RESEARCH

Exploring the relationship of sleep duration on cognitive function among the elderly: a combined NHANES 2011–2014 and mendelian randomization analysis

Peng Qiu[1†], Cheng Dong[2†], Aifen Li[3], Juanjuan Xie[4] and Junyu Wu[5*]

Abstract

Background As one of the key features of sleep, sleep duration (SD) has been confirmed to be associated with multiple health outcomes. However, the link between SD and cognitive function (CF) is still not well understood.

Methods We employed a combined approach utilizing data from the National Health and Nutrition Examination Survey (NHANES 2011–2014) and Mendelian Randomization (MR) methods to investigate the relationship between SD and CF. In the NHANES cross-sectional analysis, the association between these variables was primarily examined through multivariate linear regression to explore direct correlations and utilized smoothing curve fitting to assess potential nonlinear relationships. To ensure the robustness of our findings, subgroup analyses were also conducted. MR analysis was used to assess the causal relationship between SD and sleeplessness on CF. After excluding confounding factors, univariate and multivariate MR were performed using inverse variance weighting (IVW) as the main analysis method, and sensitivity analysis was performed.

Results The results of our cross-sectional study indicate a notable negative association between SD and CF, forming an inverted U-shaped curve with the inflection point occurring at SD = 6 h. This relationship remains consistent and robust across subgroup analyses differentiated by variables such as age, levels of physical activity, and frequency of alcohol intake. In MR analysis, IVW analysis showed no causal relationship between SD and sleeplessness on CF (Both $P > 0.05$).

Conclusion Cross-sectional studies suggest the existence of an inverted U-shaped correlation between SD and CF among the elderly. However, MR analysis did not reveal a causal relationship between SD and CF, which the lack of nonlinear MR analysis may limit. These findings provide evidence from a sleep perspective for optimizing cognitive strategies in older adults.

Keywords Sleep duration, Cognitive function, NAHENS, Mendelian randomization, Older adults

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Background

In the contemporary era marked by an unprecedented rate of population aging, the preservation of cognitive function in the elderly emerges as a critical facet of public health and geriatric medicine [1]. Cognitive function (CF)—encompassing memory, attention, executive function, and more—serves as the bedrock of autonomy, decision-making, and the overall quality of life in older adults [2, 3]. However, aging invariably brings about a decline in these crucial CF, leading to an increased prevalence of related disorders, including dementia and Alzheimer's disease [4–6]. Notably, the World Health Organization reports that dementia affects approximately 50 million individuals globally, with an estimated 10 million new cases annually [7]. Cognitive health issues impacts not only the affected individuals and their families but also society as a whole, resulting in increased healthcare costs, caregiver burden, and diminished productivity [8–10]. Consequently, elucidating the determinants of cognitive health in the elderly, particularly modifiable lifestyle factors, is critical in devising effective interventions aimed at mitigating or reversing cognitive decline.

Sleep, particularly sleep duration (SD), is increasingly recognized as a critical factor influencing cognitive health in the elderly [11–14]. The intricate relationship between sleep patterns and CF has been the subject of numerous observational studies, which have consistently indicated a correlation between SD and CF [15–17]. For example, research has shown that both short and excessively long SD are associated with impaired CF, memory deficits, and a higher risk of cognitive decline [15, 18]. Studies drawing on data from various populations have observed that optimal SD is linked to better cognitive outcomes and may play a protective role against the progression of cognitive impairment [14, 19].

However, these findings are not without their limitations. Observational studies, while valuable in highlighting associations, are often constrained by confounding factors and cannot definitively establish causality. This limitation underscores the need for employing robust research methodologies that can more effectively discern the causal relationship between SD and CF. The utilization of the National Health and Nutrition Examination Survey (NHANES) 2011–2014 data, coupled with Mendelian Randomization (MR) methods, presents a novel approach in this context. NHANES provides a comprehensive, representative dataset of the U.S. population, encompassing various health-related information, including sleep habits and CF measures [20]. On the other hand, MR uses genetic variants as instrumental variables to infer causal relationships, thereby mitigating confounding biases typical in observational studies [21]. Our study aims to illuminate the relationship between SD and CF, thereby paving the way for optimizing strategies to prevent cognitive decline and develop targeted interventions for the elderly.

Methods

NHANES study

Study design

This study aims to elucidate the relationship between SD and CF utilizing data from NHANES spanning 2011 to 2014. Conducted by the National Center for Health Statistics (NCHS) under the Centers for Disease Control and Prevention (CDC), NHANES is pivotal in evaluating the health and nutritional status of the American adult and pediatric population [20]. Distinguished by its integration of both interviews and physical examinations, NHANES employs an intricate, multistage probability sampling strategy to generate a representative sample of the U.S. civilian, noninstitutionalized demographic, inclusive of diverse ages, races, and ethnic backgrounds. Methodologically, the survey amalgamates data from in-house interviews with standardized physical assessments conducted in mobile examination centers (MECs).

In our study, we utilized this comprehensive dataset to explore the intricate relationship between sleep patterns and cognitive health. By focusing on the 2011–2014 NHANES data, we aim to derive insights into current trends and associations that can inform future research and healthcare strategies targeting the elderly population.

The study cohort was derived from the NHANES 2011–2014 dataset, initially consisting of 19,931 participants. We excluded participants with incomplete SD data (*N*=7,391) and CF data (*N*=9,681). Finally, 2,931 participants were included in this study (Fig. 1).

Variables selection

The NHANES 2011–2014 dataset includes a wide range of health-related information, making it an invaluable resource for studying various public health issues, including the dynamics of SD and its impact on CF among the elderly.

For the exposure variable of our study, we utilized self-reported SD data gathered from the NHANES 2011–2014 questionnaires. Based on previous studies, SD can be considered as a continuous and categorical variable for analyzing relevant outcomes. We categorized SD as ≤6 h (insufficient), 7–8 h (average), ≥9 h (excessive) according to previous studies and clinical rationale [22–24].

