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REVIEW

Current and Emerging Sleep Interventions for Older Adults with or without Mild Cognitive Impairment

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Abstract

Purpose of Review This systematic scoping review examines evidence from the last five years on sleep interventions in cognitive healthy older adults and those with mild cognitive impairment.

Recent Findings Sleep disturbance has been identified as a potential early, modifiable risk factor for dementia, making it crucial to investigate if these interventions also enhance cognitive function and neurodegenerative biomarkers.

Summary Since 2019, research on sleep interventions in older adults with or without cognitive impairment has gradually expanded, especially on non-pharmacological treatments including CBT-I, exercise, and multi-modal interventions, which show promise but require further study to confirm cognitive benefits. Pharmacological interventions have primarily focused on melatonin and orexin antagonists, with long-term safety remaining a concern. Tailored, clinically effective interventions that consider the presence of Alzheimer's disease biomarkers, such as amyloid, tau, cerebrovascular disease, or alpha-synuclein in key sleep-related circuits, are essential to developing feasible, cost-effective, and scalable treatments for older adults with or without cognitive impairment.

Keywords Alzheimer's disease · Dementia · Cognitive impairment · Sleep intervention · Prevention · Neurodegenerative biomarkers

Introduction

Dementia is a neurodegenerative disease that impairs cognitive ability, behaviour and functioning and is the 7th leading cause of death globally [1]. In the absence of a cure for dementia, research has recently shifted its focus to targeting modifiable risk factors that may prevent or delay cognitive decline [2]. Over the last decade, sleep and circadian (sleep–wake) disturbances have been increasingly recognised as possible risk factors for cognitive decline [3]. Sleep disturbances have shown to increase levels of beta-amyloid (Aβ) and phosphorylated tau (p-tau) [4], key pathophysiological features of Alzheimer's disease (AD), and lead to worse global cognition. Although exact mechanisms are unknown, the likely bidirectional interrelationship between sleep and AD is mainly attributed to the role of sleep in learning and memory [5], synaptic plasticity [6], and glymphatic clearance of metabolic waste from the brain [7].

Sleep disturbance affects nearly one-third of adults in the general population and increases with age, with prevalence rates from 30–70% in older adults [8]. These disturbances include subjective complaints such as insomnia, and other sleep disorders such as obstructive sleep apnea (OSA) and excessive daytime sleepiness [9]. Older adults (aged over 65) are more at risk of disorders accompanied and/or exacerbated by poor sleep. Sleep–wake disturbances are a prominent feature of AD and other dementias [10], and are linked to poorer disease prognosis [11]. Converging evidence also suggests that sleep–wake disturbances manifest in the earlier stage of the dementia continuum, such as in individuals with mild cognitive impairment (MCI). MCI is a transitional

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phase between normal aging and dementia, marked by objectively impaired cognitive function that does not significantly interfere with daily activities, and carries a higher risk of progressing to dementia [12]. Around 50–63% of MCI patients subjectively report sleep–wake disturbances, with pronounced changes in sleep macro-architecture, including greater wake after sleep onset, reduced total sleep time, lower sleep efficiency, and longer sleep onset latency compared to healthy controls [13, 14]. Even earlier on the continuum, shorter sleep duration in healthy older adults in midlife, particularly at ages 50 and 60, has been associated with an increased risk of late-onset dementia, independent of sociodemographic, behavioural, cardiometabolic, and mental health factors [15]. This highlights an opportunity to target sleep disturbance in older adults as a potential strategy to prevent cognitive decline and dementia.

The objective of this systematic scoping review was to provide an overview of sleep interventions in older adults, with or without cognitive decline, over the past five years. Research in this area is rapidly progressing with several notable recent systematic reviews [16, 17], and we therefore sought to provide an updated systematic scoping review of empirical research published since January 2019. Our primary study aim was to document types of sleep interventions being evaluated in older adults with or without cognitive impairment. Second, we wanted to determine the impact of the sleep intervention on cognitive outcomes, neurodegenerative biomarkers, and brain structure and function using neuroimaging techniques, if assessed.

Methods

This scoping review employed a systematic search strategy and a narrative synthesis of findings [18]. Our objective was to map existing research on interventions for sleep disturbances and their effects on cognitive outcomes and neurodegeneration markers in older adults with or without cognitive impairment. The search was conducted using PubMed, Scopus, Web of Science, Embase and PsycInfo databases for English-language articles from 1 January 2019 to 1 March 2024 (see flow diagram in Fig. 1). Reference lists of relevant review articles were also screened. The search strategy was discussed and agreed upon informally by the multidisciplinary team. After removing duplicates, three authors (AS, SDK, ZMS) screened titles and abstracts against the inclusion criteria. The inclusion criteria were as follows:

1. *Population:* Cognitively healthy older adults (mean age ≥ 50 years) or those with MCI or preclinical AD, confirmed by examining the inclusion criteria or baseline scores against standardized diagnostic criteria.
2. *Intervention:* Any form of pharmacological and/or non-pharmacological sleep intervention (any frequency and duration).
3. *Comparison:* Any control arm, including passive (treatment as usual, wait-list) or active (matched placebo, active comparator).
4. *Outcome:* Any validated measure evaluating changes in sleep (subjective or objective), cognitive function, neurodegenerative biomarkers, or neuroimaging data.
5. *Study design:* Any controlled, interventional studies.

Articles were excluded if they met the following criteria: (i) published before 1 January 2019; (ii) included participants with comorbid medical conditions that could potentially influence treatment effects (e.g., cancer, cardiovascular or metabolic disorders); (iii) lacked essential data or statistical analyses to ascertain treatment effects; or (iv) pooled data of older and younger adult populations. The remaining full-text articles were categorized by intervention type. Data extraction performed by five authors (AS, SK, ZMS, BT, NC), each assigned to a specific intervention type. This review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR) [19].

Results

A total of 35 full-text articles were reviewed and summarized (Table 1 and 2). Results are divided in two subsections: (i) non-pharmacological interventions, and (ii) pharmacological interventions, considering the type of interventions administered and the disease stage of participants. Of the 28 articles evaluating non-pharmacological treatments, interventions included cognitive behaviour therapy for insomnia (CBT-I) (six studies), light therapy (one study), exercise (14 studies), multi-modal intervention (two studies), mindfulness-based intervention (two studies), non-invasive brain stimulation (one study), and acoustic stimulation (two studies). Of the seven pharmacological intervention studies, one evaluated melatonin, five evaluated orexin antagonists, and one evaluated supplementation. No recent articles (2019-) on benzodiazepines or Z-drugs for treating sleep disturbances in older adults or individuals with MCI met inclusion criteria for this review.

