Review Article

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Sleep disorders in the elderly

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Nearly half of older adults report difficulty initiating and maintaining sleep. With age, several changes occur that can place one at risk for sleep disturbance including increased prevalence of medical conditions, increased medication use, age-related changes in various circadian rhythms, and environmental and lifestyle changes. Although sleep complaints are common among all age groups, older adults have increased prevalence of many primary sleep disorders including sleep-disordered breathing, periodic limb movements in sleep, restless legs syndrome, rapid eye movement (REM) sleep behaviour disorder, insomnia, and circadian rhythm disturbances. The present review discusses age-related changes in sleep architecture, aetiology, presentation, and treatment of sleep disorders prevalent among the elderly and other factors relevant to ageing that are likely to affect sleep quality and quantity.

Key words Ageing - circadian - insomnia - REM sleep - sleep - sleep-disordered breathing

Introduction

Several physical and psychological changes are known to occur with normal ageing; however, adjustment to changes in sleep quantity and quality can be among the most difficult. Although sleep disturbance is a common complaint among patients of all ages, research suggests that older adults are particularly vulnerable. A large study of over 9,000 older adults age of > 65 yr found that 42 per cent of participants reported difficulty initiating and maintaining sleep. Follow up assessment 3 yr later revealed that 15 per cent of participants who did not report sleep difficulty at baseline had disturbed sleep, suggesting an annual incidence rate of approximately 5 per cent[1]. Although changes in sleep architecture are to be expected with increasing age, age itself does not result in disturbed sleep. Rather it is the ability to sleep that decreases with age, often as a result of the other factors associated with aging[2]. In addition, there are several primary sleep disorders that are more prevalent among older adults that should receive clinical attention and treatment.

Ageing and sleep

Both subjective and objective measures of sleep quality provide support for age-related sleep changes. Subjectively, older adults report waking up at earlier times, increased sleep onset latency, time spent in bed, nighttime awakenings, and napping, and decreased total sleep compared to younger adults. Using objective measurement tools such as polysomnography (PSG), studies have been able to support subjective reports of such sleep disturbances.

Sleep consists of 2 main phases: rapid eye movement (REM) sleep and non-REM sleep (divided into three progressively "deeper" stages: N1, N2 and N3). Studies comparing sleep in older adults to younger adults found that older adults spent less time in deeper stages of sleep (N3 or slow-wave sleep). A 2004 meta-analysis including approximately 65 studies representing 3,577 (age 5 to 102 yr) participants suggested that with increasing age, time spent in lighter stages of sleep increased while time spent in REM and slow-wave sleep decreased[3]. Results from this meta-analysis suggested that age-related sleep changes are already detectable in young and middle aged participants and estimated that the percentage of slow-wave sleep linearly decreased at a rate of approximately 2 per cent per decade up to 60 yr and then stabilize through the mid-90s. Moreover, evidence suggests that sleep becomes more fragmented as we age, such that there are more frequent sleep stage shifts, arousals, and awakenings. This results in decreased sleep efficiency (i.e. the proportion of actual sleep time compared to time spent in bed), which indeed, continues to decrease with increasing age, despite slow-wave sleep proportion stabilization[3]. A second study found that among men, sleep time decreased an average of 27 min per decade from midlife until the eight decade[4].

The reasons underlying elderly sleep disturbances are complex. Accumulating evidence points towards changes in sleep architecture, increased risk for sleep disorders, circadian rhythm shifts, medical and/or psychiatric conditions, and medication use (and likely a combination of these factors) as possible factors contributing to older adult sleep disturbance. Considering the impact that sleep disturbance can have on health, it is important to pay special attention to sleep quality among older adults.

Sleep disorders in the elderly

Primary sleep disorders

Primary sleep disorders are distinguished from other sleep disorders in that these are not other mental disorders, medical conditions, medications, or substance use. There are three common primary sleep disorders frequently seen in older adults: sleep disordered breathing (SDB), restless legs syndrome (RLS)/periodic limb movements in sleep (PLMS), and REM sleep behaviour disorder (RBD).