In our study, we employed a suite of objective cognitive tests from NHANES 2011–2014 to evaluate CF among participants. These assessments included the Consortium to Establish a Registry for Alzheimer's Disease Word List (CERAD-WL) for both three-trial immediate recall (IR) and one-trial delayed recall (DR), along with the Animal Fluency (AF) test and the Digit Symbol Substitution Test (DSST) [25, 26]. The CERAD-WL test
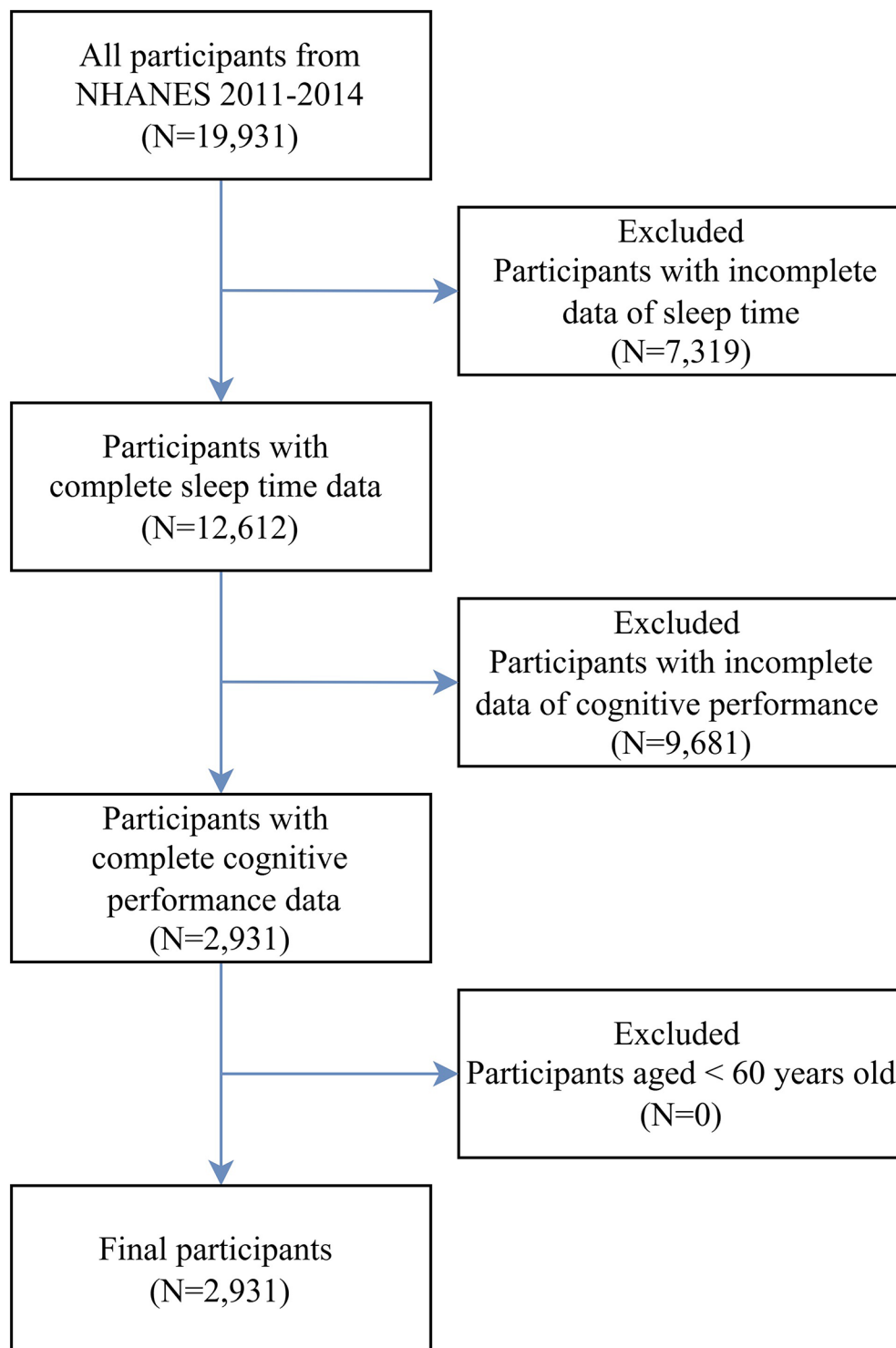
Fig. 1 Diagrammatic representation of participant selection and exclusion criteria

gauges short-term memory and learning through the IR component, where participants are asked to recall words immediately following their presentation The DR part of the CERAD-WL challenges memory retention by having participants recall the same list of words after a timed delay [26]. The AF test is a measure of verbal fluency and semantic memory, requiring participants to list as many animal names as possible within a one-minute timeframe [27]. This task assesses the rapid generation and articulation of words from a specified category, offering insight

into semantic memory and executive function [28]. The DSST is utilized to assess components of executive functioning and processing speed [29]. In this task, participants engage in a symbol-number matching exercise that evaluates their attention, speed, and visual-motor coordination. The test's demanding nature requires swift cognitive processing and has been shown to be a reliable measure of executive function [25]. For each of these tests, we calculated Z-scores to normalize the individual scores, allowing us to compare across the different cognitive domains assessed by each test [30]. The mean of these Z-scores was then computed to provide a composite score that represents an individual's overall CF [30, 31], thus facilitating a comprehensive analysis of the relationship between SD and cognitive health.

Furthermore, we controlled for a variety of covariates to isolate the effect of SD on CF. These included demographic factors (gender, race, age, education level) [31], socio-economic status (Poverty Income Ratio, PIR) [31], lifestyle factors (alcohol frequency, waist circumference, BMI, smoking status, physical activity) [32], and health-related variables (diabetes, depressive symptoms) [33].

Statistical analysis

Utilizing the NHANES 2011–2014 dataset, we performed a series of multivariate linear regression analyses to elucidate the relationship between SD and CF. Our analysis was stratified into three distinct models to incrementally adjust for potential confounders. Model 1 served as the unadjusted baseline, examining the raw association without controlling for any other variables. In Model 2, we introduced adjustments for demographic and socio-economic factors, specifically gender, age, race, education level, and PIR. Model 3 represented the fully adjusted model, which, in addition to the variables included in Model 2, also controlled for lifestyle and health-related factors—alcohol frequency, waist circumference, BMI, smoking status, physical activity, diabetes, and depressive symptoms. To assess non-linearity in the sleep-cognition relationship, we conducted threshold effect analysis and fitted smoothing curves. We used EmpowerStats to perform smooth curve fitting based on Generalized Additive Models (GAM). This approach, integrated with R's mgcv package, utilizes spline smoothing to capture the nonlinear relationship between sleep duration and cognitive function, offering flexibility without requiring a predefined functional form. These analyses allowed us to visually and statistically identify any points at which the relationship between SD and CF may change in direction or intensity. Furthermore, sensitivity analyses through subgroup analyses and interaction effect tests were performed to verify the robustness of our findings. These analyses ensured that our results were not unduly

influenced by any particular subgroup or confounding factor, thereby reinforcing the validity of our conclusions.