The review encompassed research from 15 different countries, with notable concentration of studies from China (seven studies) and the USA (six studies). Most studies included cognitively healthy older adults (mean age ≥ 50 years; 26 studies), while nine studies included individuals with MCI. Where data were provided, most studies had a majority of female participants (i.e., sample > 50% female). Nineteen studies assessed only subjective sleep measures,

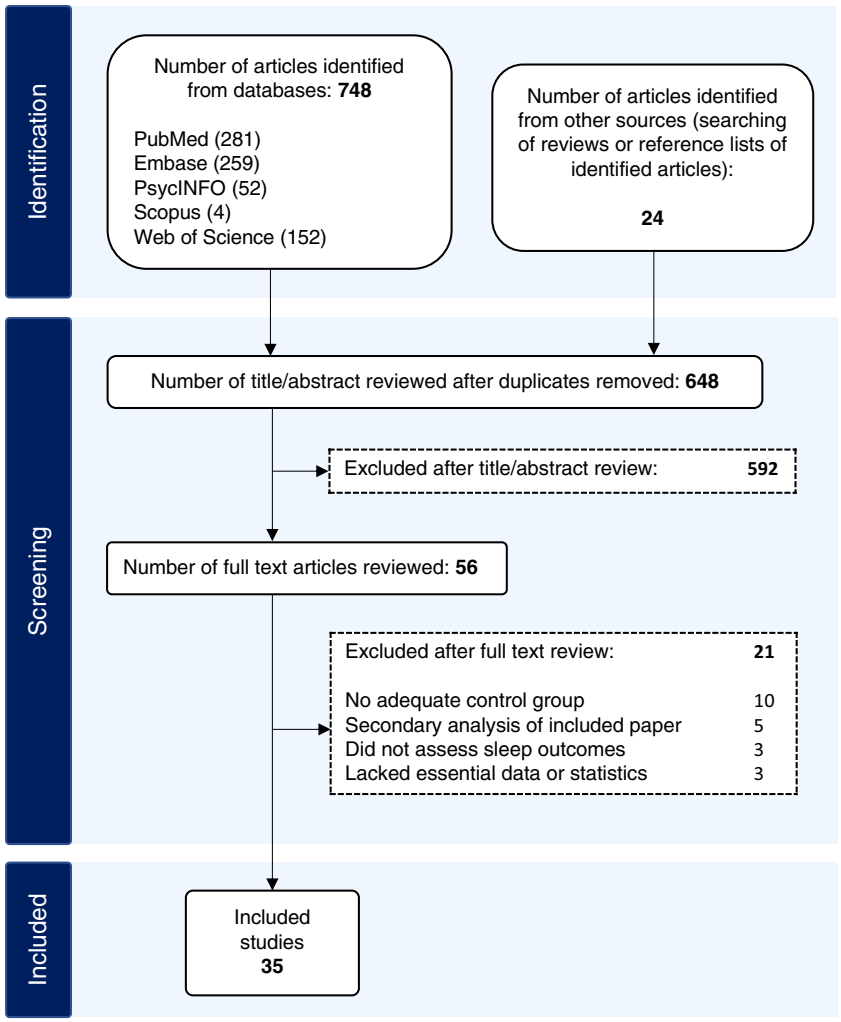


Fig. 1 Flow diagram outlining the literature search

13 studies included both subjective and objective sleep measures, and five studies examined only objective sleep measures. Nine studies examined cognitive outcomes, with one administering a discrete neuropsychological task, three using a brief measure of cognition only (e.g., the Montreal Cognitive Assessment (MoCA)), two administering comprehensive neuropsychological batteries, and three using a combination of both. Notably, no included study examined the effects of sleep interventions on neurodegenerative biomarkers or neuroimaging outcomes.

Cognitive and Behavioural Strategies and Bright Light Therapy

Four studies explored the effects of CBT-I, the gold-standard intervention for insomnia [20–23]. In a large study of 1,611 older adults with chronic insomnia, six 20-min sessions of digital CBT-I over 12 weeks significantly improved functional health, psychological well-being, and sleep-related quality of life compared to a sleep hygiene control group [22]. An RCT of digital CBT-I in adults with insomnia (mean age > 50 years) showed improvements in self-reported cognitive impairment post-treatment ($d = 0.86$) and at 6 months ($d = 0.96$), partially mediated by reduced insomnia severity and increased sleep efficiency [23]. Another study showed that 2-h weekly group CBT-I sessions for two months significantly increased the likelihood of remission of insomnia in older adults compared to the control group [21]. Those in the CBT-I group with sustained remission of insomnia also had an 82.6% decreased likelihood of experiencing incident or recurrent major depression compared to those in the control group without sustained remission of insomnia. A secondary analysis showed reduced expression of the cellular senescence blood-based biomarker $p16^{INK4a}$ in the CBT-I group at 24 months, suggesting long-term benefits for cellular aging [24]. Three studies utilizing abridged CBT-I methods, such as brief CBT-I and brief behavioural therapy for insomnia (BBT-I), reported positive effects on subjective sleep parameters, suggesting these shorter interventions may be just as effective [20, 25, 26].

Table 1 Characteristics of Randomized, Controlled Trials Assessing Efficacy of Non-Pharmacological Interventions on Sleep and Cognitive Outcomes

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Cognitive Behaviour Therapy for Insomnia												
Kyle et al., 2020	UK	410 (355 F)	DSM-5 criteria for insomnia disorder and self-reported memory difficulties	52.4 (11.5) [26–82]	2-arm, parallel RCT	Digital CBT-I	Wait-list control	10 weeks (follow-up at 24 weeks)	ISI SE (derived from PSQI)	Relative to control, ↓ISI scores and ↑SE at 10 weeks and 24 weeks ($p < 0.0001$)	BC-CCI UK Biobank Cognitive Battery	Relative to control, ↓ BC-CCI scores indicated improved self-reported cognitive impairment ($p < 0.0001$) No change on objective cognitive testing
Irwin et al., 2022	USA	291 (168 F)	Older adults with insomnia and depression (DSM-IV)	70.1 (6.7)	2-arm, parallel RCT	CBT-I	Trained public health educator	Weekly 2 h group sessions for 2 months	Sustained remission of insomnia (DSM-5)	Increased likelihood of remission of insomnia with CBT-I (26.3%) vs control (19.3%) ($p = 0.03$)	-	-
Espie et al., 2019	UK	1611 (1,329 F)	Older adults with chronic insomnia (DSM-V)	48.0 (13.8)	2-arm, parallel RCT	Digital CBT-I (n = 853)	Sleep hygiene education (n = 858)	12 weeks (24 weeks follow-up)	GSII ESS SCI	↓ sleep-related impairment at week 4 and 8 (all $p < 0.05$) ↓ in daytime sleepiness at week 4, 8 & 24 (all $p < 0.05$)	-	-
Tanaka et al., 2019	Japan	46 (36 F)	Cognitively healthy older adults	69.7 (8.1)	2-arm, parallel RCT	Brief CBT-I	Wait-list control	1 × 1 h group session, 1 × 45 min individual session; 2 × follow-up phone calls	PSQI	No sig. change in PSQI between groups	-	-