(*i*) Sleep-disordered breathing

Sleep-disordered breathing encompasses a spectrum of breathing disorders ranging from benign snoring to obstructive sleep apnoeas. Those with SDB experience complete cessation of respiration (apnoeas) and/or partial or reduced respiration (hypopnoeas) during sleep. SBD is diagnosed when each event exceeds 10 sec and recurs throughout the night, resulting in repeated arousals from sleep as well as nocturnal hypoxaemia. The total number of apnoea and hypopnoeas per hour of sleep is called the apnoea-hypopnoea index (AHI). Typically, an AHI greater than or equal to 5-10 confirms a diagnosis of SBD.

In a large series of randomly selected community dwelling older adults (age 65-95 yr), 81 per cent of participants reported an AHI > 5, with prevalence rates of 62 per cent for AHI > 10, 44 per cent for AHI > 20, and 24 per cent for AHI > 40 [5]. Furthermore, the Sleep Heart Health Study[6], in 6,400 older adults (mean age = 63.5 yr), found SDB prevalence rates of 32 per cent for AHI 5-14 and 19 per cent for AHI > 15 in 60-69 yr olds, 33 per cent for AHI 5-14 and 21 per cent for AHI > 15 in 70-79 yr olds and 36 per cent for AHI 5-14 and 20 per cent for AHI > 15 in 80-98 yr olds. These figures are staggering when compared to middle aged adults (age 30-60 yr) whose SDB prevalence rates (defined as an AHI > 5 and concomitant excessive daytime somnolence) were 4 per cent for men and 2 per cent for women[7]. Also SDB is more prevalent among institutionalized elderly adults (rates ranging from 33-70%), particularly those with dementia, compared to elderly people living independently[8].

Risk factors associated with SDB include older age, gender, obesity, and symptomatic status. In addition, other factors associated with risk for developing SDB include use of sedating medications, alcohol consumption, family history, race, smoking, and upper airway configuration. The two hallmark symptoms of SDB are snoring and excessive daytime sleepiness (EDS). Older adults with SDB may also report insomnia, nocturnal confusion, and daytime cognitive impairment including difficulty with concentration, attention, and short-term memory loss.

Snoring is caused by airway collapse and often plays a role in the breathing cessation during an apnoeic event. Research suggests that approximately 50 per cent of those who snore also have SDB[9]. Importantly, not everyone who snores has SDB and vice versa; however, snoring is associated with increased risk of ischaemic heart disease and stroke.

EDS is another symptom of SDB and is often a result of sleep fragmentation from repeated nighttime

awakenings and arousals. People with EDS may take frequent unintentional naps or fall asleep during activities such as reading, watching television, having conversations, or even while driving. Cognitive deficits and reduced vigilance are associated with EDS, placing older adults with pre-existing cognitive deficits at increased risk for EDS related impairment[2].

Patients with SDB are also at greater risk for a cardiovascular consequences such as hypertension, cardiac arrhythmias, congestive heart failure, stroke, and myocardial infarction. Specifically, among older adults, the severity of SDP was associated with increased risk for developing coronary artery disease, congestive heart failure, ischemic disease, and stroke[6].

Older adults with severe SDB are also more likely to experience cognitive impairment. A study by Aloia *et al*[10] found that older adults with AHI > 30 had deficits in attentional tasks, immediate and delayed recall of both verbal and visual stimuli, executive functioning, planning and sequential thinking, and manual dexterity. There may also be a link between SDB and dementia severity. Ancoli-Israel *et al*[11] found that dementia severity ratings were positively associated with SDB severity such that institutionalized adults who were severely demented had more severe SDB compared to mildly-moderately demented adults. This association may be partially explained by evidence suggesting that patients with many progressive dementias such as Alzheimer's disease and Parkinson's disease often experience neurodegeneration in areas of the brainstem responsible for respiration regulation and other autonomic functions relevant to sleep maintenance.

The relevance of SDB in the older adult has been questioned, specifically whether SDB in the older adult is similar to that seen in younger adults and whether it should be treated[12]. In general, if an older adult has cardiac disease, hypertension, nocturia, cognitive dysfunction, or severe SDB, treatment should be considered[13].

Evaluation of SDB usually begins with conducting a complete sleep history focusing on EDS, unintentional napping, snoring, and other sleep disorder symptoms. If possible, obtaining information from the patient's sleep partner or caregiver can provide further data. In addition, the patient's medical and psychiatric history should be reviewed in order to gain information regarding medical conditions, medication use, alcohol use, and cognitive impairment. If all evidence collected supports a diagnosis of SDB, an overnight sleep recording should be conducted to confirm diagnosis.

