Sleep Duration in Relation to Cognitive Function among Older Adults: A Systematic Review of Observational Studies

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Key Words

Sleep duration · Cognition · Older adults · Epidemiology

Abstract

Context: Increasing evidence suggests that circadian and sleep parameters influence cognitive function with aging. **Objective:** To evaluate observational studies of sleep duration and cognition in older adults. **Data Sources:** A systematic review of OVID Medline and PsycINFO through September 2015, and review of bibliographies from studies identified. **Study Selection:** English-language articles reporting observational studies of sleep duration and cognitive function in older populations. **Data Extraction:** Data extraction by 2 authors using predefined categories of desired information. **Results:** Thirty-two studies met our inclusion criteria, with nearly two-thirds published in the past 4 years. One-third of studies indicated that extreme sleep durations were associated with worse cognition in older adults. More studies favored an association with long vs. short sleep durations (35 vs. 26% of studies, respectively). Four studies found that greater changes in sleep duration over time were related to lower cognition. Study design and analytic methods were very heterogeneous across studies; therefore, meta-analysis was not undertaken. **Limitations:** We reviewed English-language manuscripts only, with a qualitative summary

of studies identified. **Conclusions and Implications of Key Findings:** Observational studies of sleep duration and cognitive function in older adults have produced mixed results, with more studies suggesting that long (rather than short) sleep durations are related to worse cognition. Studies more consistently indicate that greater changes in sleep duration are associated with poor cognition. Future studies should be prospectively designed, with objective sleep assessment and longer follow-up periods; intervention studies are also needed to identify strategies for promoting cognitive health with aging.

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Introduction

Accumulating evidence suggests that circadian disruption influences long-term health, as epidemiologic studies have identified associations of rotating night-shift work and extreme sleeping patterns with greater risks of type 2 diabetes, cardiovascular disease, stroke, and mortality [1–10]. In turn, diabetes and vascular disease have been linked to cognitive decline and dementia in older adults [11], suggesting that circadian disruption might influence cognitive health in later life. Small studies of emergency-room physicians and airline crews have dem-

onstrated that circadian disruption and related sleep problems can lead to short-term decrements in cognitive function [12–14]; however, it remains unclear whether these exposures are detrimental for the general population or whether they influence longer-term cognition. In older adults, initial studies suggest that aberrant circadian rhythms may be related to poorer cognition [15–18] and bright-light therapy may improve cognitive impairment in Alzheimer's disease [19], further supporting a link between circadian disruption and later-life cognitive impairment.

Moreover, experimental studies have identified links between sleep disturbances and beta-amyloid dynamics in the brain [20–23], and epidemiologic studies have observed associations between various sleep characteristics and cognitive function in older adults [24]. However, complexity exists in studying these associations because it is known that Alzheimer's disease causes circadian and sleep disturbances; thus, a bi-directional association may exist between sleeping patterns and cognitive function in older adults with underlying Alzheimer's disease [22]. Despite this challenge, a growing number of epidemiologic studies have examined sleep duration (an indicator of circadian rhythm) in relation to cognition in older individuals – an association that, to date, is poorly understood.

In this review, we aimed at systematically evaluating observational studies of sleep duration and cognitive function in older adults.

Methods

Using PRISMA guidelines, we conducted a systematic review of manuscripts indexed by Medline, Ovid MEDLINE(R), and PsycINFO through September 2015 [25]. Our search string was: (sleep* and (cogniti* or memory) and (elderly OR older OR geriatric OR aging OR ageing)), where the asterisk indicates that any ending may follow the beginning of the specified term. We used this search string at the beginning of a 4-phase process (identification, screening, eligibility, and inclusion) that determined manuscripts to be included in this review. The bibliographies of included manuscripts were also reviewed for additional studies of interest.

We were interested in identifying observational studies that reported the association between sleep duration and cognitive function, which were published in English, and focused on (or included) adults aged ≥ 65 years. When multiple studies were published based on the same study population, we included the study that used a prospective design, or was published most recently if all studies were cross sectional. Two authors (E.E.D. and E.S.S.) performed the literature search, reviewed search results, and extracted data from identified manuscripts based on prespecified categories of information. Inconsistencies in data extraction were reconciled by discussion between these 2 authors.

Results

Previous Epidemiologic Studies Identified in Our Search

Figure 1 is a flowchart describing the algorithm used to select studies for this review. We initially identified 4,355 records using our search criteria, and 2,423 of these were unique records that remained after removal of duplicates (Identification Phase). These articles were screened based on title and abstract, at which point 2,366 articles were excluded based on the following criteria: 225 articles were not written in English, and 2,141 articles did not evaluate the association of interest (Screening Phase). This left us with 55 full-text articles to evaluate for eligibility, of which 18 studies examined sleep characteristics other than sleep duration in relation to cognitive function [26–43], and 6 studies were based on duplicate study populations [44–49]; there were 31 remaining studies that were eligible for inclusion (Eligibility Phase). One additional study was identified based on a review of the bibliographies from these manuscripts [50]; thus, in total, 32 studies were included in our review [16, 50–80] (Inclusion Phase).

Description of Studies Included in Our Review Overall Study Design

In table 1, we present the key aspects of the overall study design for each of the studies on sleep duration and cognitive function. These studies ranged in size from 26 to 32,142 participants, and were conducted across multiple countries: United States [53, 55–57, 67, 70, 72, 73, 75, 79], United Kingdom [61, 64, 77], Spain [58, 69], Finland [50, 68], France [54, 62], Japan [65, 78], Australia [52], Germany [59], Ireland [16], Netherlands [80], Hong Kong [66], Canada [63], Korea [60], China [76], Singapore [71]. There was also a multi-country study incorporating data from China, Ghana, India, South Africa, Russia, and Mexico [74]; the location of one study was unknown [51]. Twenty-five studies used a cross sectional design [16, 50–62, 65–68, 70, 72, 74, 77–80] and 5 used a prospective design [63, 69, 71, 75, 76], with 2 additional studies including both cross-sectional and prospective analyses [64, 73]. Thus, there were a total of 27 cross-sectional analyses and 7 prospective analyses conducted across all studies in this review. We defined cross-sectional studies as those that collected information on sleep duration and cognitive function at one point in time (generally at the same time). Prospective studies were those that collected sleep information as well as multiple assessments of cognitive func-

Fig. 1. Flowchart of algorithm used to determine studies included in this review.

tion; hence, they could evaluate sleep duration in relation to change in cognitive function over time. Prospective studies had variable follow-up periods, ranging from 1 to 10 years.

Study Population

In table 1, we also describe the study population for each of the studies. Most studies included both women and men [16, 50, 51, 54, 56–69, 71, 72, 74, 76–80], although some studies focused on women only [55, 70, 73] or men only [53, 75]; 1 study did not specify the sex of participants [52]. Studies generally specified age thresholds for participants at the time of first cognitive interview: ≥ 30 years [50], ≥ 45 years [80], ≥ 50 years [74, 76, 77], ≥ 55 years [16], ≥ 59 years [71], ≥ 60 years [54, 58, 60, 65], ≥ 65 years [55, 62–64, 66, 68, 69, 75], ≥ 68 years [70], and ≥ 70 years [59, 73, 79]. Other studies provided the mean age [67] or age ranges [51–53, 56, 57, 61, 72, 78] of their participants, but did not explicitly describe an age threshold as part of the inclusion criteria; regardless, older adults were eligible for all studies. The most common ex-

clusion criteria across studies were low cognition or dementia [16, 50, 53, 56–58, 60, 63–66, 69, 71, 72, 75, 76, 78, 79], depression [57–60, 71–73, 76], other major illness [51, 54, 56, 57, 60, 62, 63, 66, 71–73, 76], and institutionalization [16, 52, 54–56, 58, 63, 65, 66, 72, 73, 75, 78, 79]. Other exclusion criteria varied widely across studies.