Table 1 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Chan et al., 2021	USA	62 (42 F)	Older adults with chronic insomnia	69.45 (7.71)	2-arm, parallel RCT	BBT-I (n = 32)	Self-monitoring control (n = 30)	4 weeks treatment (3 months follow-up)	Sleep discrepancy (Actigraphy—sleep diary) SOL, WASO, TST	↓ SOL discrepancy (explained by sleep diary but not actigraphy)	-	-
Polat et al., 2022	Turkey	124 (64 F)	Cognitively healthy older adults with self-reported daytime sleepiness (MMSE > 24)	I: 69.91 (4.28) C: 69.74 (4.18)	2-arm, parallel RCT	Sleep hygiene training (n = 67)	Control (n = 67)	2 weeks	ESS	At post-intervention, ↓ ESS ($p < 0.005$)	-	-
Bright Light Therapy												
Juda et al., 2020	Canada	14 (12 F)	Cognitively healthy older adults	82.6 (6.6)	2-arm, crossover RCT (nursing home setting)	Dynamic circadian lighting	Conventional lighting	5 weeks	PSQI Actigraphy	No difference in outcome variables between groups Higher morning light exposure (6:00–12:00) = less fragmented sleep and more stable rest-activity	NIH Toolbox	Fragmented sleep and longer sleep duration indicative of worse cognitive performance
Multimodal Interventions												
Han & Son, 2023	Korea	I: 25 (22 F) C: 30 (24 F)	MCI with sleep disturbance (IWGMCI criteria and MoCA-K < 24; PSQI > 5)	71.4 (5.3)	2-arm, parallel RCT	Sleep and Cognition Enhancement Multimodal Intervention	General education and guidance	1 session per week for 8 weeks	PSQI	Improvements in sleep quality ($p < 0.001$)	MoCA-Korean	Sig. improvement in MoCA-K score (+4.93 points; $p < 0.001$)

Table 1 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Falck et al., 2020	Canada	96 (NS F)	Probable MCI (MoCA < 26) and sleep disturbance (PSQI > 5)	65–85 y	2-arm, parallel RCT	Bright light therapy, physical activity, and sleep hygiene	Education plus attentional control	1 session per week for 24 weeks	Actigraphy PSQI	No sig. change in objective measures of sleep Improvements in subjective sleep quality ($p < 0.05$)	-	-
Exercise Interventions												
Song & Yu (2019)	China	120 (90 F)	MCI (MoCA-C score 19–26)	75.8 (6.3)	2-arm, parallel RCT Community (two healthcare centers)	Moderate-intensity aerobic exercise (n = 60)	General health education program (n = 60)	16 weeks	PSQI	Relative to control, ↓PSQI score at 16 weeks ($p < 0.001$)	MoCA (Chinese version)	Relative to control, greater improvement in MoCA-C scores ($p < 0.001$), mediated by improved sleep quality
Chen et al., 2019	Taiwan	40 (all F)	Cognitively healthy older adults with self-reported sleep disturbance	60.4 (4.7)	2-arm, parallel RCT	Light-intensity treadmill walking supervised by a certified instructor (n = 20)	Quiet rest control (n = 20)	NS	Actigraphy	Relative to control, ↓SOL ($p = 0.001$) and ↑SE ($p = 0.008$)	-	-
Cheng et al., 2021	China	51 (all F)	Community-dwelling older adults	60.4 (4.7)	2-arm, parallel RCT Community-based	3 × 60-min Tai Chi sessions per week delivered by instructor (n = 26)	Usual home lifestyle, without added regular physical exercise (n = 25)	24 weeks	PSQI	Relative to control, ↓PSQI score at 24 weeks ($p = 0.008$), maintained at 4-week follow-up ($p = 0.04$)	-	-

Table 1 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Fan et al., 2020	China	139 (105 F)	Community-dwelling, age ≥ 60 years old, PSQI ≥ 5	71.1 (6.3)	Cluster 2-arm RCT; 8 communities	5 × 45-min group exercise session per week, guided by trained tutor (n = 67)	Control group; usual lifestyle behaviors (n = 72)	24 weeks	PSQI	Relative to control, ↓PSQI score after 24 weeks relative to control (p = 0.007)	-	-
Sekerci & Bicer, 2019	Turkey	60 (23 F)	Cognitively healthy nursing home residents	F 73.56 (8.25) M 71.91 (7.98)	2-arm, parallel RCT nursing home	2 × 40-min moderate-intensity walking sessions per week (n = 32)	Control group, usual lifestyle behaviors (n = 32)	8 weeks	PSQI	Relative to control, ↓PSQI score relative to control (p < 0.001)	-	-
Jimenez-Garcia et al., 2021	Spain	73 (56 F)	Community dwelling, aged greater than 60 years, healthy	68.49 (5.18)	3-arm parallel RCT	2 × 45-min moderate or high intensity interval training per week (HIIT n = 28; MIIT n = 27)	Continued daily lifestyle, avoid regular exercise or other exercise programs (n = 27)	12 weeks	PSQI	Relative to MIIT and control, HIIT training ↓PSQI total score (p = 0.005)	-	-
Kader & Al-Jiffri, 2019	Saudi Arabia	50 (NS F)	Cognitively healthy older adults with > 3 mo sleep disturbance	I: 64.98 (4.15) C: 65.72 (3.86)	2-arm parallel RCT (Community dwelling)	3 × 40-min aerobic exercise per week (n = 25)	Usual lifestyle behaviors (n = 25)	6 months	PSG	Relative to control, ↑ TST (p = 0.004), ↑ SE (p = 0.006), ↓ WASO (p = 0.008)	-	-