While several treatments exist for SDB, continuous positive airway pressure (CPAP) is the gold standard. Older adults who adhere to CPAP treatment for three months have demonstrated improvement in cognitive performance such as psychomotor speed, executive functioning, and non-verbal delayed recall[10]. When prescribing treatment for older adults with SDB, it is important that clinicians not assume that old age is indicative of non compliance. Ayalon and colleagues[14], found that even older adults with mild-moderate Alzheimer's disease and SDB can adhere to CPAP treatment. Importantly, the results of this study indicated that the only factor related to poor CPAP compliance was depression, suggesting that treating depression concurrently with SDB might lead to improved compliance[14].

For those seeking alternatives to CPAP, other SDB treatments such as oral appliances are available; however, these have not been shown to be as effective as CPAP. Patients diagnosed with SDB should also consider weight loss, smoking cessation, and abstinence from alcohol as these factors may exacerbate SDB. Finally, elderly patients with SBD should also avoid long-lasting benzodiazepines as these medications are respiratory depressants and may increase the number and severity of apnoea events.

Restless legs syndrome(RLS) / Periodic limb movements in sleep (PLMS)

Restless legs syndrome (RLS) is characterized by dysesthesia in the legs which is usually described as "pins and needles" or a "creepy and crawly" sensation in the legs that is only relieved with movement. This dysesthesia usually occurs when the patient is in a relaxed or restful state. The diagnosis is made based on history. RLS prevalence increases with age and is about twice as prevalent among women compared to men[15]. Approximately 70 per cent of patients with RLS also have co-morbid PLMS, however only about 20 per cent of those with PLMS report RLS.

PLMS is characterized by clusters of leg jerks causing brief arousal and/or awakening occurring approximately every 20-40 sec over the course of a night. PLMS is diagnosed with an overnight sleep recording which shows patients having at least 5 kicks per hour of sleep paired with arousal. PLMS is relatively prevalent among older adults compared to younger adults, with

approximately 45 per cent prevalence among older adults compared to 5-6 per cent prevalence in younger adults[16]. The significance of this high prevalence has been questioned as many patients with repetitive leg movements do not complain of sleep difficulties.

Patients with RLS, and sometimes those with PLMS, report EDS, difficulty falling and staying asleep, and, in the case of PLMS, may or may not be aware of their leg movements. Those with RLS will complain of uncomfortable leg sensations throughout the day, which are relieved by movement. In PLMS, the patient's bed partner is the first to notice the kicking and may have even moved into a separate bed due to the disturbance. It is important that those with complaints consistent with PLMS and/or RLS be assessed for anaemia, uraemia, and peripheral neuropathy prior to treatment.

Although mechanisms underlying PLMS/RLS are not clearly understood, some research speculates that these disorders may result from dysregulation of the dopaminergic system due to the therapeutic effects of dopamine agonists on these disorders. Other theories posit that these disorders may be associated with iron homeostatic dysregulation because patients often present with reduced ferritin levels in the cerebrospinal fluid[17].

Typically, PLMS and RLS are treated with dopamine agonists, which are effective at reducing leg jerks and the associated arousals. In the United States, ropinirole and pramipexole have been approved by the Food and Drug Administration for the treatment of RLS.

Rapid eye movement (REM) sleep behaviour disorder

Rapid eye movement sleep behaviour disorder (RBD) is characterized by complex motoric behaviours that occur during REM sleep. These behaviours are likely the result of intermittent lack of the skeletal muscle atonia typically present during the REM phase of sleep. Typically, RBD behaviours present during the second half of the night, when REM sleep is more prevalent. These behaviours/movements can include walking, speaking, eating, and can also be violent and may harm the patient or the patient's bed partner. Oftentimes, patients are unaware of these actions. RBD is most prevalent among older adult males[18].

Although the aetiology of RBD is unclear, an association is suggested between acute onset of RBD and the use of tricyclic antidepressants, fluoxetine, and monoamine oxidase inhibitors, and withdrawal from alcohol or sedatives[19]. Chronic RBD, on the other hand, has been associated with narcolepsy and other idiopathic neurodegenerative disorders such as Lewy body dementia, multiple system atrophy, and Parkinson's disease.