Exposure Assessment and Categorization

We describe methods related to exposure assessment and categorization for each of the studies in table 2. Studies generally collected information on sleep duration based on the self report of participants [50, 52, 54, 56–59, 61–64, 66–69, 71, 73, 74, 76–78], with the exception of eleven studies that incorporated objective measurements of sleep duration; these studies used actigraphy [16, 55, 65, 72, 80], polysomnography [51, 53, 60], an in-home sensor device [79], and a combination of self report and actigraphy [70, 75]. Two different definitions of sleep duration were operationalized by these methods, with 20 studies defining sleep duration as night-time sleeping hours only [51, 53, 55–57, 59–64, 66, 67, 70–72, 74, 75, 77,

Table 1. Overall study design and study populations of studies identified in this review

Author, year	Study design	Study name, country, and sample size	Inclusion criteria
Berry and Webb [51], 1985	Cross sectional	No study name or location specified (n = 119)	Women and men aged 50–70. No chronic medication use, irregular sleep/wake schedules, possible psychopathology, active care by physician
Hayward et al. [52], 1992	Cross sectional	Study in Sydney, Australia (n = 124)	Participants were a random sample of residents (no sex information specified) in a retirement complex, aged 70–85. No nursing home residents
Foley et al. [53], 2003	Cross sectional	Honolulu Asia aging study, USA (n = 718)	Men aged 79–97. No dementia, CPAP/oxygen therapy
Ohayon and Vecchierini [54], 2005	Cross sectional	Cohort in France (n = 1,026)	Women and men aged ≥ 60 . No institutionalization, non-French speaking, hearing or speech impairment, illness preventing interview
Blackwell et al. [55], 2006	Cross sectional	Study of osteoporotic fractures, USA (n = 2,932)	Women aged ≥ 65 . No institutionalization, walking assistance, bilateral hip replacement
Schmutte et al. [56], 2007	Cross sectional	Bronx aging study, USA (n = 375)	Women and men aged 75–85. No institutionalization, non-English, Parkinson's disease, liver disease, terminal illness, alcoholism, severe visual/hearing impairment; no cognitive impairment (defined as >8 errors on BIMC) or dementia in first 2 years of study
Nebes et al. [57], 2009	Cross sectional	Study in USA (n = 157)	Women and men aged 65–80. No CNS pathology, substance abuse, psychoactive medication use, major depression within 5 years, GDS score ≥ 15 , or cognitive impairment (defined as repeatable battery for the assessment of cognitive status >2 standard deviations below age-group mean)
Faubel et al. [58], 2009	Cross sectional	Cohort in Spain (n = 3,212)	Women and men ≥ 60 . No institutionalization, depression requiring treatment, dementia
Kronholm et al. [50], 2009	Cross sectional	Finnish health 2000 survey, Finland (n = 5,171)	Women and men aged ≥ 30 . No dementia based on MMSE score or Alzheimer's disease medication use
Loerbroks et al. [59], 2010	Cross sectional	HeiDE study, Germany (n = 689)	Women and men ≥ 70 . No physician-diagnosed depression or mood-enhancing drugs
Kim et al. [60], 2011	Cross sectional	Study in Korea (n = 60)	Women and men aged >60 . 30 with mild cognitive impairment and 30 age- and sex-matched controls. No dementia, alcohol dependence/substance abuse, depressive/major psychiatric disorder; cerebrovascular disease, CNS disease, damage affecting cognitive function; current use of hypnotics/CNS active drugs, present illness including chronic renal failure, chronic obstructive pulmonary disease, cancer, uncontrolled diabetes/hypertension; chronic insomnia, restless leg syndrome; significant hearing/visual/language impairment; or significant abnormalities in complete blood count, liver function test, urine analysis, electrocardiogram, chest X-ray
Ferrie et al. [61], 2011	Cross sectional	Whitehall II study, United Kingdom (n = 5,431)	Women and men aged 50–74

Table 1. (continued)

Author, year	Study design	Study name, country, and sample size	Inclusion criteria
Saint Martin et al. [62], 2012	Cross sectional	PROOF trial/SYNAPSE study, France (n = 272)	Women and men aged ≥65. No CPAP or neurological disease
Cochrane et al. [16], 2012	Cross sectional	Study in Ireland (n = 26)	Women and men aged ≥55. No institutionalization, non-English, vision impairment, MMSE score ≤24
Potvin et al. [63], 2012	Prospective, with mean follow-up of 12.5 months	ESA study, Canada (n = 1,664)	Women and men aged ≥65. No institutionalization, non-French speaking, MMSE score <22, cognitive impairment, dementia, cerebrovascular disease, brain tumor/trauma/infection, multiple sclerosis, Parkinson's disease, epilepsy, schizophrenia, other psychosis
Keage et al. [64], 2012	Cross sectional and prospective, with follow-up ranging from 2 to 10 years	MRC cognitive function and ageing study, United Kingdom (n = 2,012)	Women and men aged ≥65. No MMSE score <22
Miyata et al. [65], 2013	Cross sectional	Study in Japan (n = 78)	Women and men aged ≥60. No institutionalization, impairment in basic/instrumental activities of daily living; no recent reduction in memory/cognitive performance
Auyeung et al. [66], 2013	Cross sectional	Cohort in Hong Kong (n = 2,945)	Women and men aged ≥65. No institutionalization, non-Chinese, walking assistance, bilateral hip replacement, cognitive impairment, medical conditions making survival for study duration unlikely
Ramos et al. [67], 2013	Cross sectional	Northern Manhattan study, USA (n = 927)	Women and men mean aged 75
Virta et al. [68], 2013	Cross sectional	Finnish twin cohort, Finland (n = 2,336)	Women and men aged ≥65. Restricted to same-sex twin pairs
Benito-León et al. [69], 2013	Prospective, with mean follow-up of 3.4 years	NEDICES study, Spain (n = 2,715)	Women and men aged ≥65. No dementia
Lambaise et al. [70], 2014	Cross sectional	Healthy women study, USA (n = 121)	Women aged ≥68
Lo et al. [71], 2014	Prospective, with follow-up of 2 years	Singapore longitudinal aging brain study, Singapore (n = 66)	Women and men aged ≥59. No institutionalization, non-Chinese, myocardial infarction, stroke, peripheral vascular disease, malignant neoplasia, cardiac/lung/liver/kidney failure, thyroid disease, neurological/psychiatric condition, head trauma with loss of consciousness, MMSE score <26, GDS score >5
Wilckens et al. [72], 2014	Cross sectional	Study in Pittsburgh, USA (n = 112)	Women and men in 2 age groups: 21–30 and 55–77. No institutionalization, self-reported depression, psychiatric medication use, drug/alcohol dependency, neurodegenerative disease, MMSE score <23

Table 1. (continued)

Author, year	Study design	Study name, country, and sample size	Inclusion criteria
Devore et al. [73], 2014	Cross sectional and prospective, with mean follow-up of approximately 6 years	Nurses' health study, USA (n = 15,385)	Women aged ≥ 70 . No institutionalization, stroke, antidepressant use, physician-diagnosed depression
Gildner et al. [74], 2014	Cross sectional	Study on global ageing and adult health, multi-country (n = 32,142)	Women and men aged ≥ 50
Blackwell et al. [75], 2014	Prospective, with mean follow-up of 3.4 years	Osteoporotic fractures in men study (MrOS), USA (n = 2,822)	Men aged ≥ 65 . No institutionalization, walking assistance, bilateral hip replacement, CPAP/BiPAP/oral appliances/oxygen therapy, probable dementia
Xu et al. [76], 2014	Prospective, with mean follow-up of 4.1 years	Guangzhou biobank cohort study, China (n = 13,888)	Women and men aged ≥ 50 . No non-ambulatory, dialysis, radiotherapy/chemotherapy, neurological disease, mental illness (depression, confused speech, schizophrenia, dementia, Alzheimer's disease), sleep < 3 or > 15 h daily, myocardial infarction
Miller et al. [77], 2014	Cross sectional	English longitudinal study of ageing (ELSA), United Kingdom (n = 4,129)	Women and men aged ≥ 50 . No age ≥ 90 , non-white race
Otsuka et al. [78], 2014	Cross sectional	Cohort in Japan (n = 691)	Women and men aged 75–102. No institutionalization, MMSE < 25
Seelye et al. [79], 2015	Cross sectional	Oregon center for aging and technology study, USA (n = 63)	Women and men aged ≥ 70 . No institutionalization, living with someone else, or dementia (defined as MMSE score ≤ 24 and clinical dementia rating scale score of > 0), medical illness limiting physical participation in the study or likely to lead to untimely death
Luik et al. [80], 2015	Cross sectional	Rotterdam study, Netherlands (n = 1,723)	Women and men aged ≥ 45

BiPAP = Bi-level positive airway pressure; CNS = central nervous system; CPAP = continuous positive airway pressure; GDS = Geriatric Depression Scale; MMSE = mini-mental state examination.