Table 1 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Kerkez & Erci, 2024	Turkey	114 (71 F)	Cognitively healthy adults ≥ 65 y and SMME ≥ 24	I: 70.89 (4.23) C: 71.80 (4.03)	2-arm parallel RCT	1 × 40-min group/individual Tai Chi Qigong program (n = 68)	No recommended physical, social or cognitive activities (n = 65)	6 weeks	PSQI (Turkish Version)	Relative to control, ↓PSQI total score ($p = 0.03$), and ↓PSQI sub-domain, subjective sleep quality ($p < 0.001$)	-	-
Li et al., 2021	China	41 (36 F)	Assisted living facility-dwelling sedentary adults ≥ 60 y and MoCA ≥ 18	72.2 (7.6) [60–88]	2-arm, parallel RCT	3 × 60-min resistance training per week (n = 31)	Control group, continued usual activities (n = 31)	12 weeks	Actigraphy Sleep diary	Relative to control, ↑ SE% ($p < 0.01$) and ↓WASO ($p = 0.02$)	-	-
Seol et al., 2021	Japan	10 (all F)	Healthy older women, 65–79 years	72.3 (2.3) [68–76]	3-arm crossover RCT	Low-intensity exercise (aerobic exercise) or instructed housework 3 h before bedtime for 30-min	Control group, remain stationary 3-h before bedtime	1 × overnight per group	PSG OSA-MA	Relative to control, exercise group ↓ sleep latency ($p = 0.01$) and ↑ delta EEG power density ($p = 0.007$) Exercise ↑OSA-MA total score relative to control ($p = 0.039$) and housework ($p = 0.007$)	-	-

Table 1 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Siu et al., 2021	China	320 (256 F)	Community-dwelling, aged ≥ 60 y with chronic insomnia (DSM-V)	67.3 (6.8)	3-arm, parallel RCT	3 × 1 h group-based sessions per week of conventional exercise (n = 105) or Tai Chi (n = 105)	Control (usual care) (n = 110)	12 weeks	Actigraphy DSM-5 insomnia remission PSQI ISI Sleep diary	Relative to control, both ↑SE%, ↓WASO, ↓no. of awakenings, and ↓ISI scores Tai Chi had significantly greater remission rates and ↓PSQI scores relative to exercise and control	-	-
Shree-Ganesh et al., 2021	India	96 (60 F)	Healthy, community-dwelling adults aged 60–75 y	I: 62.6 (3.9) C: 65.5 (3.4)	2-arm, parallel RCT	3 sessions of yoga-based lifestyle intervention program per week (n = 48)	Waitlist control (n = 48)	12 weeks	PSQI	Relative to control, ↓PSQI total score ($p < 0.05$)	-	-
Song et al., 2024	China	89 (68 F)	Community-dwelling adults with MoCA = 19–26 and PSQI > 5	I: 76.71 (5.96) C: 75.20 (6.63)	2-arm, parallel RCT	3 × 60-min group aerobic dancing program per week (n = 45)	8 × bi-weekly group-based health educational sessions (n = 44)	16 weeks	PSQI	Relative to control, ↓PSQI total score ($p = 0.04$)	MoCA	Relative to control, ↑MoCA score ($p = 0.008$)
Tseng et al., 2020	Taiwan	40 (33 F)	Community-dwelling, aged ≥ 40 years with poor sleep quality (PSQI > 5)	61.7 (7.0)	2-arm, crossover RCT	3 × 50-min supervised exercise per week (n = 20)	1-h educational session on sleep hygiene (n = 20)	12 weeks	Actigraphy SQI	Relative to control, ↓PSQI ($p = 0.003$), on all subdomains ($p < 0.05$)	-	-

Table 1 (continued)

Author, year	Country	Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
		N (Female sex)	Population	Mean (SD) age [range]	Study design	Intervention(s)	Comparison group	Treatment duration	Outcome Measures	Overall Findings	Outcome Measures	Overall Findings
Non-invasive Brain and Acoustic Stimulation												
Zeller et al., 2024	Switzerland	34 (20 F)	Older adults with (MoCA ≤ 25) or without (MoCA > 25) cognitive impairment	70.0 (4.9)	2-arm, crossover RCT	Phase-locked acoustic stimulation (PLAS)	Sham device (sham-PLAS)	Three consecutive nights of acoustic stimulation	PSQI PSG	No sig. difference on PSQI	Face-occupation association (FOA) task	Relative to control, PLAS improve memory performance post-treatment ($p = 0.01$) and at 1-mo ($p = 0.002$) and 3-mo ($p = 0.001$) follow-up
Papalambros et al., 2019	USA	9 (5 F)	Amnestic MCI	72 (8.7)	2-arm, crossover RCT	Phase-locked loop acoustic stimulation of slow-oscillations	Sham stimulation	Two overnight visits (1-week washout)	PSG	No change in PSG-derived sleep outcomes between groups	VPA Task NIH Toolbox Cognitive Battery	No change in VPA task outcomes between groups Change in SWA positively correlated with overnight word recall ($p = 0.012$)
Lee et al., 2021	Korea	I: 81 (52 F) C: 79 (48 F)	Community-dwelling older adults with insomnia (DSM-5)	I: 60.8 (9.3) C: 59.6 (8.7)	2-arm, parallel RCT	Low-frequency transcutaneous electric nerve stimulation (n = 81)	Sham device (n = 79)	4 weeks	PSQI Sleep diary Actigraphy	Relative to control, ↓PSQI scores ($p = 0.04$) No changes on sleep diary or actigraphy outcomes	-	-

Table 1 (continued)

Author, year	Country	Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
		N (Female sex)	Population	Mean (SD) age [range]	Study design	Intervention(s)	Comparison group	Treatment duration	Outcome Measures	Overall Findings	Outcome Measures	Overall Findings
Mindfulness-Based Intervention												
Perini et al., 2023	Singapore	127 (74 F)	Cognitively healthy older adults (MMSE ≥ 26; MoCA ≥ 23) with sleep disturbance (PSQI ≥ 5)	60.9 (6.4)	2-arm, parallel RCT	Mindfulness-based therapy (MBTI) (n = 65)	Sleep hygiene, education, and exercise program (n = 62)	1 × 2 h sessions per week for 8 weeks	PSQI ISI Actigraphy PSG	Relative to control, ↓ISI (p = 0.01) No change on PSQI or objective sleep outcomes	-	-
Cai et al., 2022	China	75 (56 F)	MCI (MoCA score cut-offs relative to education; MMSE 24–30) and sleep disturbance (PSQI > 5)	80 (9.3)	2-arm, parallel RCT (Four nursing homes)	Mindfulness intervention (n = 38)	Health education (n = 37)	1 × 1.5 h sessions per week for 8 weeks	PSQI ISI AIS	Relative to control, ↓PSQI (p = 0.001), ↓ISI (p = 0.03), and ↓ AIS (p = 0.01)	MoCA MMSE Verbal Fluency RAVLT TMT SDMT	Relative to control, ↑MoCA score (p = 0.04) and MMSE (p = 0.03) No change on specific cognitive domain tests