RBD is often treated with clonazepam, a long-acting benzodiazepine which has been shown to reduce or eliminate abnormal motor behaviour in approximately 90 per cent of RBD patients[20]. However, some patients report the side effect of residual sleepiness due to the drug's long half-life. Melatonin has also been found to be effective in the treatment of RBD[21]. Sleep hygiene education is also recommended for patients with RBD and their bed partners. Injury-preventing techniques include making the bedroom environment safer by removing potentially dangerous heavy or breakable objects, using heavy curtains on bedroom windows, keeping doors locked at night, and sleeping on a mattress placed on the floor to prevent dangerous falls.

Insomnia

Insomnia is among the most prevalent sleep complaints reported by older adults characterized by difficulty initiating or maintaining sleep, accompanied with daytime consequences. Studies have estimated that up to 40-50 per cent of adults over the age of 60 report disturbed sleep[22]. Subtypes of insomnia include sleep onset insomnia (difficulty initiating sleep), sleep maintenance insomnia (difficulty maintaining sleep throughout the night), early morning insomnia (early morning awakenings with difficulty returning to sleep), and psychophysiologic insomnia (behaviourally conditioned sleep difficulty resulting from maladaptive cognitions and/or behaviours), the most common among older adults being maintenance and early morning insomnia. Depending on the course of the sleep disturbance, insomnia can be classified as transient (lasting only a few days before or during a stressful experience), short-term (lasting a few weeks during an extended period of stress or adjustment), or chronic (enduring several months or years after a precipitating event).

People from all age groups with chronic sleep difficulty show poorer attention, slower response times, problems with short-term memory, and decreased performance levels. However, insomnia is especially problematic in older adults as it puts them at greater risk for falls, cognitive impairment, poor physical

functioning and mortality, even after controlling for medication use[23-26]. Sleep difficulty has also been linked to decreased quality of life and increased symptoms of anxiety and depression[27].

Insomnia is most often co-morbid with medical or psychiatric illnesses, medication use, circadian rhythm changes, and other sleep disorders. Foley *et al*[28] found that although 28 per cent of older adults reported chronic insomnia, only 7 per cent of the cases were in isolation of common co-morbid conditions. They concluded that ageing alone does not cause sleep disruption, but rather the conditions that often accompany ageing result in poor sleep.

This belief was supported by data from the National Sleep Foundation's survey of older adults which found a positive relationship between the amount of sleep complaints and the medical conditions, such as cardiac disease, pulmonary disease, stroke and depression. Likewise, as the number of medical conditions increased, so did the likelihood of having sleep difficulties[29]. In a large epidemiological study of older adults, heart disease, diabetes mellitus, and respiratory disease measured at baseline were all associated with long-term persistence of insomnia measured at a 3 yr follow up assessment[28]. Medical conditions such as arthritis, diabetes, chronic pain and cancer have all been associated with difficulty sleeping.

Insomnia is also often co-morbid with psychiatric disorders. Indeed, sleep disturbance among depressed patients is extremely prominent and is also one of the nine diagnostic criteria for depression[30]. Research supports a bidirectional relationship between depression and insomnia, such that mood disturbance can result in disturbed sleep and insomnia can place one at risk for developing depression[31]. Oftentimes, people undergoing significant life stressors such as divorce or loss of a loved one, may experience depression resulting chronic insomnia. Similarly, Buysee & colleagues[31], found that the presence of insomnia at baseline was predictive of developing depression 1 to 3 yr later. A study conducted among older adults found similar results[32]. Insomnia also is a common comorbidity for other psychiatric disorders. Ohayon & Roth[33] found that 65 per cent of depressed patients, 61 per cent of patients with panic disorder and 44 per cent of those with generalized anxiety disorder complained of insomnia.

Certain medications are also known to affect sleep quality. Among older adults, this is especially relevant considering the number of elderly patients on polypharmacy regimens. Medications known to have negative effects on sleep include β-blockers, bronchodilators, corticosteroids, decongestants, diuretics, stimulating antidepressants, and other cardiovascular, neurologic, psychiatric, and gastrointestinal medications. When possible, clinicians should advise patients to modify their medication schedule such that stimulating medications and diuretics are taken earlier in the day and sedating medications are taken shortly before bedtime.