In our study, categorical variables were depicted as percentages, with intergroup disparities assessed via the weighted chi-square test. Continuous variables were articulated as mean±standard deviation and analyzed using the weighted Student's t-test. These statistical evaluations were performed utilizing R software (version 4.2.3) and EmpowerStats (version 2.0). A significance threshold was established at $P<0.05$ for all analyses, delineating the level of statistical significance.
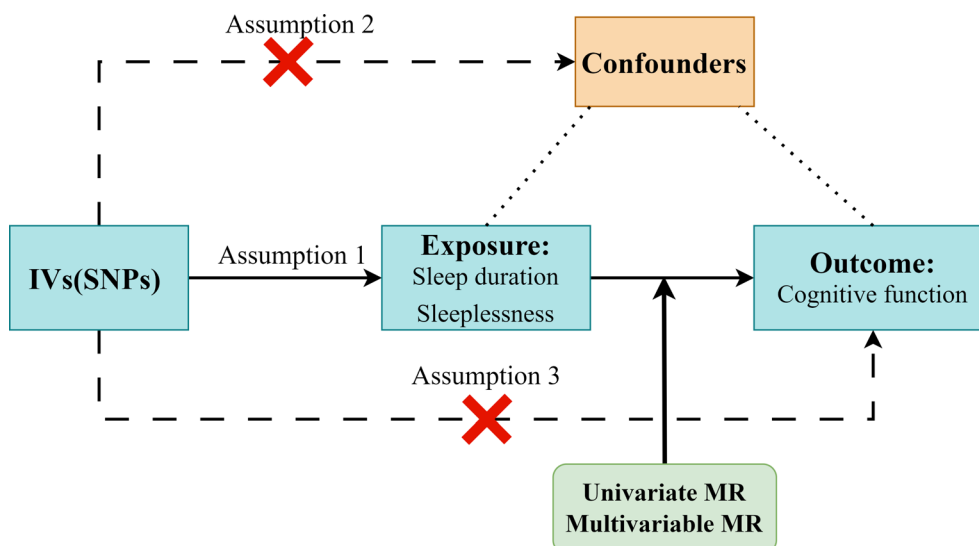
Mendelian randomization study
Study design
Our study utilized a two-sample MR approach to explore the causal link between genetically predicted SD and sleeplessness on CF. To ensure the validity of our MR analysis, we adhered to three critical criteria: firstly, the genetic variants must have a significant association with SD or sleeplessness; secondly, these variants should be free from any association with potential confounding factors; and thirdly, the influence of these variants on CF ought to occur solely through SD or sleeplessness [34]. Figure 2 illustrates the study's methodology. Leveraging single nucleotide polymorphisms (SNPs) linked to SD or sleeplessness as instrumental variables (IVs), our strategy capitalized on the extensive Genome-Wide Association Study (GWAS) datasets. This approach effectively circumvents the limitations typically encountered in observational studies.

Genetic instruments selection
The GWAS summary statistics for SD and sleeplessness were obtained from the UK Biobank public database, encompassing data from 460,099 to 462,341 European participants, respectively [35, 36]. For SD, ACE touchscreen question "About how many hours sleep do you get in every 24 hours? (please include naps)". The following examinations were conducted: Reject answers less than 1 or more than 23. If the response is less than 3, the participant is prompted to affirm. If the response is more than 12, the participant is prompted to confirm. When the participant clicked on the Help button, they were shown the message: Provide the average duration of sleep for a 24-hour day over the last 4 weeks if your sleep patterns have been inconsistent. For sleeplessness, ACE touchscreen question "Do you have trouble falling asleep at night or do you wake up in the middle of the night?". When the participant pressed the "Help" button, they saw the message "If this changes a lot, answer this question in terms of the last 4 weeks."

This MR analysis capitalized on SNPs that demonstrated robust associations—surpassing the genome-wide significance threshold ($P<5\times10^{-8}$)—with the exposure

Fig. 2 Principles of Mendelian randomization and assumptions. Assumption (1): the instrumental variables must be significantly associated with exposure. Assumption (2): they should not have any correlation with potential confounding variables. Assumption (3): their impact on cognitive function should be exclusively mediated through exposure. IVs, instrumental variables; MR, Mendelian randomization; SNPs, single nucleotide polymorphisms

variables of SD or sleeplessness as IVs [37]. To ensure the independence of these IVs, we implemented stringent criteria: a linkage disequilibrium correlation coefficient (r²) less than 0.001 and a clumping window exceeding 10,000 kilobases. Further refinement was conducted through the PhenoScanner V2 [38] database to excise any SNPs potentially linked with confounders at the genome-wide significance level ($P<5\times10^{-8}$), with a comprehensive list of these confounders presented in Supplementary File 1: Table S1. In the harmonization phase for exposure and outcome data, we rigorously excluded SNPs that were missing, palindromic, incompatible, or directly related to the outcomes under study from the set of IVs. To address and mitigate the impact of weak instrument bias on our causal inference, we computed the F-statistic for each IV, using the formula: $F_{\text{exposure}} = \frac{Beta^2_{exposure}}{SE^2_{exposure}}$. This metric was integral to evaluating the robustness of the IVs [39]. IVs with F-statistics below 10 were excluded from the analysis to avoid potential biases associated with weak IVs [40]. This stringent criterion ensured that only robust IVs were utilized in our MR study, enhancing the reliability of our causal estimates.

Summary dataset of outcome

The outcome data for our study come from the 2022 CF dataset (GWAS ID: ieu-b-4838), which is provided by the IEU Open GWAS project [41]. The dataset contains information on 22,593 male and female participants from Europe and includes 6,719,661 SNPs.