Symbol '- ' indicates that the study did not include cognitive outcome measures. Abbreviations: *AIS* Athens Insomnia Scale, *BBT-I* Brief Behavioral Therapy for Insomnia, *BC-CCI* British Columbia Cognitive Complaints Inventory, *C* Control group, *CBT-I* Cognitive Behavioural Therapy for Insomnia, *CFQ* Cognitive Failures Questionnaire, *DSM-IV* Diagnostic and Statistical Manual of Mental Disorders 4th Edition, *DSM-5* Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, *ESS* Epworth Sleepiness Scale, *GSII* General Sleep Inventory for Insomnia, *HIIT* High-Intensity Interval Training, *I* Intervention group, *ISI* Insomnia Severity Index, *IWGMCI* International Working Group on Mild Cognitive Impairment, *MCI* mild cognitive impairment, *MBTI* Mindfulness-Based Therapy for Insomnia, *MIIT* Moderate-Intensity Interval Training, *MMSE* Mini-Mental State Examination, *MoCA* Montreal Cognitive Assessment, *NIH* National Institutes of Health, *NS* not specified, *OSA* Obstructive Sleep Apnea, *OSA-MA* Oguri-Shirakawa-Azumi Sleep Inventory, *PSG*, Polysomnography, *PSQI* Pittsburgh Sleep Quality Index, *RAVLT* Rey Auditory Verbal Learning Test, *RCT* randomised controlled trial, *SCI* Sleep Condition Indicator, *SDMT* Symbol Digit Modalities Test, *SE* Sleep Efficiency, *SMMSE* Standardized Mini-Mental State Examination, *SOL* Sleep Onset Latency, *SWA* Slow-Wave Activity, *TMT* Trail Making Test, *TST* Total Sleep Time, *WASO* Wake After Sleep Onset

No controlled interventional studies in the past five years examining CBT-I in MCI met criteria for this review. Nonetheless, a recent open-label RCT found that administering six weekly sessions of digital CBT-I was feasible in 40 older adults with MCI, with high adherence rates (79% completed > 4 out of the 6 CBT-I sessions) and an improvement on the Insomnia Severity Index after 12 weeks (NCT05568381). This suggests that digital delivery of standard CBT was acceptable and feasible in an MCI population, warranting further long-term studies in individuals with MCI. Although no studies have explored the effects of CBT-I on AD-related biomarkers, emerging studies (e.g., NCT0395210), aim to investigate the efficacy of CBT-I on cognitive function and its potential impact on Aβ accumulation in cognitively healthy older adults with insomnia, indicating a promising direction for future research.

Bright light therapy (BLT) is a non-pharmacological treatment aimed at treating the physiological changes associated with alternations of circadian rhythm in cognitively healthy older adults and those with dementia (for review, see [27]). Although some evidence supports its use to improve sleep disturbances in individuals with cognitive impairment or AD, several recent systematic reviews and meta-analyses indicate that the current evidence is at best equivocal [17, 28–31]. Larger, more rigorously conducted trials are needed before BLT can be recommended in clinical practice. Existing studies have administered heterogenous BLT protocols administered across different settings (institutions, nursing homes, or hospital settings) which raises the question whether BLT is an effective strategy in individuals with cognitive impairment or AD and highlights the need for early intervention. Juda et al. (2020) showed that a 5-week treatment with dynamic circadian lighting in cognitively healthy older adults did not significantly change subjective and actigraphy-derived measures of sleep; however, higher morning light exposure (between 6am-12 pm) resulted in less fragmented sleep and more stable rest-activity pattern [32].

Exercise-based Interventions

A 2022 systematic review and network meta-analysis of 35 RCTs found that muscle endurance training combined with walking improved sleep quality in older adults more than usual care (standardized mean difference, SMD = -2.2), but was less effective than face-to-face CBT-I (SMD = -4.7) [33]. Expanding on this, our review identified 14 studies on exercise interventions for sleep published since 2019. These studies align with recent systematic reviews showing that various exercise types (walking, aerobic exercise, moderate-to-high intensity interval training, resistance training, yoga, Tai Chi, and dance) improve both subjective and objective sleep outcomes.

No controlled interventional studies in the past five years on exercise interventions for MCI met our criteria. However, a recent systematic review and meta-analysis found moderate-to-high-quality evidence that exercise, regardless of intensity, benefits both subjective (e.g., Pittsburgh Sleep Quality Index) and objective sleep outcomes (e.g., polysomnography, actigraphy) in older adults with MCI or Alzheimer's disease and related dementias (AD/ADRD) [34]. A pre-registered trial (NCT03939286) will investigate the effects of exercise on brain structure, function, and metabolism using various brain imaging outcomes in patients with amnestic MCI and Alzheimer's pathology.

Multi-modal Interventions

Three studies on non-pharmacological multi-modal interventions for sleep disturbance in MCI were identified. Han & Son (2023) found that an once weekly intervention combining walking, light exposure, and behavioural strategies for eight weeks, significantly improved subjective sleep quality and MoCA-Korean scores in MCI patients compared to a general education control group [35]. Weekly telephone coaching was provided to promote adherence to the intervention. Falck et al. (2020) showed that individualized BLT, physical activity, and sleep hygiene training improved subjective sleep quality but not actigraphy-derived sleep outcomes in older adults with probable MCI and sleep disturbance [36]. Adherence to treatment was not assessed. Current pre-registered trials will test various multi-modal lifestyle interventions on brain health including sleep, cognition, and AD-related biomarkers, such as inflammatory and neurodegenerative biomarkers and structural and functional brain imaging (for example, ACTRN12621001760864, NCT01041989, NCT03978052, NCT04364191).

Mindfulness-based Interventions

Mindfulness-based interventions (MBI) have shown improvements in sleep quality, mental wellbeing, and cognition in older adults, including those with MCI and dementia (for reviews, see [37] and [38]). We identified two studies that met criteria for this review. Perini et al. (2023) found that eight weekly MBI sessions significantly improved subjective sleep outcomes, but not objective sleep measures, in cognitively healthy older adults with sleep disturbances, compared to an education-only control group, with effects sustained at 6-month follow-up [39]. Cai et al. (2022) found that eight weekly MBI sessions improved subjective sleep and general cognitive measures (e.g., MoCA), but not on discrete neuropsychological tests, in 75 MCI patients with sleep disturbance [40]. A recent systematic review and meta-analysis reported negligible effects of MBI on attention and memory, with a small effect on executive function ($g = 0.14$)

Table 2 Characteristics of Randomised, Controlled Trials Assessing Efficacy of Pharmacological Interventions on Sleep and Cognitive Outcomes

