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Study protocol for a longitudinal observational study of disparities in sleep and cognition in older adults: the DISCO study

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ABSTRACT

Introduction Cognitive dysfunction, a leading cause of mortality and morbidity in the USA and globally, has been shown to disproportionately affect the socioeconomically disadvantaged and those who identify as black or Hispanic/Latinx. Poor sleep is strongly associated with the development of vascular and metabolic diseases, which correlate with cognitive dysfunction. Therefore, sleep may contribute to observed disparities in cognitive disorders. The Epidemiologic Study of Disparities in Sleep and Cognition in Older Adults (DISCO) is a longitudinal, observational cohort study that focuses on gathering data to better understand racial/ethnic sleep disparities and illuminate the relationship among sleep, race and ethnicity and changes in cognitive function. This investigation may help inform targeted interventions to minimise disparities in cognitive health among ageing adults.

Methods and analysis The DISCO study will examine up to 495 individuals aged 55 and older at two time points over 24 months. An equal number of black, white and Hispanic/Latinx individuals will be recruited using methods aimed for adults traditionally under-represented in research. Study procedures at each time point will include cognitive tests, gait speed measurement, wrist actigraphy, a type 2 home polysomnography and a clinical examination. Participants will also complete self-identified assessments and questionnaires on cognitive ability, sleep, medication use, quality of life, sociodemographic characteristics, diet, substance use, and psychological and social health.

Ethics and dissemination This study was approved by the Northwestern University Feinberg School of Medicine Institutional Review Board. Deidentified datasets will be shared via the BioLINCC repository following the completion of the project. Biospecimen samples from the study that are not being analysed can be made available to qualified investigators on review and approval by study investigators. Requests that do not lead to participant burden or that conflict with the primary aims of the study will be reviewed by the study investigators.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Multiple race and ethnic groups are examined in a single study with identical instrumentation and methodology applied across groups.
⇒ This is a longitudinal follow up study to determine temporality.
⇒ Gold-standard instruments illustrate objective determination of habitual sleep and sleep architecture.
⇒ Sample is not generalisable for the population since random sampling is not used.

INTRODUCTION AND RATIONALE

Dementia, including Alzheimer's disease, is a severe manifestation of cognitive dysfunction and among the top 10 causes of death in the USA and globally.[1] Morbidity from less severe cognitive dysfunction is equally notable, since cognitive dysfunction alone, although not terminal in most cases, still requires progressive social and medical support. The prevalence of cognitive dysfunction is higher among persons with fewer socioeconomic resources, less education or those who identify as black or Hispanic/Latinx race and ethnicity.[2] Disparities in the cardiovascular and metabolic correlates of cognitive dysfunction are hypothesised to account for differences in cognitive function by race and ethnicity.[3] However, while these disparities are observed by race and ethnicity, they are likely attributable to differences in socioeconomic resources that provide access to preventive medical care and offer differential access to environmental resources (eg, healthy foods, safe spaces for physical activity) that promote ideal health. Given the irreversibility of cognitive dysfunction, identifying and addressing these modifiable factors that are associated with cognitive decline could reduce disparities in cognitive dysfunction.[4]

Sleep disturbances are one such potentially modifiable correlate of cognitive dysfunction that vary by race/ethnicity and socioeconomic

status.[5–7] Habitual sleep duration and sleep disordered breathing may influence cognition indirectly through the biologically plausible development of cardiovascular and metabolic disorders.[8–12] Alternatively, short sleep duration or sleep disorders may influence cognition dysfunction and dementia via inflammation and endothelial dysfunction.[13 14]

Non-Hispanic black and Hispanic/Latinx adults have less favourable patterns of habitual sleep, sleep architecture and sleep disordered breathing as compared with white adults.[15–18] These patterns are observed across the lifecourse, including in epidemiological studies of middle-aged and older-aged adults.[19] Based on prior evidence that sleep characteristics are worse among non-white older adults and the biologically plausible pathways by which poor sleep could influence cognitive functioning, we formed a longitudinal observational epidemiological study to investigate how disparities in sleep among older adults influence cognitive outcomes.

Specific aims

The primary objectives of the Disparities in Sleep and Cognition (DISCO) study are twofold. The first is to examine numerous social, behavioural and health-related characteristics as possible explanations for racial and ethnic sleep health disparities. The second is to determine whether disparities in sleep health by race and ethnicity are significant contributors to disparities in the rate of cognitive decline over the course of approximately 2 years.

The study has two primary aims:

1. Define the contribution of psychological well-being, social well-being and clinical characteristics to sleep disparities among older adults.

We will test the hypotheses that sleep disparities by race and ethnicity are partially explained by lower psychological well-being, greater stress, lower self- efficacy and lower social support among non-white adults; and by a higher burden of prevalent comorbidities, such as heart failure or diabetes among non-white adults.

2. Determine whether sleep disturbances mediate racial or ethnic differences in the change in cognitive function over 24 months.

We hypothesise that inadequate sleep will be associated with greater cognitive decline and will partially mediate the racial and ethnic differences in change in cognitive function over 2 years. We will additionally explore mechanistic pathways to account for these associations, including the presence of cerebral small vessel dysfunction and insulin resistance.

METHODS

Study design

The DISCO study is a longitudinal observational cohort study that will examine 450 older adults with an equal proportion of non-Hispanic black, non-Hispanic white and Hispanic/Latinx adults of any race aged 55 years and older. Participants will be examined at baseline and again approximately 24 months later. To account for 10% lost to follow-up, we are enrolling approximately 495 participants at baseline. Women and men will be enrolled at proportions that reflect older age distribution according to the 2019 US Census (54% and 46%, respectively). Study participant enrolment began in July 2019 and will continue through December 2023. Participant follow-up will take place through March 2024.