Statistical analysis

In our study, MR analyses were conducted employing the Inverse Variance Weighting (IVW) method as the principal analytical framework [42]. We utilized both the Fixed Effect (IVW-FE) and Random Effect (IVW-RE) IVW models to enhance the robustness of our findings. Further reinforcing the validity of our results, complementary MR methodologies, including MR-Egger and the weighted median approaches, were incorporated. The MR-Egger method is predicated on the assumption that a majority (over 50%) of the IVs are subject to horizontal pleiotropy [43], whereas the weighted median model presupposes that a minority (less than 50%) of IVs are influenced by such pleiotropy [44]. Integral to our sensitivity analyses were Cochrane's Q test, employed to scrutinize heterogeneity, and the MR-Egger regression intercept tests, utilized to investigate the presence of pleiotropy [45, 46]. Additionally, the MR-PRESSO test was applied to evaluate whether MR estimates remained robust after the exclusion of potential pleiotropic outliers [47]. To ensure the integrity of our MR findings, we conducted a leave-one-out analysis, recalculating the causal effect while sequentially excluding each SNP from the instrumental variables, thus verifying the stability of our results [46]. To address potential reverse causality, Steiger filtering analysis was undertaken, examining the directionality between CF and the outcomes of SD and sleeplessness [48]. We established causality only for those exposure-outcome pairs that maintained a consistent direction across all employed MR methodologies and demonstrated significant findings in the IVW analysis.

Statistical significance for our analyses was predetermined at a threshold of $P<0.05$. The results, indicating causal relationships, were quantitatively expressed through beta coefficients (β), standard errors (SE), and 95% confidence intervals (95% CIs). These statistical

evaluations were executed utilizing the "TwoSampleMR" (version 0.5.6) and "MR-PRESSO" (version 1.0) packages within the R computational environment (version 4.2.3) [49, 50].

Multivariable Mendelian randomization analysis
We employed Multivariable Mendelian Randomization (MVMR) to assess the impacts of multiple exposures on an outcome while adjusting for confounders: smoking, diabetes, depression, obesity, and alcohol intake frequency (IEU GWAS IDs: ieu-b-4877, ukb-b-10753, ukb-b-12064, ukb-b-15541, ukb-b-5779) [51]. Post integration of GWAS summaries for these variables, IVs were validated for strong associations ($P < 5 \times 10^{-8}$) with the exposures or confounders. We pruned SNPs within a 10,000 kilobases and $r^2 < 0.001$ to mitigate linkage disequilibrium effects. Subsequently, the IVW method discerned causal relationships, excluding palindromic SNPs and those missing in outcome data, while accounting for these confounders.

Results
Results of NHANES
Basic information
In the demographic data (Table 1), the three SD categories (≤6 h, 7–8 h, ≥9 h) exhibited significant differences in age, ethnicity, education level, and PIR, but not in gender. In terms of other covariates, notable differences were found among the SD groups in the prevalence of diabetes, symptoms of depression, levels of physical activity (PA), frequency of alcohol consumption, Body Mass Index (BMI), and waist circumference. With respect to CF outcomes, all three SD groups showed significant disparities in overall cognitive performance as well as in individual tests (IR, DR, AF, DSST).

Negative relationship between SD and CF
The results of the regression analysis revealed a notable negative association between SD and overall CF (Table 2). In the stratified analysis, elderly subjects with SD ≥9 h showed significant differences in their overall cognitive scores compared to those with SD ≤6 h. More precisely, an increase of 1 h in sleep time led to a 0.02-point reduction in the total cognitive score for the SD ≥9 h relative to the SD ≤6 h. This pattern was also evident in individual cognitive tests (detailed in Supplementary File1: Table S2-S5), where each additional hour of SD corresponded to decreases of 0.19, 0.35, 0.18, and 0.16 in the scores of IR, DR, AF, and DSST.

Smoothing curves and analysis of threshold effects
Smoothing curve fitting (Fig. 3) and threshold effect analysis (Table 3) demonstrated a pronounced inverted U-shaped correlation between SD and overall CF, with the curve's inflexion point at SD=6 h. In detail, for SD less than 6 h, an increase of 1 h in SD is associated with a 0.07 score increase in overall CF scores. When SD exceeds 6 h, each additional hour of sleep leads to a 0.07 score decreases in these scores. Furthermore, similar analyses were performed for SD and various cognitive tests (IR, DR, AF, DSST), as elaborated in the supplementary file (Supplemental File1: Table S6-S9). The results showed that SD's relationship with IR and DR also exhibits an inverted U-shaped curve, with inflection points at SD=6 and 5 h, respectively (detailed in Supplemental File 2: Figure S1).

Subgroup analysis
After conducting subgroup analysis based on age, PA levels, and alcohol frequency (Table 4), the negative association between SD and overall CF was consistently observed across all subgroups, without any significant interaction effects (P for interaction > 0.05). Furthermore, detailed subgroup analyses were performed for the relationship between SD and each cognitive test (IR, DR, AF, DSST), stratified similarly by age, PA levels, and alcohol frequency, as outlined in the supplementary file (Supplemental File1: Table S10-13).

Results of MR analysis
Results of univariate MR analysis
In our study, 24 SNPs were chosen as IVs for SD and 14 SNPs for sleeplessness. For an in-depth overview of these IVs utilized in MR analysis, please refer to Supplementary File 1: Table S14. The F-statistics of each IV varied, ranging from 30.05 to 224.46. For SD and sleeplessness, the results of the four MR methods showed that the $β$ coefficients obtained by all methods were not significant ($P > 0.05$; Table 5).

In our study, heterogeneity within SD measures was assessed using Cochrane's Q test, revealing significant diversity ($P < 0.05$; Table 6), thereby guiding our application of the IVW-RE model for the MR analysis. Conversely, the lack of significant heterogeneity in sleeplessness metrics justified the use of the IVW-FE model ($P > 0.05$; Table 6). Additionally, MR-Egger intercept tests were performed, indicating no substantial influence of horizontal pleiotropy on the MR outcomes for both conditions (Both $P > 0.05$; Table 6).