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Melatonin												
Duffy et al., 2022	USA	24 (13 F)	Cognitively healthy older adults	64.2 (6.3)	RCT; Crossover (vs placebo) and Parallel (dose)	I: 0.3 mg melatonin (n = 12) II: 5 mg melatonin (n = 12)	Placebo (n = 24)	2 weeks	PSG MEQ	Relative to placebo, 0.3 mg melatonin ↑stage N1, N2 and NREM sleep, but ↓SWS 5.0 mg melatonin ↑TST (p = 0.0007) and ↑SE (p = 0.0007) due to ↑stage N2 sleep	-	-
Orexin Receptor Antagonists												
Rosenberg et al., 2019	North America/ Europe	1,006 (869 F)	Community-dwelling older adults (55–88 y) with DSM-5 insomnia disorder	63.9 (6.8)	RCT, Parallel [67 sites in Nth America and Europe)	Lemborexant (LEM) 5 mg, LEM 10 mg	Placebo	30 nights	PSG Sleep diary ISI	Relative to placebo and zolpidem, both LEM doses ↓PSG-derived SOL (p < 0.001), ↑%SE (p < 0.001), and ↓WASO (p < 0.001)	-	-
Karppa et al. (2020)	North America, Europe, Asia, Oceania	949 (647 F)	Insomnia disorder (DSM-5 and ISI ≥ 15)	54.5 (13.8)	RCT; Parallel; 119 sites	Lemborexant (5 mg, 10 mg)	Placebo	6 months	Sleep diary	Relative to placebo, both doses ↓sSOL (p < 0.0001), ↑sTST (p ≤ 0.003), ↑sSE (p ≤ 0.0001), and ↓sWASO (p ≤ 0.01)	-	-

Table 2 (continued)

		Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
Author, year	**Country**	**N (Female sex)**	**Population**	**Mean (SD) age [range]**	**Study design**	**Intervention(s)**	**Comparison group**	**Treatment duration**	**Outcome Measures**	**Overall Findings**	**Outcome Measures**	**Overall Findings**
Lucey et al., 2023	USA	38 (26 F)	Cognitively healthy adults with poor sleep efficiency (actigraphy)	I (10 mg): 56.95 (4.35) I (20 mg): 54.30 (5.66) C: 55.94 (6.10)	RCT Parallel community	Suvorexant 10 mg, Suvorexant 20 mg	Placebo	1 night	PSG	No change on any PSG-derived sleep outcome	-	-
Zammit et al., (2020)	Germany-USA	58 (39 F)	Community-dwelling older adults with ISI ≥ 15 & DSM-5 insomnia disorder	Median age 69 (range 65–85 y)	RCT; Crossover; 10 centers	Daridorexant 5, 10, 25, and 50 mg	Placebo	2 nights	PSG	Relative to placebo, ↓WASO ($p < 0.001$) and ↓latency to persistent sleep ($p < 0.025$) with all doses ≥ 10 mg (not 5 mg)	-	-
Mignot et al., (2020)	Global (18 countries)	Study 1: 930 (638 F) Study 2: 924 (363 F)	Community-dwelling older adults with ISI ≥ 15 & DSM-5 insomnia disorder	Mean age 50 years	RCT; Parallel; 156 sites	Study 1: 25 mg, 50 mg daridorexant Study 2: 10 mg, 25 mg daridorexant	Placebo	12 weeks	PSG Sleep diary IDSIQ	Relative to placebo, both 25 mg and 50 mg of daridorexant ↓WASO ($p < 0.0001$) and ↓latency to persistent sleep ($p < 0.005$) 25 mg and 50 mg of daridorexant also ↑sTST ($p < 0.03$) and ↓sleepiness scores on IDSIQ sleepiness subdomain ($p < 0.01$)	-	-

Table 2 (continued)

Author, year	Country	Participants			Study Characteristics				Sleep Outcomes		Cognitive Outcomes	
		N (Female sex)	Population	Mean (SD) age [range]	Study design	Intervention(s)	Comparison group	Treatment duration	Outcome Measures	Overall Findings	Outcome Measures	Overall Findings
Supplementation												
Stavrinou et al., 2020	Cyprus	36 (22 F)	MCI (Petersen criteria and ACE-R score ≤ 88)	78.8 (7.3)	RCT; Parallel; community	High dose omega-3 and omega-6 fatty acid and antioxidants (n = 18)	Placebo (n = 18)	6 months	PSQI	Relative to placebo, ↓PSQI at mid-treatment (3 mo; p = 0.02) but not at post-treatment (6-mo; p = 0.06)	ACE-R MMSE TMT-A TMT-B SCWT DSST	Relative to placebo, ↑ACE-R (p = 0.003) and ↑MMSE at 6 mo (p = 0.03) Relative to placebo, ↑correct responses on Stroop Color Test (p = 0.004) and ↓DSST errors (p = 0.001)

Symbol '- ' indicates that the study did not include cognitive outcome measures. Abbreviations *ACE-R* Addenbrooke's Cognitive Examination-Revised, *C* Control, *DSM-5* Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, *DSST* Digit Symbol Substitution Test, *I* intervention group 1, *II* intervention group 2, *IDSIQ* Insomnia Daytime Symptoms and Impacts Questionnaire, *ISI* Insomnia Severity Index, *LEM* lemborexant, *MCI* mild cognitive impairment, *MEQ* Morningness-Eveningness Questionnaire, *MMSE* Mini-Mental State Examination, *N1* non-rapid eye movement sleep stage 1, *N2* non-rapid eye movement sleep stage 2, *NA* not applicable, *NREM* non-rapid eye movement sleep, *PSG* polysomnography, *PSQI* Pittsburgh Sleep Quality Index, *RCT* randomized controlled trial, *REM* rapid eye movement sleep, *SCWT* Stroop Color and Word Test, *SE* sleep efficiency, *SD* standard deviation, *SOL* sleep onset latency, *SWS* slow-wave sleep, *TMT-A* Trail Making Test Part A, *TMT-B* Trail Making Test Part B, *TST* total sleep time, *WASO* wake after sleep onset

in older adults with or without cognitive impairment [41]. It is hypothesized that longer lifetime experience with mindfulness practice and integration with existing therapies (e.g., CBT-I) may enhance cognitive benefits, particularly in specific cognitive domains.

Non-invasive Brain and Acoustic Stimulation Techniques

One study exploring non-invasive brain stimulation was included in the review. Lee et al. (2021) investigated the effects of low-frequency transcutaneous electric nerve stimulation (LF-TENS) compared to a sham device on sleep outcomes in 160 older adults with insomnia [42]. Significant improvement in subjective sleep quality was observed in participants aged > 60 years, but not in the middle-aged group (aged 40–60 years), suggesting age-specific effects. Current pre-registered trials are exploring other techniques, including transcranial electrical stimulation (NCT05771844) and transcranial alternating current stimulation (NCT05544201) on memory performance and neurodegenerative biomarkers.