Table 2. Approaches to exposure, outcome, and covariates in studies identified in this review

Author, year	Exposure assessment	Exposure categories with reference category	Outcome assessment	Outcome definition	Covariate adjustments
Berry and Webb [51], 1985	Night-time sleep duration by polysomnography in unknown year	Continuous	In-person cognitive testing in unknown year, using WAIS, WMS, Ravens progressive matrices, test 7 of army alpha	Continuous scores for verbal intelligence quotient and performance intelligence quotient (from WAIS), memory quotient (from WMS), Ravens progressive matrices, army alpha	None reported
Hayward et al. [52], 1992	Sleep duration (night-time or 24-hour sleep duration not specified) by self report in unknown year	Continuous	In-person cognitive testing in unknown year, using WMS subtests (logical memory, visual reproduction, digit span, paired associate learning), TMT, controlled oral word association, token test, Stroop color-word test, grooved pegboard, and NART	Continuous scores for neuropsychological factors: general ability, memory, motor, and cerebral efficiency (from principal components analysis)	None reported
Foley et al. [53], 2003	Night-time sleep duration by polysomnography in 1999–2000	Continuous	In-person cognitive testing in 1999–2000, using CASI	Low CASI score: <74 points	Not reported
Ohayon and Vecchierini [54], 2005	Night-time and 24-hour sleep duration by self report in 1999–2000	Categories: ≤ 4.5 , > 4.5 – 6 , 8 – < 9.5 , ≥ 9.5 h of sleep per night Reference: > 6 – < 8 h of sleep per night	Telephone cognitive testing in 1999–2000, using CDS	Cognitive impairment based on CDS scores: ≥ 46 points	Age, gender, education, alcohol, coffee, smoking, exercise, health perception, physical disease, hypertension, BMI, depressive mood, anxiety, stress, IADL, social network
Blackwell et al. [55], 2006	Night-time sleep duration by actigraphy in 2002–2004	Continuous	In-person cognitive testing in 2002–2004, using MMSE and TMT part B	Continuous MMSE and TMT part B scores Cognitive impairment based on MMSE scores: < 26 points Cognitive impairment based on TMT part B scores: > 1.5 SDs above the mean	Age, race, education, depression, BMI, health status, stroke, hypertension, IADL, smoking, alcohol, caffeine, antidepressant use, physical activity
Schmutte et al. [56], 2007	Night-time sleep duration by self report in 1980–1983	Categories: ≤ 4 , 5 – 6 , 7 – 8 , ≥ 9 h of sleep per night Reference: none designated	In-person cognitive testing in 1980–1983, using WAIS subtests (vocabulary, information, similarities, digit span, block design, digit symbol substitution, object assembly), months backward from Blessed-Memory-Information-Concentration, selective reminding, Purdue pegboard	Continuous scores on all cognitive tests	Age, education, depression, physical comorbidity, and hypnotic use
Nebes et al. [57], 2009	Night-time sleep duration by self report in unknown year	Continuous	In-person cognitive testing in unknown year, using repeatable battery for the assessment of cognitive status, test of nonverbal intelligence, TMT part B, n-back test, WAIS letter-number sequencing, Stroop interference ratio, Hayling interference ratio, conceptual comparison, perceptual comparison, WMS immediate/delayed recall of logical memory	Continuous scores on all cognitive tests	Depression

Table 2. (continued)

Author, year	Exposure assessment	Exposure categories with reference category	Outcome assessment	Outcome definition	Covariate adjustments
Faubel et al. [58], 2009	24-Hour sleep duration by self report in 2001	Categories: ≤5, 6, 8, 9, 10, ≥11 h of sleep per 24-hour period Reference: 7 h of sleep per 24-hour period	In-person cognitive testing in 2001, using MEC	Continuous MEC scores Cognitive impairment based on MEC scores: ≤22 points	Age, gender, physical activity, tobacco, alcohol, coffee, education, mental health score, physical health score, night time awakenings, anxiolytic medication, social ties, head of household employment, number of medications, BMI, chronic disease, hypertension, antihypertensive medication
Kronholm et al. [50], 2009	24-Hour sleep duration by self report in 2000–2001	Categories: ≤6, 7, 8, ≥9 h of sleep per 24-hour period Reference: none designated	In-person cognitive testing in 2000–2001, using CERAD subtests (verbal fluency and immediate/delayed word recall)	Continuous verbal fluency, learning effect, and recall rate scores	Age, gender, education, depression, alcohol dependency, neuroleptic use, antidepressant use, hypertension, musculoskeletal disease, arthrosis, circulatory system disease, coronary artery disease, diabetes, allergic reaction, vascular disease symptoms, neurological disease, cerebrovascular disease, and chronic respiratory system inflammation
Loerbroeks et al. [59], 2010	Night-time sleep duration by self report in 1992–1995 and 2002–2003	Categories: ≤6, 8, ≥9 h of sleep per night Reference: 7 h of sleep per night	Telephone cognitive testing in 2003 and 2006, using TICS, EBMT (immediate and delayed recall), ANT, delayed recall of TICS 10-word list, and digit span backward	Cognitive impairment based on TICS scores: <31 points Cognitive impairment based on verbal scores (average z-scores on verbal tests): ≤13th percentile Cognitive impairment based on total score (average of z-scores on all tests): ≤13th percentile	Age, gender, education, physical activity, alcohol, BMI, smoking, sleep medication, depressive symptoms, hypertension, myocardial infarction, stroke, diabetes
Kim et al. [60], 2011	Night-time sleep duration by polysomnography in 2005–2007	Continuous	Clinical diagnosis of mild cognitive impairment based on Petersen's criteria (subjective or objective memory impairment without dementia and scoring >1.5 SDs below the normative score on at least one cognitive test in Korean version of CERAD)	Mild cognitive impairment vs. no mild cognitive impairment	Age, gender, education
Ferrie et al. [61], 2011	Night-time sleep duration by self report in 1997–1999 and 2003–2004	Categories: 6, 7, 8, ≥9 h of sleep per night Reference: ≤5 h of sleep per night	In-person cognitive testing in 2003–2004, using MMSE, 20-word recall (memory), Alice Heim 4-1 test (reasoning), Mill Hill test (vocabulary), ANT (semantic fluency), naming words starting with 's' (phonemic fluency)	Continuous scores on all 6 cognitive tests	Age, education, occupation, gender (when both sexes included in the same model)

Table 2. (continued)

Author, year	Exposure assessment	Exposure categories with reference category	Outcome assessment	Outcome definition	Covariate adjustments
Saint Martin et al. [62], 2012	Night-time sleep duration by self report in 2009–2011	Continuous	In-person cognitive testing in 2009–2011, using MMSE, selective reminding, Benton visual retention test, TMT parts A and B, WAIS subtests (code test and similarity test), Stroop test, and alphabetic/category fluency tasks	Continuous	Gender, anxiety, depression, sleep medication, sleep apnea
Cochrane et al. [16], 2012	24-hour sleep duration by actigraphy in unknown year	Continuous	In-person cognitive testing in unknown year, using NART, WMS subtests (logical memory, visual reproduction, and visual paired associated), ANT, Stroop color word test, and MMSE	Continuous	Age, anxiety, depression, general health
Potvin et al. [63], 2012	Night-time sleep duration by self report in 2005–2006	Categories: ≤ 5 , ≥ 9 h of sleep per night Reference: >5 – <9 h of sleep per night	In-person cognitive testing in 2005–2006 and 1 year later, using French-version MMSE	Cognitive impairment based on MMSE scores: <15 th percentile at follow-up (according to age, sex, and education norms) and loss of ≥ 2 points between baseline and follow-up	Age, education, baseline MMSE score, depression, anxiety, psychotropic medication, cardiovascular conditions, chronic diseases
Keage et al. [64], 2012	Night-time sleep duration by self report in 1991–1993	Categories: ≤ 6.5 , ≥ 8.5 h of sleep per night Reference: >6.5 – <8.5 h of sleep per night	In-person cognitive testing in 1991–1993, 2 and 10 years later, using MMSE	Cross sectional analyses. Mild cognitive impairment based on MMSE scores: 22–25 points Prospective analyses. Cognitive impairment based on MMSE scores: ≤ 21 points	Age, gender, BMI, education; baseline cognitive score in prospective analyses
Miyata et al. [65], 2013	24-hour sleep duration by actigraphy in unknown year	Continuous	In-person cognitive testing in unknown year, using continuous performance subtest (identical pairs) and n-back test	Continuous scores on identical pairs, 0-back, and 1-back	Age and measures of sleep quality and sleep apnea
Auyeung et al. [66], 2013	Night-time sleep duration by self report in approximately 2005	Categories: <4 , 4–4.9, 5–5.9, 6–6.9, 7–7.9, 8–8.9, 9–9.9, ≥ 10 h of sleep per night Reference: none designated	In-person cognitive testing in approximately 2005, using MMSE	Continuous MMSE scores	Age, gender, education, smoking, alcohol, tea, coffee, snoring, depression, psychotropic medication, diabetes, hypertension, stroke, COPD, coronary heart disease
Ramos et al. [67], 2013	Night-time sleep duration by self report in 2006	Categories: <6 , ≥ 9 h of sleep per night Reference: 6–8.9 h of sleep per night	In-person cognitive testing in 2006–2007, using English- or Spanish-version MMSE	Continuous MMSE scores Low MMSE scores: <24 points for >8 years of education and <20 points for ≤ 8 years of education	Age, gender, education, race/ethnicity, insurance status, alcohol, hypertension, diabetes, depression, medications, high risk of sleep disordered breathing
Virta et al. [68], 2013	24-hour sleep duration by self report in 1975 and 1981	Categories: <7 , >8 h of sleep per 24-hour period Reference: 7–8 h of sleep per 24-hour period	Telephone cognitive testing in 1999–2001, using TICS and TELE	Continuous TICS + TELE scores	Age, gender, education, apolipoprotein E genotype, follow-up time, life satisfaction, obesity, hypertension, physical inactivity, heavy drinking, binge drinking; also considered smoking, sleep quality, hypnotics