The MR-PRESSO test identified an outlier SNP (rs7016314) within the SD analysis; however, the association remained consistent upon this SNP's exclusion ($P = 0.09$; Table 6), underscoring the resilience of our findings. Furthermore, a comprehensive leave-one-out sensitivity analysis substantiated the robustness of our MR results, demonstrating no significant alteration in outcomes upon the sequential exclusion of individual SNPs (Supplemental File 2: Figures S2-S3). Lastly, our Steiger

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Table 1 Basic information on the study population

	Total	SD (hour)			P-value
		≤ 6	7–8	≥ 9	
Categorical scalar (%)					
Gender					0.5229
Male	45.55	43.90	46.11	46.70	
Female	54.45	56.10	53.89	53.30	
Race					< 0.0001
Mexican American	3.39	4.79	2.84	2.89	
Other Hispanic	3.64	5.50	3.02	2.27	
Non-Hispanic White	79.44	67.79	83.70	85.77	
Non-Hispanic Black	8.48	13.81	6.33	6.70	
Other	5.05	8.11	4.11	2.37	
Education level					0.0004
< 9th grade	5.71	7.17	4.60	8.22	
9-11th grade	10.26	11.52	9.78	9.67	
High school graduate/GED	22.04	23.62	21.39	21.59	
College or AA degree	31.42	32.96	31.45	27.21	
College graduate or above	30.56	24.72	32.77	33.31	
Smoking status					0.9704
Yes	50.40	50.69	50.35	49.90	
No	49.60	49.31	49.65	50.10	
Diabetes					< 0.0001
Yes	19.28	24.10	16.26	23.82	
No	76.64	72.09	79.73	71.03	
Boundary	4.08	3.81	4.01	5.15	
Depressive symptoms					< 0.0001
Yes	8.33	14.27	5.47	9.01	
No	91.67	85.73	94.53	90.99	
Physical activity					< 0.0001
High level	51.25	49.94	54.42	36.63	
Low level	48.75	50.06	45.58	63.37	
Continuous variables (M ± SD)					
Age (year)	69.22 ± 6.65	68.48 ± 6.36	69.25 ± 6.68	71.00 ± 6.89	< 0.0001
PIR	3.08 ± 1.53	2.90 ± 1.53	3.18 ± 1.52	3.00 ± 1.56	< 0.0001
Alcohol frequency (time)	4.89 ± 22.20	2.96 ± 8.92	5.64 ± 26.05	5.69 ± 22.50	0.0128
BMI (kg/m^2)	29.04 ± 6.21	29.83 ± 7.02	28.63 ± 5.72	29.28 ± 6.41	< 0.0001
Waist circumference (cm)	102.34 ± 14.21	103.45 ± 15.05	101.60 ± 13.89	103.59 ± 13.46	0.0020
IR	0.17 ± 0.96	0.15 ± 0.95	0.23 ± 0.95	-0.11 ± 1.03	< 0.0001
DR	0.14 ± 0.99	0.21 ± 0.92	0.17 ± 0.99	-0.23 ± 1.07	< 0.0001
AF	0.28 ± 1.04	0.20 ± 1.00	0.35 ± 1.05	0.06 ± 1.07	< 0.0001
DSST	0.36 ± 0.97	0.29 ± 0.98	0.44 ± 0.96	0.11 ± 0.96	< 0.0001
Cognitive function (score)	0.24 ± 0.79	0.21 ± 0.77	0.30 ± 0.78	-0.04 ± 0.82	< 0.0001

PIR: Ratio of family income to poverty; SD: sleep duration; IR: Word list learning trials (immediate recall); DR: Word list learning trials (delayed recall); AF: Animal fluency; DSST: Digit symbol substitution test. Continuous variables are described using mean ± standard deviation(M ± SD), while categorical variables are represented by percentages (%). Individuals with a score > 9 on the Patient Health Questionnaire [PHQ-9] were considered to have depressive symptoms. High level of physical activity was defined as ≥ 600 MET-min/week and low level of physical activity was defined as < 600 MET-min/week

filtering analysis did not unveil any evidence of reverse causation within the analyzed datasets (Table 6), reinforcing the directional integrity of our inferred causal relationships.

Results of multivariable MR analysis

MVMR analysis was conducted to further assess the causal relationship between SD and sleeplessness on CF. After individually adjusting for five confounding factors: smoking, diabetes, depression, obesity, and alcohol consumption frequency, both SD and sleeplessness continued to exhibit no causal relationship with CF (All

Table 2 Association between SD and overall cognitive function

	β(95%CI)		
	Model 1	**Model 2**	**Model 3**
SD (hour)	-0.04 (-0.06, -0.02) 0.0003	-0.04 (-0.05, -0.02) < 0.0001	-0.04 (-0.06, -0.02) < 0.0001
≤ 6	0(reference)	0(reference)	0(reference)
7–8	0.08 (0.02, 0.15) 0.0114	0.01 (-0.04, 0.06) 0.6370	-0.01 (-0.06, 0.05) 0.8463
≥ 9	-0.26 (-0.36, -0.16) < 0.0001	-0.22 (-0.30, -0.14) < 0.0001	-0.22 (-0.30, -0.14) < 0.0001
P for trend	0.007	< 0.001	< 0.001

SD: sleep duration

Model 1: Unadjusted Variables. Model 2: Race, gender, age, education level, ratio of family income to poverty were adjusted. Model 3: Race, age, gender, education level, ratio of family income to poverty, alcohol frequency, waist circumference, BMI, smoking status, diabetes, depressive symptom, and physical activity were adjusted
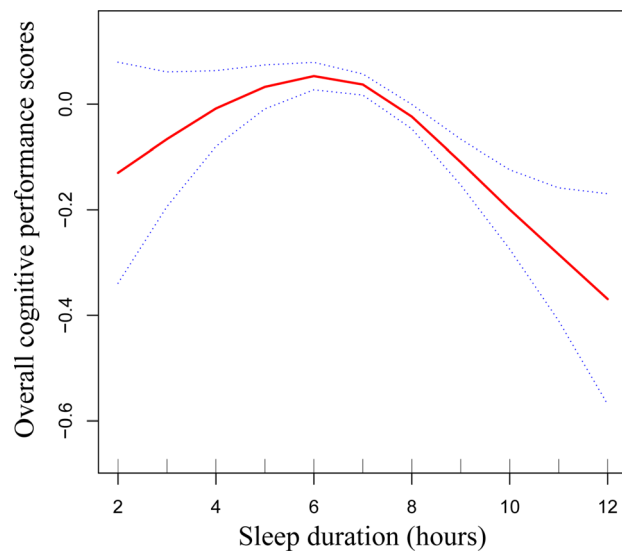
Fig. 3 Smoothed curves of the relationship between sleep duration and cognitive function