Slow wave sleep (SWS)-enhancing technologies, such as acoustic stimulation, are being explored as a way to improve sleep and cognitive function in cognitively healthy older adults [43–47] and those with MCI [48]. Papalambros et al. (2019) found that one night of acoustic stimulation did not change PSG-derived sleep outcomes in amnestic MCI patients, but the magnitude of change in slow wave activity correlated positively with overnight memory recall on a verbal paired-associated task, suggesting a link between slow wave activity and memory consolidation [48]. Zeller et al. (2024) showed no effect of phase-locked acoustic stimulation (PLAS) versus sham on sleep outcomes in older adults with or without cognitive impairment [49]. However, PLAS induced significant electrophysiological responses and improved memory performance in both groups, with a delayed response in the cognitively impaired group. Stronger electrophysiological responses in the cognitively impaired group were significantly associated with improved Aβ ratios. These results suggest that PLAS could enhance SWS electrophysiology, memory, and amyloid burden in older adults with cognitive impairment, although longer interventions may be needed for more pronounced memory improvements.

OSA Therapies

Given the limited number of published RCTs and the prevalence of observational, cross-sectional, or population-based study designs exploring the effects of CPAP [50, 51], no controlled interventional studies met the inclusion criteria for this review. However, a systematic review of 11 studies (N = 60,840 OSA patients) found that CPAP therapy had a protective effect on the incidence of MCI and AD, suggesting OSA as a modifiable risk factor for cognitive decline [52]. Long-term research studies investigating whether CPAP delays the accumulation of AD pathology and cognitive and functional decline are currently underway. These include two multi-site RCTs: one in 180 older adults with moderate-to-severe OSA [53] [54] and another in 400 older adults with moderate-to-severe OSA (NCT05988385). Both trials will administer personalized OSA therapy by any combination (i.e., CPAP, oral appliance therapy, positional therapy) for dementia prevention. Additionally, three pre-registered trials will examine how CPAP affects brain health and cognition: one on Aβ deposition using PET imaging in those with subjective cognitive decline and MCI (NCT06150352); another on delaying progression of cognitive impairment in amnestic MCI (NCT03113461), and a third on the effect of CPAP withdrawal on brain waste clearance in OSA (NCT05606991).

Pharmacological Approaches for the Treatment of Sleep Disturbances

Melatonin

Exogenous melatonin is considered a safe alternative to hypnotic medications, with modest efficacy for insomnia and circadian rhythm disorders in older adults [55]. Duffy et al. (2022) tested 0.3 mg and 5 mg doses of melatonin for two weeks in 24 healthy older adults [56]. The higher dose showed more consistent improvements in sleep parameters than the lower dose and placebo. Although melatonin trials in older adults demonstrate a favorable safety profile, long-term safety data are limited, with most studies lasting less than 12 weeks (for review, see [55]). A pre-registered trial will examine the effects of 5 mg melatonin over a 9-month period in older adults with and without MCI, measuring actigraphy-derived sleep outcomes, AD biomarkers (p-tau, t-tau, Aβ-42 ratio) from cerebrospinal fluid (CSF), and cognitive outcomes through neuropsychological tests (NCT03954899). Melatonin, a potent antioxidant with potential anti-amyloid properties, is being increasingly studied at higher doses (> 10 mg) for various conditions, including cancer, cardiometabolic disease, and neurodegenerative disorders [57, 58]. One study will evaluate the feasibility of 25 mg melatonin for 12 weeks in 40 adults with MCI (aged 60–80 years) on measures of brain oxidative stress using magnetic resonance spectroscopy and blood-based biomarkers (ANZCTRN12619000876190).

Orexin Receptor Antagonists

Orexin receptor antagonists such as lemborexant, daridorexant, and suvorexant are being explored for treating insomnia

in older adults. In one study, 38 cognitively healthy older adults (mean age > 50 years) received suvorexant, which reduced tau phosphorylation at threonine-181 (p-tau181) and Aβ levels (Aβ38, Aβ40, and Aβ42) in human CSF, despite no significant group differences in sleep outcome measures [59]. This suggests potential neuroprotective properties beyond its effects on sleep and underscores the need for long-term studies on cognitive function and neurodegenerative biomarkers. A pre-registered Phase II RCT of suvorexant (20 mg) in those aged > 65 years with amyloid pathology but no cognitive impairment will assess impact on the rate of Aβ accumulation via PET imaging (NCT04629547).

Rosenberg et al. (2019) showed that 4-week treatment with lemborexant (5 or 10 mg) significantly improved sleep onset and maintenance compared to placebo and zolpidem in 1,006 adults with insomnia (aged ≥ 55 years) and was well-tolerated [60]. Kärppä et al. (2020) tested the effects of 6-month treatment with lemborexant (5 or 10 mg) in adults with insomnia (mean age 54.4 years) [61]. Both doses improved subjective sleep parameters at 6 months, including sleep onset latency, wake after sleep onset (WASO), sleep efficiency (SE), and sleep quality, with low rates of adverse events. The effects on subjective sleep parameters were sustained at 12 months [62]. A secondary analysis confirmed these findings in a subgroup of older adults (≥ 65 years; n = 262) [63]. The safety and tolerability of lemborexant in elderly patients was similar to younger patients, with no age-based dose adjustments required. Previous studies reported no effects on postural stability [64] and driving performance [65], though 10 mg lemborexant negatively affected attention and memory in healthy older adults [64]. While preliminary work with lemborexant in AD patients with sleep disturbance is promising [66], more studies in older adults with cognitive impairment are needed. A pre-registered trial will examine the effect of lemborexant in cognitively healthy older adults with amyloid deposition on AD biomarkers including CSF and plasma markers of tau and Aβ accumulation, neurofilament light chain (NfL), and soluble triggering receptor expressed on myeloid cells 2 (sTREM2) (NCT06274528).

Zammit et al. (2020) assigned 58 adults (aged ≥ 65 years) with insomnia to receive ascending doses of daridorexant and placebo over five two-night treatment periods [67]. Dose-dependent improvements in PSG-derived WASO and latency to persistent sleep (dose range 10–50 mg) were observed. Two subsequent Phase 3 RCTs (N = 1,854) showed that both 25 mg and 50 mg of daridorexant improved sleep outcomes, while 50 mg also improved daytime functioning, in adults with insomnia (mean age > 50 years) after 12 weeks [68]. A secondary analysis indicated that 50 mg of daridorexant was most effective for improving both sleep outcomes and daytime function, without increasing adverse events or next-morning residual effects [69]. The same participants joined a 40-week extension trial (n = 550) [70] showing 50 mg daridorexant consistently improved sleep and daytime functioning without next-morning sleepiness, withdrawal, or rebound effects. A pre-registered trial will test daridorexant for insomnia in MCI and mild-to-moderate AD, with outcomes including PSG, neuropsychological assessments, and neurodegenerative biomarker assays (NCT05924425).