Table 2. (continued)

Author, year	Exposure assessment	Exposure categories with reference category	Outcome assessment	Outcome definition	Covariate adjustments
Benito-León et al. [69], 2013	24-Hour sleep duration by self report in 1994–1995	Categories: ≤5, ≥9 h of sleep per 24-hour period Reference: 6–8 h of sleep per 24-hour period	In-person cognitive testing in 1994–1995 and 1997–1998, using MEC	Cognitive decline based on MMSE scores: decline of ≥4 points	Age, gender, geographical area, education, diabetes, COPD, depressive symptoms or antidepressant use, medications with central nervous system effects
Lambiase et al. [70], 2014	Night-time sleep duration by actigraphy and self report in 2010–2011	Continuous	In-person cognitive testing in 2010–2011, using 3MS, digit symbol substitution, TMT parts A and B, letter fluency, animal fluency	Continuous	Age, education, BMI, hypertension, depressive symptoms; race and sleep medications also considered
Lo et al. [71], 2014	Night-time sleep duration by self report in 2009–2011	Continuous	In-person cognitive testing in 2009–2011 and 2011–2013, using symbol digit modalities, WMS subtests (symbol search task, digit span, spatial span, verbal paired associates, visual reproduction), TMT part A, categorical verbal fluency, design fluency in Delis-Kaplan executive function system, TMT part B, Rey auditory verbal learning, visual paired associates	Continuous composite scores for global performance (average of z-scores on all tests) and 5 cognitive domains (processing speed, executive function, attention, verbal memory, and visuospatial memory)	Age, gender, education, BMI
Wilckens et al. [72], 2014	Night-time sleep duration by actigraphy in unknown year	Continuous	In-person cognitive testing in unknown year, using Sternberg working-memory, n-back, Stroop task, flanker task, NART, categorical/lexical fluency, TMT part A, WAIS digit symbol substitution, CERAD word memory test	Continuous composite scores for working memory, inhibition, verbal fluency, processing speed, and recall	Age, gender, education
Devore et al. [73], 2014	24-Hour sleep duration by self report in 1986 and 2000	Categories: ≤5, 6, 8, ≥9 h of sleep per 24-hour period Reference: 7 h of sleep per 24-hour period	Telephone cognitive testing in 1995–2001 and 3 subsequent times at 2-year intervals, using TICS, EBMT (immediate and delayed recall), ANT, delayed recall of TICS 10-word list, and digit span backward	Continuous TICS scores, verbal scores (average of z-scores on verbal tests), and global scores (average of z-scores on all tests) averaged across cognitive assessments over time Slopes of decline for TICS, verbal, and global scores over time	Age, education, shift work, smoking, alcohol, physical activity, BMI, hypertension, mental health score, living alone, tranquilizer use
Gildner et al. [74], 2014	Night-time sleep duration by self report in 2007–2010	Categories: ≤6, >9 h of sleep per night Reference: >6–9 h of sleep per night	In-person cognitive testing in 2007–2010, using immediate and delayed verbal recall test, digit span forward and backward, and ANT	Continuous composite scores (average of z-scores on all tests)	Education

Table 2. (continued)

Author, year	Exposure assessment	Exposure categories with reference category	Outcome assessment	Outcome definition	Covariate adjustments
Blackwell et al. [75], 2014	Night-time sleep duration by self report and actigraphy in 2003–2005	Categories: ≤ 5 , >5 –7, >8 h of sleep per night Reference: >7 –8 h of sleep per night	In-person cognitive testing in 2003–2005, 2005–2007, and 2007–2009, using 3MS and TMT part B	Change in continuous 3MS and TMT part B scores Clinically significant cognitive decline based on 3MS scores: decline by ≥ 5 points Clinically significant cognitive decline based on TMT part B scores: decline in the worst decile	Age, clinic site, race, BMI, education, depressive symptoms, co-morbidities, IADL, benzodiazepine use, antidepressant use, self-reported health status, physical activity, alcohol, smoking
Xu et al. [76], 2014	24-hour sleep duration by self report in 2003–2008	Categories: 3–4, 5, 6, 8, 9, ≥ 10 h of sleep per 24-hour period Reference: 7 h of sleep per 24-hour period	In-person cognitive testing in 2003–2008 and 2008–2012, using CERAD delayed recall (with Chinese words) and MMSE	Change in continuous CERAD delayed recall and MMSE scores Memory impairment based on CERAD delayed recall scores: <4 points Memory impairment based on MMSE scores: <25 points	Age, gender, occupation, education, smoking, drinking, physical activity, objective and self-rated health status, baseline cognitive score, waist-to-hip ratio, daytime napping, morning tiredness, insomnia
Miller et al. [77], 2014	Night-time sleep duration by self report in 2008	Categories: <6 , 6–8, >8 h of sleep per night Reference: none designated	In-person cognitive testing in 2008, using memory, orientation, immediate and delayed recall, verbal fluency, processing speed, visual search accuracy, and numeracy tasks	Continuous amnesic and non-amnesic test scores (average of t-scores on these respective tests)	Age, gender, education, employment, depression, physical activity, smoking, general health
Otsuka et al. [78], 2014	Sleep duration by self report in unknown year; night-time or 24-hour duration unknown	Continuous	Cognitive testing with unknown method and year, using MMSE	Categories of MMSE scores: 25–26, 27–28, and 29–30 points	None reported
Seelye et al. [79], 2015	Night-time sleep duration by an in-home sensor system in 2011–2012	Continuous	In-person cognitive testing in 2011–2012, using WMS subtests (letter-number sequencing, logical memory, and visual reproduction), WAIS subtests (digit span backward, digit span forward, digit symbol, block design, picture completion), TMT parts A and B, CERAD word-list recall, letter fluency, Stroop color word conflict	Continuous composite scores for global cognition (average of z-scores on all tests) and 5 cognitive domains (working memory, attention/processing speed, memory, executive function, visual perception/construction)	None reported
Luik et al. [80], 2015	Night-time sleep duration by actigraphy in 2004–2007	Continuous	In-person cognitive testing in 2004–2007, using immediate/delayed recall of word learning, word fluency, letter digit substitution, and Stroop color word test	Continuous global composite scores (average of z-scores on all tests) and individual cognitive scores	Age, gender, employment status, education, depressive symptoms, BMI, activities of daily living, stroke, myocardial infarction, diabetes, apnea

3MS = Modified MMSE; ANT = animal naming test; BMI = body mass index; CASI = cognitive abilities screening instrument; CDS = Cognitive Difficulties Scale; CERAD = consortium to establish a registry for Alzheimer's disease; COPD = chronic obstructive pulmonary disease; EBMT = east boston memory test; IADL = independent activities of daily living; MEC = Spanish version of MMSE; MMSE = mini-mental state examination; NART = national adult reading test; RBANS = repeatable battery for the assessment of neuropsychological status; SD = standard deviations; TELE = telephone screening to identify potential dementia cases; TICS = telephone interview of cognitive status; TMT = trail making test; WAIS = Weschler adult intelligence; WMS = Weschler Memory Scale.

79, 80], and 9 studies including all sleeping hours within a 24-hour period [16, 50, 58, 65, 68, 69, 73, 76]; 1 study incorporated both of these definitions into analyses [54], and 2 studies did not provide information on the specific definition used [52, 78]. Two of these studies reported results of midlife sleep duration and cognitive function in older individuals [68, 73]. In addition, 4 studies assessed sleep duration at 2 different time points, enabling the evaluation of changes in sleep duration over time [59, 61, 68, 73]. Finally, sleep duration was examined categorically in some studies [50, 54, 56, 58, 59, 61, 63, 64, 66–69, 73–77], but continuously in other studies [16, 51–53, 55, 57, 60, 62, 65, 70–72, 78–80]; exposure categories and corresponding reference groups varied widely across studies.