Table 3 Threshold effect analysis of SD on overall cognitive function

	β(95%CI)
One-line linear regression model	-0.04 (-0.06, -0.02) < 0.0001
Two-piecewise linear regression model	
Inflection point (K)	6
SD < K(hours)	0.07 (0.02, 0.13) 0.0059
SD ≥ K(hours)	-0.07 (-0.10, -0.05) < 0.0001
Log-likelihood ratio	< 0.001

SD: sleep duration;

This model adjusted for various variables including race, age, gender, education level, ratio of family income to poverty, alcohol frequency, waist circumference, BMI, smoking status, diabetes, depressive symptom, physical activity

$P > 0.05$, Fig. 4). This lack of causality persisted even after simultaneously adjusting for all five confounders (Both $P > 0.05$, Fig. 4), indicating a robust finding across multiple analytical conditions.

Discussion

In our cross-sectional study of NHANES 2011–2014 data, we discovered a notable inverse U-shaped correlation between SD and CF in the elderly. This pattern indicates that both insufficient and excessive sleep are associated with poorer cognitive performance compared to moderate SD. Interestingly, our findings reveal that the cognitive function of elderly individuals sleeping excessively is lower than those with insufficient sleep. However, our Mendelian Randomization analysis did not establish a causal relationship between SD and CF. These results underscore the complexity of the sleep-cognition nexus in the elderly and highlight the need for further research to explore the underlying mechanisms and potential interventions to support cognitive health in aging populations.

Consistent with earlier research, our study reaffirms the complex relationship between SD and cognitive function in the elderly. Many prior studies have also identified a non-linear association, typically suggesting that both short and long SD could be detrimental to cognitive health [11, 52, 53]. This is in line with our observation of an inverse U-shaped relationship, reinforcing the notion that an optimal SD exists for cognitive health. However, a unique aspect of our study is the emphasis on the more pronounced cognitive decline in elderly individuals with excessive SD compared to those with insufficient sleep. This contrasts with some earlier findings where the focus has been predominantly on the adverse effects of short SD [13, 54]. Our results thereby contribute to a more nuanced understanding of the sleep-cognition dynamic, suggesting that excessive sleep might be an equally or more important factor to consider in cognitive health. It's important to note that while our study adds to the growing body of literature, the lack of a demonstrated causal link between SD and CF through Mendelian Randomization analysis presents a divergence from some studies that have suggested a potential causal relationship [55, 56]. Previous research by Henry et al. demonstrated the importance of considering non-linear MR approaches when investigating SD and cognitive outcomes [55]. Similarly, Chen et al. found a U-shaped association

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Table 4 Subgroup analyses of the relationship between SD and overall cognitive function

	Model 1	Model 2	Model 3
SD (hour)	-0.04 (-0.06, -0.02) 0.0003	-0.04 (-0.05, -0.02) < 0.0001	-0.04 (-0.06, -0.02) < 0.0001
Stratified by age			
≤ 70	-0.01 (-0.04, 0.01) 0.3118	-0.05 (-0.07, -0.03) < 0.0001	-0.05 (-0.08, -0.03) < 0.0001
> 70	-0.03 (-0.06, 0.01) 0.1128	-0.04 (-0.07, -0.01) 0.0033	-0.04 (-0.06, -0.01) 0.0100
P for interaction	0.5847	0.6038	0.3675
Stratified by PA			
High level	-0.02 (-0.06, 0.01) 0.1539	-0.02 (-0.05, 0.00) 0.0688	-0.03 (-0.05, -0.00) 0.0265
Low level	-0.04 (-0.07, -0.01) 0.0047	-0.05 (-0.07, -0.03) < 0.0001	-0.05 (-0.07, -0.02) < 0.0001
P for interaction	0.4125	0.1419	0.3203
Stratified by alcohol frequency			
High level	-0.05 (-0.08, -0.03) 0.0002	-0.05 (-0.07, -0.02) < 0.0001	-0.05 (-0.07, -0.03) < 0.0001
Low level	-0.03 (-0.06, 0.00) 0.0846	-0.04 (-0.06, -0.01) 0.0059	-0.05 (-0.07, -0.02) < 0.0001
P for interaction	0.2410	0.5141	0.3004

SD: sleep duration

Model 1: Unadjusted Variables. Model 2: Race, gender, age, education level, ratio of family income to poverty were adjusted. Model 3: Race, age, gender, education level, ratio of family income to poverty, alcohol frequency, waist circumference, BMI, smoking status, diabetes, depressive symptom, and physical activity were adjusted

Table 5 Mendelian randomization analysis results

Exposure	Method	SNPs	MR		
			β (95%CI)	SE	P
Sleep duration	IVW-FE	24	-0.08 (-0.42, 0.26)	0.17	0.66
	IVW-RE	24	-0.08 (-0.55, 0.39)	0.24	0.75
	MR Egger	24	-0.05 (-1.51, 1.41)	0.74	0.95
	WM	24	0.14 (-0.40, 0.68)	0.28	0.61
Sleeplessness	IVW-FE	14	-0.22 (-0.74, 0.31)	0.27	0.42
	IVW-RE	14	-0.22 (-0.79, 0.36)	0.29	0.47
	MR Egger	14	-0.57 (-3.90, 2.77)	1.70	0.75
	WM	14	-0.28 (-1.02, 0.46)	0.38	0.46