Pharmacological intervention is the most common treatment for insomnia. Several different medications are used to treat insomnia such as sedative-hypnotics, antihistamines, antidepressants, antipsychotics, and anticonvulsants. However, the National Institutes of Health State-of-the-Science Conference on Insomnia concluded that there is no systematic evidence that antihistamine, antidepressant, antipsychotic, and anticonvulsant treatment is effective for insomnia and that the risks outweigh the benefits. These treatments therefore are not recommended for the elderly[34]. Research suggests that selective short-acting nonbenzodiazepines [type-1 γ-aminobutyric acid (GABA) benzodiazepine receptor agonists; *e.g*., eszopiclone, zaleplon, zolpidem, zolpidem ER (extended release)] and melatonin receptor agonists (*e.g*., ramelteon) are safe and effective for older adults[35-38].

The most effective treatment for insomnia, however, is cognitive behavioural therapy[34]. Behavioural treatment of insomnia often involves teaching sleep hygiene techniques in combination with other behavioural treatments to counteract poor sleep habits and cognitive therapy to counteract maladaptive or dysfunctional beliefs. Basic sleep hygiene rules for older adults are listed in the Table, however the clinician needs to be aware that sleep hygiene education alone is not as effective as cognitive behavioural therapy for insomnia (CBT-I).

Table. Sleep hygiene tips

1.	Do not spend too much time in bed.
2.	Maintain consistent sleep and wake times.
3.	Get out of bed if unable to fall asleep.
4.	Restrict naps to 30 min in the early afternoon.
5.	Exercise regularly.
6.	Spend more time outside, without sunglasses, especially late in the day.
7.	Increase overall light exposure.
8.	Avoid caffeine, tobacco, and alcohol after lunch.
9.	Limit liquids in the evening.

The two most effective behavioural treatments included within CBT for insomnia are stimulus control and sleep restriction. The theory underlying stimulus control is that insomnia results from maladaptive classical conditioning. Therefore, patients are instructed eliminate in-bed activity other than sleep and to get out of bed if unable to fall asleep within 20 min. The patient can only return to bed when he/she feels adequately sleepy. If unable to fall asleep within 20 min, they are asked to repeat the process. Sleep restriction therapy aims to increase sleep efficiency by limiting the amount of time the patient is allowed to stay in bed. Typically, patients are instructed that they can stay in bed for 15 min longer than the time of actual sleep they report each night. This results in daytime sleepiness that allows for an increased sleep drive the following night. As sleep improves each week, the amount of time allowed in bed in gradually increased.

Research supports the efficacy of CBT for insomnia as an effective treatment for older adults. Morin & colleagues[39] tested the efficacy of CBT for insomnia compared to temazepam, a combination of CBT and temazepam, and placebo in a group of older adults. After 8 wk of treatment, results showed that each active treatment was more effective than the placebo in reducing wake time at night. However, at 3, 12, and 24 month follow up assessment, patients treated with CBT maintained clinical gains better than those who were not treated with CBT[37]. Although CBT for insomnia typically consists of 6-8 weekly meetings with a clinically-trained therapist, emerging research supports the efficacy of briefer interventions (2 sessions) using similar techniques in the primary care setting[40]. For some patients, combining pharmacological and behavioural treatment may be a more effective regimen for treating insomnia as medications can provide acute relief while patients learn techniques helpful for long-term efficacy.

Circadian rhythm disturbances

Changes in circadian rhythms, i.e., biologic rhythms entrained to a 24 h cycle that control many physiological functions, can also contribute to sleep disturbance. Circadian rhythms, such as the sleep-wake cycle, are controlled by the superchiasmatic nucleus (SCN) in the anterior hypothalamus. This brain region controls the internal circadian pacemaker, which is synchronized to the hour of the day by both external zeitgebers (time givers, or cues) and internal cues. External cues include light which is processed through the retinohypothalamic visual pathway. Internal cues include core body temperature and melatonin. Research suggests that the secretion of endogenous melatonin decreases with age resulting in decreased sleep efficiency and in increased incidence of circadian rhythm disturbance[41].

As people age, they experience deterioration of the SCN, resulting in less synchronized sleep-wake circadian rhythms due to decreased responsiveness to external cues[42]. This results in less consistent periods of sleeping and waking across the 24 h day. Additionally, the amplitude of the circadian rhythm may decrease with age. This can result in increased nighttime awakenings and subsequent EDS[43].