Outcome Assessments and Definitions

We describe methods related to outcome assessment and definition for each of the studies in table 2. Most studies obtained information on cognitive function using in-person neuropsychological assessments [16, 50–53, 55–58, 61–67, 69–72, 74–77, 79, 80], although 5 studies collected this information over the telephone [54, 59, 68, 73]; 1 study did not report whether in-person or telephone assessment was used [78] and another study made a clinical diagnosis of mild cognitive impairment [60]. Studies used a variety of different cognitive tests, although the most commonly used test was the mini mental state exam (MMSE) [16, 55, 58, 61–64, 66, 67, 69, 76, 78], the modified MMSE [70, 75], or the telephone interview of cognitive status (TICS; i.e. a telephone version of the MMSE) [59, 68, 73]; 22 studies used more than 1 cognitive test [16, 50–52, 55–57, 59, 61, 62, 65, 68, 70–77, 79, 80]. There was little consistency across studies in specifying how cognitive test scores were used to define the outcome of interest; in part, this stemmed from differences in tests or test batteries utilized, although cognitive outcomes were defined differently even among those studies that used the same test (e.g. the cutoff for ‘cognitive impairment’ based on the MMSE). As noted previously, 7 studies assessed cognitive function at more than 1 time point, which enabled the analysis of changes in cognition over time [63, 64, 69, 71, 73, 75, 76].

Covariates

In table 2, we describe covariate adjustments used in statistical analyses for each of the studies. Studies generally accounted for age, gender (unless the population was restricted to one gender only), and education in their statistical models, except 5 studies that did not re-

port any covariate adjustments [51–53, 78, 79]. Many studies also accounted for important health and lifestyle variables that might be confounding factors of the association between sleep duration and cognition in older adults, including alcohol intake [50, 54, 55, 58, 59, 66–68, 73, 75, 76], physical activity [54, 55, 58, 59, 68, 73, 75–77], body mass index or obesity [54, 55, 58, 59, 64, 68, 70, 71, 73, 75, 76, 80], depression or antidepressant medication use [16, 50, 54–57, 59, 62, 63, 66, 67, 69, 70, 75, 77, 80], overall health status [16, 54, 55, 58, 75–77], and other co-morbidities [50, 54–56, 58, 59, 62, 63, 65–69, 73, 75, 80]. Only a few studies incorporated sleep-related covariates in their analyses, including measures of sleep quality [58, 68, 76], sleep-related medications [56, 58, 59, 62, 68, 70, 73, 75], and indications of sleep-disordered breathing [62, 65, 67, 80].

Results of Studies on Sleep Duration and Cognitive Function

We describe the findings for each of the studies included in our review, separately for short and long sleep durations in relation to cognitive function, in table 3. When short sleep durations were examined, 5 of 27 cross-sectional studies [54, 61, 65, 73, 74] and 4 of 7 prospective analyses [63, 64, 71, 76] reported an association with worse cognitive function in older adults. For long sleep durations, 9 out of 27 cross-sectional studies [16, 56, 58, 67, 68, 70, 73, 74, 78] and 3 of 7 prospective studies [63, 69, 76] identified relations with worse cognition in elderly participants. All studies that reported significant associations between sleep durations and cognitive function utilized subjective assessment of sleep duration; there were no studies that found extreme objective sleep durations to be related to worse cognitive function. For example, self-reported sleep durations of 3–4 h and ≥ 10 h per 24-hour period were significantly related to greater decline in cognitive scores in a large prospective study among 13,888 Chinese older adults (mean differences in MMSE change scores over 4 years = -0.28 points (95% CI -0.47 to -0.10) and -0.48 points (95% CI -0.67 to -0.28) for these sleep durations vs. 7 h of sleep in 24 h, respectively) [76]. In contrast, a prospective study utilizing actigraphy-derived sleep durations reported that modified MMSE score decline over 3 years was similar between older participants sleeping ≤ 5 or >8 h nightly compared to those sleeping >7 – 8 night-time hours (group mean scores = -0.44 vs. -0.34 points for ≤ 5 vs. >7 – 8 h, and -0.48 vs. -0.34 points for >8 vs. >7 – 8 h; $p \geq 0.05$) [75]. However, specific estimates were difficult to compare due to varying methods across studies, includ-

Table 3. Results of epidemiologic studies on sleep duration and cognition identified in this review*

Author, year	Short sleep duration	Long sleep duration
Berry and Webb [51], 1985	Correlations between sleep duration and cognitive scores were not significant (for women: -0.081 for verbal intelligence quotient, 0.090 for performance intelligence quotient, -0.129 for memory quotient, -0.111 for Ravens progressive matrices, -0.110 for army alpha; for men: -0.209 for verbal intelligence quotient, -0.135 for performance intelligence quotient, -0.034 for memory quotient, 0.227 for Ravens progressive matrices, and 0.075 for army alpha)	See results under short sleep duration
Hayward et al. [52], 1992	Correlations between sleep duration and neuropsychological factor scores were not significant: -0.01 for general ability, -0.04 for memory, -0.02 for motor, and 0.13 for cerebral efficiency	See results under short sleep duration
Foley et al. [53], 2003	Mean night-time sleep duration: 5.9 h both for those with low CASI scores vs. all other scores	See results under short sleep duration
Ohayon and Vecchierini [54], 2005	OR for cognitive impairment: 1.5 (1.0-2.2) and 2.2 (1.2-4.2) for those with night-time sleep durations >4.5-6 and ≤4.5 vs. >6-8 h, respectively No association for 24-hour sleep durations (point estimates not reported)	OR for cognitive impairment: 1.1 (0.8-1.6) and 1.2 (0.5-2.7) for those with night-time sleep durations 8-9.5 and ≥9.5 vs. >6-8 h, respectively No association for 24-hour sleep durations (point estimates not reported)
Blackwell et al. [55], 2006	Mean percent difference in MMSE and TMT part B scores: 0.17% better scores (0.05-0.33) and -0.34% less time to completion (-0.38 to 0.53) for each 30 min increase in night-time sleep duration, respectively No association for cognitive impairment (point estimates not reported)	See results under short sleep duration
Schmutte et al. [56], 2007	Cognitive scores were not significantly associated with short sleep durations in multivariable-adjusted models	Night-time sleep durations of ≥9 h were associated with lower selective reminding scores (p < 0.03); no other cognitive scores were related to sleep duration in multivariable-adjusted models
Nebes et al. [57], 2009	Night-time sleep duration was not significantly correlated with cognitive scores (estimates not reported)	See results under short sleep duration
Faubel et al. [58], 2009	Mean difference in MEC scores: 0.09 points (-0.48 to 0.67) for those with 24-hour sleep durations ≤5 vs. 7 h; p trend = 0.7 across short sleep durations OR for cognitive impairment: 1.0 (0.7-1.6) for those with 24-hour sleep durations ≤5 vs. 7 h; p trend = 1.0 across short sleep durations	Mean difference in MEC scores: -1.48 points (-2.12 to -0.85) for those with 24-hour sleep durations ≥11 vs. 7 h; p trend < 0.001 across long sleep durations OR for cognitive impairment: 1.2 (0.8-1.9) for those with 24-hour sleep durations ≥11 vs. 7 h; p trend = 0.008 across long sleep durations
Kronholm et al. [50], 2009	Sleep duration was significantly associated with verbal fluency, learning effect, and recall rate scores with multivariable adjustment (p-values = 0.001, <0.0001, and 0.011, respectively); however, these associations were not statistically significant after restriction of the sample to those without medical illness and with good self-reported health	See results under short sleep duration
Loerbroks et al. [59], 2010	OR for cognitive impairment based on TICS, verbal, and total scores: 0.83 (0.45-1.54), 0.77 (0.39-1.49), and 0.97 (0.52-1.81) for those with night-time sleep durations ≤6 vs. 7 h, respectively	OR for cognitive impairment based on TICS, verbal, and total scores: 1.37 (0.68-2.74), 1.71 (0.98-2.97), and 1.55 (0.80-2.98) for those with night-time sleep durations ≥9 vs. 7 h, respectively

Table 3. (continued)