IVW-FE, inverse variance weighted (fixed effects); IVW-RE, inverse variance weighted (multiplicative random effects); WM, Weighted median; *β*, beta; SE, standard error

between SD and dementia risk, highlighting the potential genetic susceptibilities influencing both short and long SD [56]. The MR analysis employed in this study utilized a linear model, which may not be suitable for capturing the observed non-linear, U-shaped relationship. Linear MR models assume a constant effect size across the range of the exposure, potentially overlooking complex associations where the effect varies at different levels of exposure. Consequently, our MR analysis may not have detected a causal relationship due to its inability to model non-linear effects. Future studies should consider employin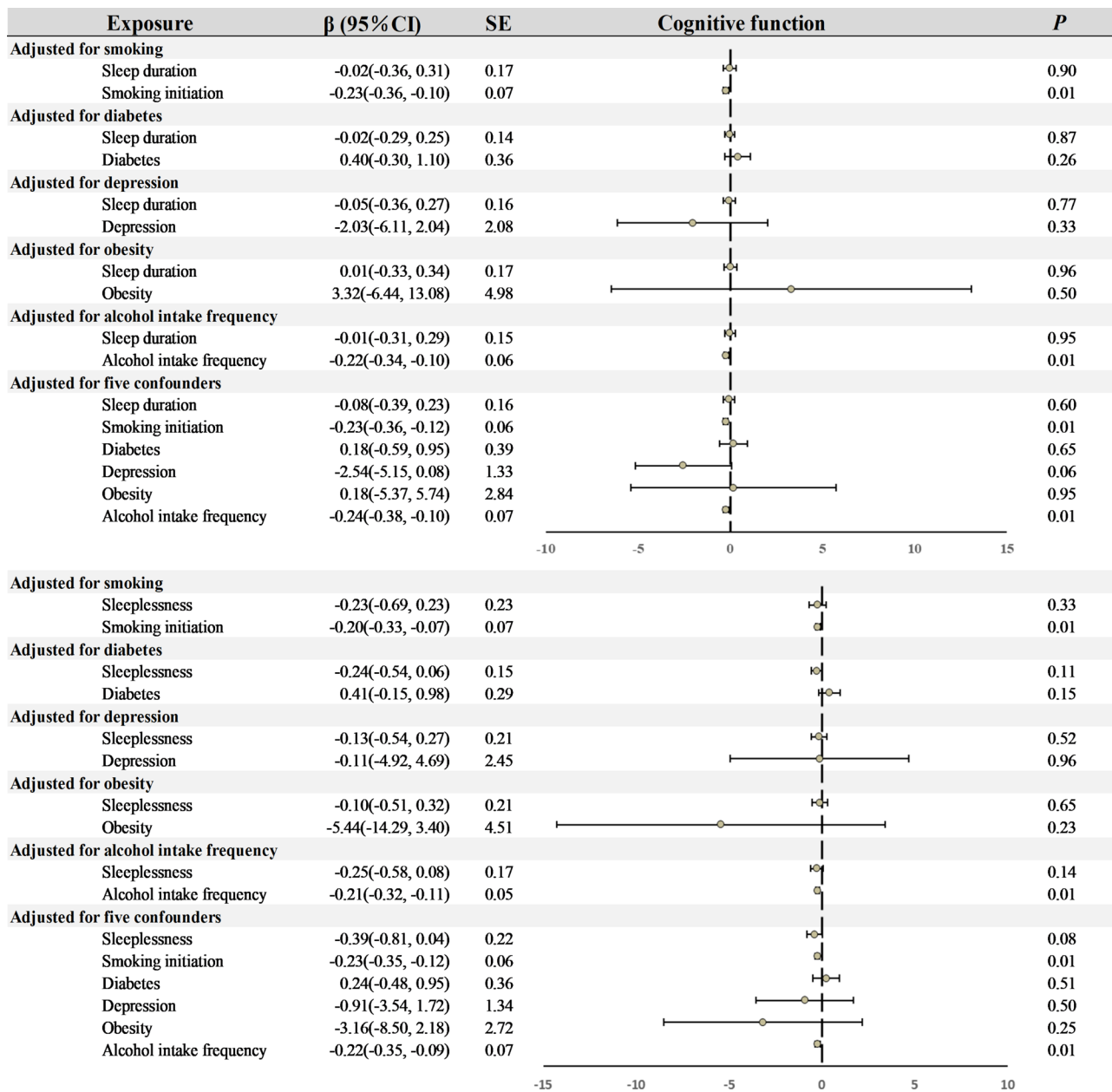g non-linear MR methods to better understand the complex interplay between SD and CF. This discrepancy underscores the complexity of the relationship and the need for ongoing research using diverse methodological approaches to fully understand the interplay between sleep and cognitive health in the elderly.

Our study suggests that in older adults, excessive SD may exert a more adverse effect on CF than short SD. However, the mechanisms driving this association are not definitively established. We propose several potential mechanisms for consideration. Firstly, the correlation between excessive sleep and underlying health conditions might be a key factor. Diseases such as depression and cardiovascular conditions [57, 58], which are linked to prolonged SD, are independently associated with cognitive decline [59, 60]. This suggests that excessive sleep may be more symptomatic of these underlying conditions rather than a direct cause of cognitive impairment. Another mechanism to consider is the disruption of the brain's clearance processes due to excessive sleep. Sleep facilitates the elimination of metabolic waste from the brain, but overextension of this state could potentially interfere with these processes, potentially leading to an accumulation of neurotoxic substances like beta-amyloid plaques [61, 62]. In addition, poor sleep quality, often masked by prolonged SD, is also a potential factor. This can result in disrupted sleep cycles and frequent

Table 6 Results of sensitivity analyses

Exposure	Heterogeneity (Cochran's Q test)				Pleiotropy				Steiger filtering	
	MR-egger		IVW		MR egger		MR-PRESSO			
	Q	P	Q	P	Intercept	P	*n* Outliers	P	Correct causal direction	P
Sleep duration	43.78	0.01	43.78	0.01	0.01	0.97	1	0.09	TRUE	0.57
Sleeplessness	15.72	0.21	15.78	0.26	0.01	0.84	NA	NA	TRUE	0.36