Most older adults also experience a shift, or advance, in circadian sleep rhythms. Circadian rhythm advancement may be a result of changes in core body temperature cycle, decreased light exposure, and may also be related to genetic factors. Advanced rhythms cause patients to become sleepy early in the evening (typically between 1900 and 2000 h) and awaken very early in the morning (typically around 0300 to 0400 h). If these older adults went to bed when they began getting sleepy, they would be able to get an adequate amount of sleep at night. However, some feel pressure from societal norms to stay up later in the evening, despite begin sleepy and despite continuing to wake up too early in the morning. This can result in restricted sleep and daytime sleepiness similar to that in insomnia.

Presenting complaints of those with circadian rhythm disturbances can be similar to those with insomnia. However, it is important to carefully differentiate between the two diagnoses because treatment approaches differ. Circadian rhythm disturbance is effectively treated with bright light therapy. Using a light box that mimics natural daylight, patients can get exposure to light at specific times of the day which helps advance or delay sleep-wake rhythms and can also shift core body temperature and endogenous melatonin rhythms. Indeed, studies suggest that bright light exposure via a light box is efficacious in improving sleep continuity among healthy and institutionalized older adults[44,45].

Sleep and menopause

Older women are at particular risk for sleep difficulties. One possible contributing factor placing women at increased risk for sleep difficulties are changes related to menopause. In fact, sleep difficulty is one of the hallmark symptoms of menopause, with approximately 25-50 per cent of women undergoing

menopause reporting sleep complaints compared to approximately 15 per cent of the general population[46]. Evidence suggests that sleep architecture disruption in menopausal women is associated with vasomotor symptoms, such as hot flashes[46].

Hormone changes are also likely to cause sleep disruption in post-menopausal women. Progesterone, injected intravenously, has direct sedative qualities resulting from stimulation of benzodiazepine receptors that stimulate the production of the NREM-associated GABA receptors[47]. During a normal menstrual cycle, the rapid peak and drop-off of progesterone levels in the mid-luteal phase is associated with sleep difficulties and increased arousals[47]. The effects of estrogen on sleep are somewhat more complex, however, evidence suggests that estrogen is associated with increased sleep time and decreased sleep latency, nighttime awakenings, and arousals[48]. Considering that estrogen is also involved in temperature regulation of the body, decreased estrogen in menopause may also be associated with hot flashes, and thus increased arousals[46]. Further, estrogen is complexly related to melatonin and menopause-related changes in melatonin are also likely to affect sleep. A study by Okatani & colleagues[49] found that post-menopausal women with insomnia have lower levels of melatonin compared to their cohorts.

The decision to undergo hormone replacement therapy (HRT), a controversial treatment for menopause-related symptoms, should be carefully considered and the risks (*i.e.*, increased risk of incident cancer, and thromboembolic phenomena) and benefits (*i.e.*, reduced menopausal symptoms, decreased risk for osteoporotic fractures) associated with this line of treatment should be weighed[50]. Welton *et al*[51] examined the effects of HRT on health related quality of life in 3721 randomized postmenopausal women with one group receiving HRT and one group receiving placebo. After one year of treatment, women who received HRT reported significant improvement in vasomotor symptoms and sleep problems compared to women in the placebo group. Also, less women in the HRT group reported night sweats and insomnia compared to the placebo group.

Summary

Among several changes that occur with ageing, changes in sleep quality and quantity can be the most difficult for many older adults. With age, older adults experience normal changes in sleep architecture and sleep-wake cycles, however, there are other factors that accompany ageing which are associated with poor sleep. When rigorous exclusion criteria for co-morbidities are used, the prevalence of insomnia is very low in healthy older adults[52]. There are several treatments for the various sleep disturbances that older adults experience. Careful assessment of sleep such as a comprehensive sleep history and, when appropriate, sleep studies should be conducted in order to be certain of the nature of a patient's sleep complaint. In addition, evaluation of the patient's medical history, psychiatric history, and lifestyle and environmental factors should be carefully considered while choosing treatment modalities. Treatment should target both the sleep problem and any co-morbidities thus optimizing the chance for improvement in quality of life and functioning in older adults.

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