytime sedation and direct adverse effects of these drugs on reaction times, balance, gait, and vision.⁷⁹⁻⁸¹

Reduced drug metabolism and increased drug effects in the elderly contribute to increased risks of falls, delirium, fractures, and motor vehicle accidents. The AGS recommends that all benzodiazepine drugs, including nonbenzodiazepine hypnotics, should be avoided in older patients.^{78,79} The 2015 Beers Criteria update specifically stated that “nonbenzodiazepine receptor agonists (such as eszopiclone, zolpidem, and zolpidem) are unambiguously to be avoided regardless of duration of use,” based on high-quality evidence.⁷⁸

The AGS criteria suggest seeking alternatives to sedating CNS-active medications, such as anticonvulsants, opioid-receptor agonists, antipsychotics, antidepressants, benzodiazepine-receptor agonists, and other sedatives and hypnotics. They also recommend using nonpharmacologic therapies for chronic insomnia aimed at reduction of fall risk.⁷⁸

Cognitive Impairment

Short- and long-term cognitive effects on memory, learning, attention and visuospatial relations have been reported with benzodiazepine use, even after discontinuation.⁸²⁻⁸⁴ These effects have not been clearly identified to be caused by benzodiazepine drugs, but may result from increased prescriptions of these medications in patients with anxiety and other preclinical signs of dementia.⁷⁹ Tapering of benzodiazepines is also associated with improvement in cognitive decline.⁸³

SUMMARY

Insomnia in the elderly presents a number of unique challenges to diagnosis and management. Prompt and accurate identification of insomnia, along with physiologic, psychological/behavioral, environmental, and comorbid factors, are necessary to address the causes of insomnia. Cognitive-behavioral therapies are recommended as first-line treatment when available and feasible. Pharmacologic treatments can be efficacious, but should be used cautiously after considering comorbidities, polypharmacy and the greater potential for AEs among older patients.

* During publication of this supplement, a new 2019 update of the Beers Criteria was released that did not substantially change recommendations regarding treatment of insomnia in the elderly.

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APPENDIX

The Berlin Questionnaire

PDF Available at: www.sleepapnea.org/wp-content/uploads/2017/02/berlin-questionnaire.pdf

The OSA50

PDF Available at: www.clmsleep.com/wp-content/.../11/OSA-50-Screening-Questionnaire.pdf

The STOP-BANG Questionnaire for Sleep Apnea

Available at: <http://www.stopbang.ca/osa/screening.php>

Patient-Reported Outcomes Measurement Information System (PROMIS)

Available at: <http://www.healthmeasures.net/explore-measurement-systems/promis>

Pittsburgh Sleep Quality Index (PSQI)

PDF Available at: <https://www.opapc.com/uploads/documents/PSQI.pdf>

Epworth Sleepiness Scale (ESS) & Functional Outcomes of Sleep Questionnaire 30 (FOSQ-30)

Available at: https://www.edsandosa.com/tools-and-resources/screening/?gclid=EAIaIQobChMIv7O5od2E4AIVJh6tBh0RbQ9QEAAAYASAAEgJUKPD_BwE&gclidsrc=aw.ds

AAPA CME / AANP CE POST TEST

1. Which of the following symptoms is the most common type of complaint reported by people over age 60?

- a. Trouble falling asleep
- b. Daytime sleepiness/drowsiness
- c. Difficulty staying asleep
- d. a and c only
- e. all of the above

2. Which of the following factors is not considered in the 3P Model of Insomnia?

- a. Predisposing
- b. Precipitating
- c. Predominating
- d. Perpetuating

3. Disruptions of the 24-hour sleep-wake cycle are referred to as:

- a. Circadian rhythm sleep-wake disorders
- b. REM sleep disturbances
- c. Narcolepsy
- d. Homeostatic disequilibrium

4. The pineal gland is responsible for the release of which hormone?

- a. Melatonin
- b. Prolactin
- c. Cortisol
- d. Thyroid Stimulating Hormone
- e. All of the above

5. The information from a sleep diary is used as the basis for which aspect of CBTi?

- a. Bright Light Therapy
- b. Stimulus Control Therapy
- c. Relaxation Therapy
- d. Sleep Restriction Therapy

6. A 2008 study of community-dwelling elderly people reported that what percentage of participants aged 57-85 surveyed were taking 5 or more medications?

- a. 20
- b. 30
- c. 50
- d. 70

7. The only recommended therapy that is specifically noted not to cause CNS depression is:

- a. Zolpidem
- b. Temazepam
- c. Ramelteon
- d. Doxepin

8. Suvorexant is from the _____ class of therapies.

- a. Non-benzodiazepine receptor agonists
- b. Melatonin receptor agonists
- c. Benzodiazepine receptor agonists
- d. Orexin receptor agonists

9. Which of the following drugs is specifically not recommended by the Academy of Sleep Medicine for treatment of insomnia?

- a. Doxepin
- b. Trazodone
- c. Mirtazapine
- d. Estazolam

10. Hypnotic medications for chronic insomnia in the elderly should be used:

- a. For a minimum of 12 months
- b. For a minimum of 24 months
- c. As a long-term chronic therapy
- d. For the shortest feasible duration



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