IVW, inverse variance weighted; SE, standard error

Exposure	β (95%CI)	SE	Cognitive function	*P*
Adjusted for smoking				
Sleep duration	-0.02(-0.36, 0.31)	0.17		0.90
Smoking initiation	-0.23(-0.36, -0.10)	0.07		0.01
Adjusted for diabetes				
Sleep duration	-0.02(-0.29, 0.25)	0.14		0.87
Diabetes	0.40(-0.30, 1.10)	0.36		0.26
Adjusted for depression				
Sleep duration	-0.05(-0.36, 0.27)	0.16		0.77
Depression	-2.03(-6.11, 2.04)	2.08		0.33
Adjusted for obesity				
Sleep duration	0.01(-0.33, 0.34)	0.17		0.96
Obesity	3.32(-6.44, 13.08)	4.98		0.50
Adjusted for alcohol intake frequency				
Sleep duration	-0.01(-0.31, 0.29)	0.15		0.95
Alcohol intake frequency	-0.22(-0.34, -0.10)	0.06		0.01
Adjusted for five confounders				
Sleep duration	-0.08(-0.39, 0.23)	0.16		0.60
Smoking initiation	-0.23(-0.36, -0.12)	0.06		0.01
Diabetes	0.18(-0.59, 0.95)	0.39		0.65
Depression	-2.54(-5.15, 0.08)	1.33		0.06
Obesity	0.18(-5.37, 5.74)	2.84		0.95
Alcohol intake frequency	-0.24(-0.38, -0.10)	0.07		0.01
Adjusted for smoking				
Sleeplessness	-0.23(-0.69, 0.23)	0.23		0.33
Smoking initiation	-0.20(-0.33, -0.07)	0.07		0.01
Adjusted for diabetes				
Sleeplessness	-0.24(-0.54, 0.06)	0.15		0.11
Diabetes	0.41(-0.15, 0.98)	0.29		0.15
Adjusted for depression				
Sleeplessness	-0.13(-0.54, 0.27)	0.21		0.52
Depression	-0.11(-4.92, 4.69)	2.45		0.96
Adjusted for obesity				
Sleeplessness	-0.10(-0.51, 0.32)	0.21		0.65
Obesity	-5.44(-14.29, 3.40)	4.51		0.23
Adjusted for alcohol intake frequency				
Sleeplessness	-0.25(-0.58, 0.08)	0.17		0.14
Alcohol intake frequency	-0.21(-0.32, -0.11)	0.05		0.01
Adjusted for five confounders				
Sleeplessness	-0.39(-0.81, 0.04)	0.22		0.08
Smoking initiation	-0.23(-0.35, -0.12)	0.06		0.01
Diabetes	0.24(-0.48, 0.95)	0.36		0.51
Depression	-0.91(-3.54, 1.72)	1.34		0.50
Obesity	-3.16(-8.50, 2.18)	2.72		0.25
Alcohol intake frequency	-0.22(-0.35, -0.09)	0.07		0.01

Fig. 4 MVMR analysis for evaluating the causal effect of sleep duration and sleeplessness on cognitive function. MVMR, multivariable Mendelian randomization; *β*, beta; SE, standard error

awakenings, which are detrimental to the hippocampus and memory consolidation, hence impacting CF [14, 63–65]. Lastly, the lifestyle associated with excessive sleep, characterized by reduced physical and cognitive activity, could contribute to cognitive decline. Regular engagement in stimulating activities is crucial for cognitive health, and a sedentary lifestyle due to prolonged sleep could limit these beneficial activities [66–68]. In conclusion, while our study highlights the potential greater harm of excessive sleep on CF compared to insufficient sleep in the elderly, the exact mechanisms remain unclear and require further exploration.

Our study shares similarities with Yu et al. [69], which also explored the relationship between sleep duration and cognitive function using NHANES and UK Biobank data. However, key differences exist. Yu et al. used a bidirectional MR approach with SNPs categorized for short and long sleep durations, whereas our study applied a linear MR analysis using sleep duration as a continuous variable. This difference stems from our lack of access to individual-level UK Biobank data, which is necessary for such categorization. While Yu et al. identified a causal link between extreme sleep durations and cognitive risks, our study did not establish such a relationship, likely

due to differences in methodology and data availability. These contrasting findings highlight the complexity of the sleep-cognition relationship and the need for further research.

Despite yielding valuable insights, our study has several limitations. The cross-sectional design of the NHANES dataset curtails our capacity to deduce temporal relationships and longitudinal changes. Moreover, while MR serves as a potent mechanism for causal inference, it presumes that the genetic instruments employed are specifically associated with SD and sleeplessness without influencing CF via alternate pathways. This study also does not encompass other potential confounding variables, including nutritional intake, lifestyle behaviors, and environmental factors, all of which could influence both SD and CF. A key limitation is the use of a linear MR model, which may not capture the nonlinear U-shaped relationship between SD and CF. Future studies should explore nonlinear MR methods to more accurately assess causal relationships in such complex associations. Additionally, our study has another limitation, which is that only a portion of participants in NHANES completed the sleep questionnaire and the full CF tests. The missing data could potentially introduce bias into the results. Future research should aim to overcome these constraints and further dissect the intricate relationships among physical health, genetic predispositions, and CF with greater granularity.

Conclusion

In our study, cross-sectional study findings indicate an inverted U-shaped relationship between SD and CF, with excessively long SD having a more detrimental effect on CF than insufficient sleep. However, MR analysis did not reveal a causal relationship between these variables. These findings underscore the importance of optimal SD for the cognitive health of older adults, offering potential intervention strategies to prevent cognitive decline associated with aging. And highlight the criticality of maintaining an optimal SD for safeguarding the cognitive health of the elderly. It propels the discourse on devising tailored sleep management strategies as preventive measures against the cognitive decline associated with aging.

Abbreviations

SD	Sleep duration
CF	Cognitive function
NHANES	The National Health and Nutrition Examination Survey
MR	Mendelian randomization
IVW	Inverse variance weighting
CERAD-WL	Consortium to Establish a Registry for Alzheimer's Disease Word List
IR	Immediate recall
DR	Delayed recall
AF	Animal Fluency
DSST	Digit Symbol Substitution Test
PIR	Poverty Income Ratio
SNPs	Single nucleotide polymorphisms
IVs	Instrumental variables
IVW-FE	Fixed effect inverse variance weighted model
IVW-RE	Random effect inverse variance weighted model
GWAS	Genome-wide association study
MVMR	Multivariable Mendelian randomization
PA	Physical activity
BMI	Body mass index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-024-05511-2.

Supplementary Material 1

Supplementary Material 2

Declarations

Ethics approval and consent to participate
Ethical approval and consent were not specifically for this study as we used summary data that is publicly available.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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