Author, year	Short sleep duration	Long sleep duration
Kim et al. [60], 2011	No significant difference between sleep duration comparing those with mild cognitive impairment vs. no mild cognitive impairment (group means = 358.15 vs. 366.50, $p = 0.523$)	See results under short sleep duration
Ferrie et al. [61], 2011	For women: mean memory, reasoning, vocabulary, phonemic fluency, and MMSE scores: 49.5 vs. 50.1 points, 48.8 vs. 50.8 points , 48.3 vs. 50.8 points , 49.2 vs. 50.5 points, 49.5 vs. 50.6 points, and 47.8 vs. 50.5 points, respectively, for those with sleep durations ≤ 5 vs. 7 h For men: mean memory, reasoning, vocabulary, phonemic fluency, and MMSE scores: 49.9 vs. 50.4 points, 48.8 vs. 50.3 points , 49.6 vs. 50.3 points, 49.5 vs. 50.1 points, 49.1 vs. 50.4 points , and 49.1 vs. 50.4 points , respectively, for those with sleep durations ≤ 5 vs. 7 h	For women: mean memory, reasoning, vocabulary, phonemic fluency, semantic fluency, and MMSE scores: 49.0 vs. 50.1 points, 48.4 vs. 50.8 points, 48.0 vs. 50.8 points, 47.0 vs. 50.5 points, 49.3 vs. 50.6 points, and 46.1 vs. 50.5 points, respectively, for those with sleep durations ≥ 9 vs. 7 h (pairwise significance testing not reported for these comparisons) For men: mean memory, reasoning, vocabulary, phonemic fluency, semantic fluency, and MMSE scores: 48.6 vs. 50.4 points, 49.2 vs. 50.3 points, 48.8 vs. 50.3 points, 48.5 vs. 50.1 points, 47.8 vs. 50.3 points, and 48.2 vs. 50.4 points, respectively, for those with sleep durations ≥ 9 vs. 7 h (pairwise significance testing not reported for these comparisons)
Saint Martin et al. [62], 2012	Sleep duration was not significantly correlated with cognitive test scores ($p \geq 0.05$)	See results under short sleep duration
Cochrane et al. [16], 2012	See results under long sleep duration	Longer 24-hour sleep duration was associated with worse logical memory scores ($r = -0.539$, $p < 0.05$)
Potvin et al. [63], 2012	For women: OR for cognitive impairment: 1.31 (0.65–2.65) for those with night-time sleep durations ≤ 5 vs. > 5 – < 9 h For men: OR for cognitive impairment: 2.91 (1.24–6.82) for those with night-time sleep durations ≤ 5 vs. > 5 – < 9 h	For women: OR for cognitive impairment: 2.10 (1.10–4.00) for those with night-time sleep durations ≥ 9 vs. > 5 – < 9 h For men: OR for cognitive impairment: 0.26 (0.03–2.03) for those with night-time sleep durations ≥ 9 vs. > 5 – < 9 h
Keage et al. [64], 2012	Cross-sectional analyses. OR for mild cognitive impairment: 1.10 (0.78–1.56) for those with night-time sleep durations ≤ 6.5 vs. > 6.5 – < 8.5 h Prospective analyses. RR for cognitive impairment: 2.02 (1.17–3.48) for those with night-time sleep durations ≤ 6.5 vs. > 6.5 – < 8.5 h	Cross sectional analyses: OR for mild cognitive impairment: 1.30 (0.93–1.81) for those with night-time sleep durations ≥ 8.5 vs. > 6.5 – < 8.5 h Prospective analyses: RR for cognitive impairment: 1.27 (0.64–2.48) for those with night-time sleep durations ≥ 8.5 vs. > 6.5 – < 8.5 h
Miyata et al. [65], 2013	Shorter 24-hour sleep duration was associated with less accuracy on 0-back test after multivariable adjustment ($r = 0.267$, $p = 0.033$)	See results under short sleep duration
Auyeung et al. [66], 2013	Mean MMSE scores: 25.3 vs. 25.8 points for those with night-time sleep durations < 4 vs. 7–7.9 h (CIs are overlapping in the figure presented); p trend = 0.5 across short sleep durations	Mean MMSE scores: 24.9 vs. 25.8 points for those with night-time sleep durations ≥ 10 vs. 7–7.9 h (CIs are overlapping in the figure presented); p trend = 0.006 across long sleep durations

Table 3. (continued)

Author, year	Short sleep duration	Long sleep duration
Ramos et al. [67], 2013	Mean difference in MMSE scores: 0.01 points for those with night-time sleep durations <6 vs. 6–8.9 h ($p = 0.39$) OR for low MMSE score: 0.8 (0.4–1.6) for those with night-time sleep durations <6 vs. 6 to 8.9 hours	Mean difference in MMSE scores: –0.06 points for those with night-time sleep durations ≥9 vs. 6–8.9 h ($p = 0.012$) OR for low MMSE score: 2.4 (1.1–5.0) for those with night-time sleep durations ≥9 vs. 6–8.9 h
Virta et al. [68], 2013	Mean difference in TICS + TELE scores: –0.79 points for those with 24-hour sleep durations <7 vs. 7–8 h ($p = 0.019$) This mean difference was attenuated to –0.52 points after adjusting for sleep quality and hypnotics ($p = 0.138$)	Mean difference in TICS + TELE scores: –1.61 points for those with 24-hour sleep durations >8 vs. 7–8 h ($p < 0.001$) This mean difference was attenuated to –1.60 points after adjusting for sleep quality and hypnotics ($p < 0.001$)
Benito-León et al. [69], 2013	OR for cognitive decline: 1.1 (0.8–1.5) for those with 24-hour sleep durations ≤5 vs. 6–8 h	OR for cognitive decline: 1.3 (1.1–1.6) for those with 24-hour sleep durations ≥9 vs. 6–8 h
Lambiase et al. [70], 2014	See results under long sleep duration	Shorter self-reported night-time sleep duration was associated with decreased time to complete TMT part B after multivariable adjustment (β = 0.001 , $p < 0.04$); no association between actigraphy-measured sleep duration and cognitive scores See results under short sleep duration
Lo et al. [71], 2014	Each 1-hour decrease in night-time sleep duration was associated with annual decline in global cognitive performance over 2 years, after multivariable adjustment (β = 0.670 , $p < 0.05$); no associations for any of the individual cognitive domains	See results under short sleep duration
Wilckens et al. [72], 2014	Shorter and longer night-time sleep durations were associated with worse working memory and verbal fluency in younger, but not older, adults after multivariable adjustment	See results under short sleep duration
Devore et al. [73], 2014	For midlife sleep duration: mean TICS, verbal, and global scores: 33.3–33.7 vs. 33.7 points (33.5–33.9), 0.04 standard units (–0.03 to 0.10) vs. 0.03 standard units (–0.01 to 0.07), and –0.06 standard units (–0.12 to 0.00) vs. –0.02 standard units (–0.06 to 0.02) for those with 24-hour sleep durations ≤5 vs. 7 h, respectively; p value for quadratic terms for TICS, verbal, and global scores: <0.001 , 0.2, and 0.002 across all sleep durations For later life sleep duration: mean TICS, verbal, and global scores: 33.5 points (33.3–33.7) vs. 33.7 points (33.5–33.9), 0.00 standard units (–0.05 to 0.05) vs. 0.04 standard units (–0.02, 0.08), and –0.07 standard units (–0.11 to –0.02) vs. –0.01 standard units (–0.04 to 0.02) for those with 24-hour sleep durations ≤5 vs. 7 h, respectively; p value for quadratic terms for TICS, verbal, and global scores: <0.001 for all outcomes across all sleep durations For midlife and later life sleep duration: no association for slopes of decline for TICS, verbal, or global scores	For midlife sleep duration: mean TICS, verbal, and global scores: 33.5 points (33.3–33.7) vs. 33.7 points (33.5–33.9), –0.02 standard units (–0.09 to 0.04) vs. 0.03 standard units (–0.01 to 0.07), and –0.09 standard units (–0.15 to –0.04) vs. –0.02 standard units (–0.06 to 0.02) for those with 24-hour sleep durations ≥9 vs. 7 h, respectively; p value for quadratic terms under short sleep duration For later life sleep duration: mean TICS, verbal, and global scores: 33.4 points (33.2–33.6) vs. 33.7 points (33.5–33.9), –0.05 standard units (–0.10 to 0.00) vs. 0.04 standard units (–0.02 to 0.08), and –0.11 standard units (–0.15 to –0.06) vs. –0.01 standard units (–0.04 to 0.02) for those with 24-hour sleep durations ≥9 vs. 7 h, respectively; p value for quadratic terms under short sleep duration For midlife and later life sleep duration: no association for slopes of decline for TICS, verbal, or global scores
Gildner et al. [74], 2014	Mean difference in composite scores: –0.367 for those with night-time sleep durations ≤6 vs. >6–9 h ($p < 0.001$)	Mean difference in composite scores: –0.657 for those with night-time sleep durations >9 vs. >6–9 h ($p < 0.001$)

Table 3. (continued)