Supplementation

One RCT examined the effects of a high-dose omega-3 and omega-6 fatty acids with antioxidant vitamins on sleep, cognitive function and functional capacity in 47 older adults with MCI over six months [71]. The supplementation group showed significant cognitive improvements on the ACE-R and MMSE compared to placebo, indicating potential for reducing cognitive and functional decline in MCI. A pre-registered RCT (NCT06029894) will explore the effects of a dietary supplement, citicoline, on sleep and cognition, including neuropsychological tests and changes in CSF-derived Aβ-42 and tau and p-tau levels.

Discussion

Since 2019, research on sleep interventions in older adults with or without cognitive impairment has significantly expanded, involving multiple countries and a higher proportion of female participants, reflecting increased representation of women in dementia research [72]. While most studies focused on subjective measures of sleep, an increasing number of studies included both subjective and objective measures, such as wearable devices. Few studies incorporated measures of cognition, with most using only gross measures of cognition and a subset administering discrete neuropsychological tasks. Additionally, few studies incorporated long-term follow-up to determine lasting clinical benefits and efficacy on sleep and cognitive outcomes, aligning with a recent meta-analysis calling for longer follow-up durations and use of supporting biomarkers [73]. Despite the growing interest in sleep, dementia, and neurodegenerative research [74], none of the included studies from the past five years examined the effect of sleep interventions on biomarkers of neurodegeneration (e.g., glial fibrillary acidic protein, NfL, p-tau217) or brain structure and function via neuroimaging. However, several emerging pre-registered trials include these outcomes, indicating a promising direction for future research.

Over the past five years, research has established non-pharmacological treatments such as CBT-I, exercise, and multimodal interventions as the mainstay for treating sleep disturbances in older adults, with or without cognitive impairment. CBT-I remains a safe and effective method for improving sleep in this population, though further research is needed to optimize

its delivery in older adults, including length and type of therapy (e.g., CBT-I, BBT-I) and mode of delivery (e.g., individual, group, or digital). Digital or web-based CBT-I interventions are particularly promising due to their accessibility, especially since the majority of individuals with MCI use e-tools like the internet and smartphones [75]. Indeed, a recent pilot RCT (N = 246) demonstrated that digital CBT-I is feasible and acceptable for those with MCI, showing a 5.9-point improvement in ISI scores at week 12 compared to the control group [76]. Similar results were observed in another pilot RCT involving a four-session multi-modal group intervention ("Sleep Well, Think Well") for individuals with MCI [77]. Exercise intervention is a widely accessible intervention that can improve or protect against both functional and cognitive decline and improve depressive symptoms – a known risk factor for dementia [78]. A systematic review of 218 controlled studies (N = 14,170 participants) found that exercise was an effective treatment for depression, with walking/jogging, yoga, and strength training more effective than other exercises, and yoga somewhat more effective among older adults [79].

Given the complex and multifactorial nature of cognitive decline in older adults, multidomain lifestyle interventions targeting several risk factors simultaneously show promise in improving sleep and cognitive decline. Large-scale, long-term RCTs, such as The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) and World-Wide FINGER (WW-FINGER), are in progress, with follow-ups of up to 11 years [80]. These studies involve the addition of metformin as a potential disease-modifying drug for AD and dementia, as well as the analysis of cognitive outcomes, sleep parameters, and genetic factors such as apolipoprotein E (APOE) [81]. Emerging non-pharmacological sleep interventions, including time-restricted feeding [82] and music-based interventions, are also being explored. Early evidence suggests that music-based interventions may improve sleep in older adults [83] and cognition among those with MCI and AD [82]. However, more research is needed to determine the type, duration, and dose of music required to produce lasting effects on sleep and cognition.

In acute cases of sleep disturbance or as adjuncts to non-pharmacological intervention, short-term pharmacological therapies may be offered. Melatonin is considered a safe alternative to hypnotic medications such as benzodiazepines and Z-drugs, which are not recommended due to their off-target effects and heightened risk of falls and injury [84, 85]. Orexin receptor antagonists are increasingly shown to be relatively safe and effective for improving sleep in older adults, without the need for aged-based dose adjustments. Preliminary studies suggest potential neuroprotective effects of suvorexant, emphasising the need for further long-term research to evaluate their impact on cognitive function and neurodegenerative biomarkers. The effects of AD-specific drugs on sleep are noteworthy. Memantine, an N-methyl-D-aspartate receptor antagonist (NMDA) receptor antagonist, has shown positive effects on sleep behavior in AD and dementia with Lewy bodies and Parkinson's disease dementia [86–88]. Anti-amyloid monoclonal antibodies (MABs), including donanemab and lecanemab, offer new avenues for research, particularly regarding their potential effects on sleep, which remain largely unexplored. Targeting amyloid burden early may reduce sleep disturbances and improve patient outcomes [89]. Future studies involving MABs and emerging pharmacological agents targeting neuroinflammation (e.g., NCT05904717) should incorporate validated objective and subjective measures of sleep-related outcomes.

The field of sleep-focused clinical trials is limited by an incomplete understanding of the neurobiology underlying sleep disturbances in older adults and those with MCI, and and how the regional distribution of neurodegenerative disease in the brain predisposes to and/or perpetuates sleep disorders and vice versa. Some studies suggest that distinct clusters of individuals attending memory clinics exhibit altered sleep neurophysiology, which correlates with distinct cognitive profiles and brain network connectivity [90]. Future research must consider the type of sleep disorder, environmental factors, and the neurodegenerative pathologies that contribute to sleep disturbances and cognitive decline. It is also pertinent that future research account for the heterogeneity of cognitive deficits in pre-dementia periods and tailor interventions accordingly, with insights into the neuroscience of sleep in MCI informing these efforts.

Conclusions

The field of sleep-focused clinical trials in older adults with or without cognitive impairment is progressing, but still needs robust evidence through well-designed studies targeting objective markers of sleep, cognition, and neurodegeneration. Personalized, clinically effective interventions, considering the presence of amyloid, tau, cerebrovascular disease, or alpha-synuclein in key sleep-related circuits, are needed to develop feasible, cost-effective, and scalable treatments in older adults with or without cognitive impairment.

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Declarations

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