Author, year	Short sleep duration	Long sleep duration
Blackwell et al. [75], 2014	For subjective sleep duration: mean annual decline in 3MS and TMT part B scores: -0.22 vs. -0.40 points and 2.99 vs. 2.34 s to completion for those with night-time sleep durations ≤ 5 vs. $>7-8$ h, respectively OR for clinically significant cognitive decline based on 3MS and TMT part B scores: 0.99 ($0.68-1.43$) and 1.41 ($0.89-2.22$) for those with night-time sleep durations ≤ 5 vs. $>7-8$ h, respectively For objective sleep duration: mean annual decline in 3MS and TMT part B scores: -0.44 vs. -0.34 points and 2.69 vs. 2.63 s to completion for those with night-time sleep durations ≤ 5 vs. $>7-8$ h, respectively OR for clinically significant cognitive decline based on 3MS and TMT part B scores: 1.24 ($0.85-1.79$) and 1.34 ($0.82-2.19$) for those with night-time sleep durations ≤ 5 vs. $>7-8$ h, respectively	For subjective sleep duration: mean annual decline in 3MS and TMT part B scores: -0.39 vs. -0.40 points and 3.61 vs. 2.34 s to completion for those with night-time sleep durations >8 vs. $>7-8$ h, respectively OR for clinically significant cognitive decline based on 3MS and TMT part B scores: 0.75 ($0.43-1.29$) and 1.01 ($0.52-1.93$) for those with night-time sleep durations >8 vs. $>7-8$ h, respectively For objective sleep duration: mean annual decline in 3MS and TMT part B scores: -0.48 vs. -0.34 points and 2.20 vs. 2.63 s to completion for those with night-time sleep durations >8 vs. $>7-8$ h, respectively OR for clinically significant cognitive decline based on 3MS and TMT part B scores: 1.10 ($0.70-1.72$) and 1.00 ($0.55-1.81$) for those with night-time sleep durations >8 vs. $>7-8$ h, respectively
Xu et al. [76], 2014	Mean difference in CERAD delayed recall and MMSE change scores: -0.16 (-0.27 to -0.05) and -0.28 (-0.47 to -0.10) for those with 24-hour sleep durations 3–4 vs. 7 hours, respectively; p-trends for CERAD delayed recall and MMSE change scores: <0.001 for both outcomes across short sleep durations RR for memory impairment based on CERAD delayed recall scores: 1.53 ($1.21-1.93$) for those with 24-hour sleep durations 3–5 vs. 7 h RR for memory impairment based on MMSE scores: 1.32 ($0.84-2.08$) for those with 24-hour sleep durations 3–6 vs. 7 h	Mean difference in CERAD delayed recall and MMSE change scores: -0.31 (-0.43 to -0.20) and -0.48 (-0.67 to -0.28) for those with 24-hour sleep durations ≥ 10 vs. 7 h, respectively; p trends for CERAD delayed recall and MMSE change scores: <0.001 for both outcomes across long sleep durations RR for memory impairment based on CERAD delayed recall scores: 1.22 ($0.92-1.61$) for those with 24-hour sleep durations ≥ 9 vs. 7 h RR for memory impairment based on MMSE scores: 1.58 ($0.85-2.92$) for those with 24-hour sleep durations ≥ 9 vs. 7 h
Miller et al. [77], 2014	Mean t-scores for amnesic and non-amnesic tests: 49.7 vs. 49.7 and 49.8 vs. 49.7 standard units for those with night-time sleep durations <6 vs. $6-8$ h (pairwise significance testing not reported for these comparisons)	Mean t-scores for amnesic and non-amnesic tests: 47.7 vs. 49.7 and 48.4 vs. 49.7 standard units for those with night-time sleep durations >8 vs. $6-8$ h (pairwise significance testing not reported for these comparisons)
Otsuka et al. [78], 2014	Mean sleep durations across groups with MMSE scores 25–26, 27–28, and 29–30 points: 8.22 , 7.97 , and 7.86 h, respectively ($p = 0.008$)	See results under short sleep duration
Seelye et al. [79], 2015	No statistically significant correlations between night-time sleep duration and cognitive scores ($r = -0.02$, 0.02 , 0.07 , -0.05 , -0.09 , and -0.08 for global, executive function, memory, visuospatial, attention/processing speed, and working memory, respectively)	See results under short sleep duration
Luik et al. [80], 2015	24-hour sleep duration was not significantly associated with global cognition ($\beta = 0.01$, $p = 0.75$), immediate word recall ($\beta = -0.11$, $p = 0.47$), delayed word recall ($\beta = 0.00$, $p = 0.96$), word fluency ($\beta = -0.07$, $p = 0.62$), letter digit substitution ($\beta = 0.16$, $p = 0.28$), and Stroop color word test ($\beta = 0.00$, $p = 0.99$)	See results under short sleep duration

* Statistically significant results are indicated in bold type.

3MS = Modified MMSE; CASI = cognitive abilities screening instrument; CERAD = consortium to establish a registry for Alzheimer's disease; MEC = Spanish version of MMSE; MMSE = mini-mental state examination; OR = odds ratio; RR = relative risk; TELE = telephone screening to identify potential dementia cases; TICS = telephone interview of cognitive status; TMT = trail making test.

ing differences in study population, exposure assessment and categorization (including reference categories), outcome assessment and definition, and covariate adjustments.

Results of Studies on Change in Sleep Duration and Cognitive Function

We describe the results of 4 studies included in our review that examined change in sleep duration over time with cognitive function in table 4. Three studies reported that decreased sleep duration over time was associated with lower cognitive function [61, 68, 73], and 4 studies found that increased sleep duration was related to worse cognition [59, 61, 68, 73]. One of these studies included prospective data on cognitive function, enabling analyses of changes in sleep duration with cognitive decline; however, there was no indication of association in these results [73]. The length of time between the first and second assessment of sleep duration in these studies ranged from 6 to 14 years.

Discussion

Based on our review, the epidemiologic literature on sleep duration and cognitive function in older adults is growing rapidly. We identified 32 existing studies of this association, of which 20 studies have been published since 2012. On average, 31% of these studies indicated associations of short sleep duration, long sleep duration, or short and long sleep durations with worse cognitive function in older individuals, with a slightly greater percentage of analyses yielding an association for long sleep durations (35%) compared to short sleep durations (26%). There was more consistency across 4 studies that examined changes in sleep duration over time, with each study suggesting that greater deviations from earlier life sleep duration were associated with cognition decrements in later life. There was large heterogeneity across all studies comparing their approaches to important aspects of study design, including overall study design, study population, exposure and outcome assessment, and statistical analysis (as described in the results section); thus, we did not think it was appropriate to conduct a meta-analysis of these results.

Most studies involved cross-sectional analyses of exposure and outcome data collected at the same time point, although two studies reported on midlife sleep duration assessed 1–2 decades prior to cognitive function testing [68, 73]. There were a limited number of

prospective studies, with repeated cognitive assessments conducted over varying follow-up periods; however, these studies more often indicated an association between extreme sleep duration and poor cognitive function. Because prospective study designs are inherently stronger than cross-sectional ones (i.e. they provide more information about the direction of association, with less concern for bi-directional effects), this difference is somewhat intriguing. In the meantime, this body of literature should be interpreted cautiously due to its reliance on mainly cross-sectional studies. More prospective studies are clearly needed to evaluate sleep duration in relation to cognitive trajectories over time among older adults.

Studies generally assessed subjective sleep duration using self-reported information from study participants, with few studies utilizing more extensive actigraphy or polysomnography to measure objective sleep duration. Of studies that identified an association between extreme sleep durations and worse cognitive function, each ascertained subjective sleep duration via participant self report. This is interesting, considering the fact that previous studies have reported a discrepancy between subjective vs. objective assessments of sleep duration; indeed, there is some indication that older adults with perceived or actual problems with sleep quality may report more extreme sleep durations [44, 81]. A minority of studies in this review considered sleep-related variables other than sleep duration (i.e. sleep quality, sleep medication use, and sleep-disordered breathing) as part of their statistical analyses, but one study did find that results were attenuated with adjustment for self-reported sleep quality [68]. This is consistent with two other studies included in our review that indicated objective measures of sleep disturbances, but not sleep duration, were related to worse cognitive outcomes in older adults [55, 75]; additional literature also supports a link between poor sleep quality and lower cognition in later life [24]. Clearly, more research is necessary to understand the interplay among subjective and objective sleep characteristics, and cognitive function, in older adults.

The effects of other methodologic differences across studies are more difficult to predict. First, exposure categories and corresponding reference groups varied widely across studies, leading us to characterize observed associations broadly by ‘short’ or ‘long’ sleep durations. However, we were limited in our ability to draw more detailed conclusions about specific sleep durations. Second, studies collected sleep duration information based on night time only or a 24-hour period. The inclusion of

Table 4. Results of epidemiologic studies on change in sleep duration and cognition identified in this review*

Author, year	Decreased sleep duration	Increased sleep duration
Loerbroks et al. [59], 2010	OR for cognitive impairment based on TICS and verbal scores: 0.90 (0.40–2.03) and 1.07 (0.50–2.27) for those with a decrease vs. no change in sleep duration Models for total score did not converge	OR for cognitive impairment based on TICS and verbal scores: 2.13 (1.01–4.48) and 1.98 (1.04–3.78) for those with an increase vs. no change in sleep duration Models for total score did not converge
Ferrie et al. [61], 2011	Mean differences in memory, reasoning, vocabulary, phonemic fluency, semantic fluency, and MMSE scores: –0.12 (–0.80 to 0.57), –1.08 (–1.69 to –0.47) , –0.72 (–1.34 to –0.10) , –0.33 (–0.99 to 0.33), –0.62 (–1.27 to 0.02), and –1.19 (–1.90 to –0.49) points for those with sleep durations that decreased from 6, 7, or 8 h vs. no change in sleep duration	Mean differences in memory, reasoning, vocabulary, phonemic fluency, semantic fluency, and MMSE scores: 0.23 (–0.61 to 1.06), –0.13 (–0.87 to 0.61), 0.09 (–0.67 to 0.85), –0.34 (–1.15 to 0.47), –0.04 (–0.82 to 0.75), and –0.26 (–1.12 to 0.60) points for those with sleep durations that increased from 5 or 6 hours vs. no change in sleep duration Mean differences in memory, reasoning, vocabulary, phonemic fluency, semantic fluency, and MMSE scores: –0.98 (–1.96 to –0.01) , –1.11 (–1.98 to –0.25) , –1.39 (–2.28 to –0.50) , –1.19 (–2.14 to –0.25) , –1.47 (–2.39 to –0.55) , and –1.73 (–2.74 to –0.72) points for those with sleep durations that increased from 7 or 8 h vs. no change in sleep duration
Virta et al. [68], 2013	Significantly lower TICS + TELE scores observed in those with 24-hour sleep durations <7 h in 1975 or 1981 and those with 24-hour sleep durations <7 h in 1975 and 1981 vs. 7–8 h in both years (point estimate not reported)	Significantly lower TICS + TELE scores observed in those with 24-hour sleep durations >8 h in 1975 or 1981 and those with 24-hour sleep durations >8 h in 1975 and 1981 vs. 7–8 h in both years (point estimates not reported)
Devore et al. [73], 2014	Mean TICS, verbal, and global scores: 33.4 points (33.2–33.6) vs. 33.7 points (33.5–33.9), 0.00 standard units (–0.06 to 0.06) vs. 0.05 standard units (–0.02 to 0.09), and –0.08 standard units (–0.13 to –0.02) vs. –0.02 standard units (–0.06 to 0.02) for those with a decrease in 24-hour sleep duration ≥2 h vs. no change; p value for quadratic terms for TICS, verbal, and global scores: <0.001 for all outcomes across all change in sleep categories No association for slopes of decline for TICS, verbal, or global scores	Mean TICS, verbal, and global scores: 33.3 points (33.1–33.5) vs. 33.7 points (33.5–33.9), –0.04 standard units (–0.10 to 0.02) vs. 0.05 standard units (–0.02 to 0.09), and –0.12 standard units (–0.17 to –0.07) vs. –0.02 standard units (–0.06 to 0.02) for those with an increase in 24-hour sleep duration ≥2 h vs. no change; p value for quadratic terms under decreased sleep duration No association for slopes of decline for TICS, verbal, or global scores

* Statistically significant results are indicated in bold type.

TELE = Telephone screening to identify potential dementia cases; TICS = telephone interview of cognitive status; MMSE = mini-mental state examination; OR = odds ratio.

daytime napping hours in total sleep duration over 24 h might be most likely to increase sleep durations for individuals on the shorter end of the spectrum, although it is perhaps just as likely that those who take regular daytime naps are the most fragmented sleepers, which could increase sleep durations among very short and very long sleepers because both groups tend to have more fragmented sleep. However, in this review, we did not observe trends in study findings according to this difference. Likewise, there were large differences in methods of cognitive assessment and outcome definition across studies,

but findings were not systematically different based on these factors.

Third, most studies accounted for covariates that might influence the association between sleep duration and cognition among older individuals. Potential confounders are factors that affect both exposure and outcome, with the possibility of inducing a non-causal (biased) association. Most studies accounted for such factors by excluding individuals with certain characteristics from the study population (e.g. depression or other co-morbidities) or by adjusting for these characteristics in statis-

tical analyses. In addition to comorbidities, other factors that might confound the association of sleep duration and cognitive function include age, alcohol intake, body mass index, physical activity, and sleep-related factors. Although most studies accounted for some of these factors, these adjustments varied across studies and the potential for residual confounding remains in all observational studies; in particular, sleep-related factors were not accounted for in most studies. There is also the possibility that health and lifestyle factors might be mediators of this association, which would suggest that controlling for these factors could attenuate part of the association of interest. For studies that yielded different results before and after inclusion of these factors, it is probably most appropriate to control for possible confounding effects and interpret results accordingly, with the understanding that some associations may be underestimated. Thus, we interpreted results based on estimates adjusted for key potential confounders.

There may be several biologic explanations for studies that observed associations between extreme sleep durations and worse cognitive function in older adults. The central pacemaker for circadian rhythms is located in the suprachiasmatic nuclei of the brain, and circadian rhythms are important for optimal sleeping patterns and cognitive function [83]. However, circadian rhythms tend to weaken with aging, such that sleep and cognition can become dysregulated in older adults [84]. Thus, observed associations between sleep disturbances (including extreme sleep durations) and worse cognitive function in elderly individuals could be driven, at least in part, by this common factor. Moreover, sleeping patterns and Alzheimer's disease pathology may interact in a bidirectional manner [22]. It is known that Alzheimer's disease, even in stages of early cognitive impairment, induces sleep disturbances that become more pronounced with disease progression [22, 85].

However, recent studies have supported the notion that sleep disturbances can also promote beta-amyloid accumulation (the hallmark pathology of Alzheimer's disease) in the absence of cognitive impairment and Alzheimer's disease. One study found that sleep deprivation and poor sleep quality promoted beta-amyloid accumulation in mouse brain [20], while human studies identified self-reported short sleep duration, worse sleep efficiency, and frequent daytime napping as being associated with greater beta-amyloid burden in older adults [21, 32]. An additional study reported that greater sleep fragmentation was associated with a higher risk of cognitive decline and Alzheimer's disease in the elderly popu-

lation [86]. Further research on the sleep-wake cycle and beta-amyloid dynamics supports these observations, suggesting a diurnal pattern of beta-amyloid clearance with sleep and beta-amyloid accumulation with wakefulness in both mice and human brains [20, 23]. On a molecular level, it appears that sleep disturbances could induce neuronal excitability via altered potassium currents, leading to beta-amyloid accumulation [87]. Thus, there is growing evidence to support a central role of beta-amyloid accumulation in explaining associations between sleep disturbances and cognitive impairment. Still, other studies implicate increased tau protein, neuroinflammation, neurodegeneration, hypoxia, and vascular changes, as well as decreased synaptic plasticity as mediators of this association, any of which may also interact with beta-amyloid to promote further cognitive decrements [24, 88].

Interestingly, the Osteoporotic Fractures in Men Study suggests that self-reported extreme sleep durations may be a marker for objective sleep disturbances. In this study, wake after sleep onset (an objective measure of sleep disruption) was significantly higher among participants with the shortest and longest self-reported sleep durations (average wake-after-sleep-onset times: 85.4, 75.6, 78.4, and 93.0 min for individuals with night-time sleep durations ≤ 5 , $>5-7$, $>7-8$, and >8 h, respectively; $p < 0.001$) [44]. The authors posited that individuals with self-reported long sleep might perceive their sleep as long due to multiple night awakenings, or because they spend long periods in bed (although they are not necessarily sleeping). If this were true, then the link between sleep disturbances and beta-amyloid accumulation could help explain observed associations between extremes of self-reported sleep duration and worse cognitive function in observational studies of older adults. It might also contribute to our understanding of studies that did not find objectively measured extreme sleep durations to be associated with lower cognition, as these studies eliminate the influence of sleep quality on an individual's perception of sleep duration.

In conclusion, there is increased attention being paid to associations between sleep duration and cognitive function in older populations. Existing observational studies have produced mixed results, but epidemiologic research on objective sleep assessments and later-life cognition has begun to enhance our understanding of these findings. Future observational studies incorporating such assessments are clearly necessary, and may help elucidate potential biologic mechanisms of these associations. Intervention studies will also be needed to identify effective

strategies (e.g. improved sleep hygiene, increased physical activity, and sleep-promoting medications) [88] for ameliorating cognitive impairment among affected individuals, and preventing cognitive decrements among those not yet affected.

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