Study setting

This is a single-site study in the metropolitan Chicago area and surrounding suburbs, and nearby northwest Indiana and southern Wisconsin.

Recruitment methods

Participants are recruited through a combination of strategies including random sampling of commercially available telephone listings, institutional electronic health records, advertisements on social media and in publicly available locations, community engagement strategies and word of mouth (ie, snowball sampling).

1. Our recruitment strategy using commercially available sampling and the electronic health record sampling are similar. Our staff mails a letter to potential participants or sends an email to explain the study and invite them to contact study staff to assess eligibility. If potential participants do not attempt to reach us, then our staff call participants to explain the study, invite participation, screen for eligibility and obtain consent.
2. Advertisements for our study are placed in newspapers, at community sites (eg, public libraries, cafes, senior living facilities), on public transportation and on Facebook. The advertisements include a link to our study website and staff phone numbers so that individuals can request more information about the study and complete preliminary screening questions to determine their eligibility.
3. Community engagement activities call for the active involvement of community leaders, organisations and other sectors or stakeholders (such as departments of health) working with academic institutions in the development, implementation, and evaluation of research priorities and activities.[20] The DISCO team engaged with a number of Chicago-area community-based grassroots and health and human services organisations, local and state government representatives, professional organisations and other sectors that are not traditionally involved in research. DISCO convenes a Community Advisory Board (CAB) approximately every 6 months to provide recommendations on project activities, suggest community engagement opportunities, discuss strategies for recruitment and retention, build relationships with community groups, and inform our team about community events. Most CAB members were identified from organisations that serve black and Hispanic/Latinx communities in the city of Chicago. While a core group of 3–4 CAB mem-

bers remain engaged in the study since its inception, the CAB also includes some older adults who enrolled in the DISCO study and joined the CAB after their study participation. When study results are available, the CAB will advise on strategies to disseminate the findings back to the community who contributed to the research.

4. The DISCO staff are also using 'snowball sampling,' to recruit participants. Staff ask participants who complete the study to refer us to people outside of their household who are sociodemographically similar (based on race, ethnicity and age) who might also be interested in participating. Study staff ask the participants to share our study flyer and website with these friends and family.

Impact of the COVID-19 pandemic on recruitment

The COVID-19 pandemic greatly impacted study recruitment due to the vulnerability of older adults to severe outcomes from SARS-CoV-2.[21] The research clinic was closed from 16 March 2020 to 1 June 2020. DISCO pivoted to virtual-only engagement strategies and recruitment activities from March 2020 to June 2022. Following advice from our CAB, we provided virtual educational sessions on relevant topics to increase the community's familiarity with our research team. Additionally, we expanded our digital and print recruitment campaigns and tailored them to our target audience. During this period, we maintained a slower but steady rate of enrolment.

Eligibility criteria

Table 1 summarises the inclusion and exclusion criteria.

Eligible participants are given the Montreal Cognitive Assessment (MOCA) test either in-person or via the telephone.[22] To administer over the phone (a process that was approved following the pandemic to avoid unnecessary in-person contact), the BLIND MOCA is used, which is a version designed for people with visual impairment. Both versions contain cognitive domains such as attention, concentration, memory, language, conceptual thinking, calculation and orientation. A pass score on the original MOCA is 26/30, and a pass score on the BLIND MOCA is 18/22. Participants who indicate that their preferred language is Spanish are administered the validated Spanish-language version of the MOCA. If they pass, study staff solicit verbal consent over the telephone and obtain a signed consent using REDCap.

Table 1 Inclusion and exclusion criteria

Inclusion	Exclusion
At least 55 years of age at the time of enrolment	Currently undergoing treatment for cancer (other than non-melanoma skin cancer)
Non-Hispanic black, non-Hispanic white or Hispanic/Latinx of any race	Clinical vascular event including myocardial infarction, stroke, transient ischaemic attack or procedure to treat those conditions within the previous 6 months
Able to read and understand either English or Spanish	Chronic heart failure classes II–IV
	Diagnosis of dementia (including Alzheimer's disease)
	Living in a group home, assisted living or other institution
	Overnight shift work or swing shift work that spans midnight (12:00 hours)
	Severe vision or hearing deficits that would interfere with testing
	Regular use of medications in the following classes: hypnotics, psychoactive medications with anti-cholinergic and antihistaminic effects or opioids
	Severe chronic obstructive pulmonary disease
	Inability to move both arms
	Prior diagnosis of severe neurological disorders
	Montreal Cognitive Assessment score <23 if administered the in-person version or <18 if administered the over-the-phone version
	Inability to give consent

DATA COLLECTION

Examination structure

Between July 2019 and March 2020, most participants came to the research clinic twice during the baseline examination—first to provide consent, complete questionnaires described in table 2 and undergo the clinical examination to undergo a fasting blood draw, anthropometric measures, blood pressure assessment, 6 min walk test, National Institutes of Health (NIH) Toolbox to assess cognitive function and to receive the sleep equipment that they will wear in their homes. On or around the eighth day, participants returned to the research clinic to complete additional cognitive function testing, gait analysis and measurement of cerebral blood flow.

From October 2020 going forward, participants are consented to join the study remotely via REDCap and invited to complete the questionnaires prior to the in-person clinical examination. Following receipt of the questionnaires, they attended the clinical examination and to receive the sleep devices (Actiwatch and Sleep Profiler). Participants are provided with the option of returning on the eighth morning or completing the remaining set of cognitive testing elements on that same day. We document the order with which the examination components were captured and devices administered and can account for any variability in our analyses, though we do not anticipate that it will influence our associations.

Table 2 List of survey instruments used in this study

Instrument	Description
Cognitive Domain	
MOCA[59]	Assessment tool for the early detection of mild cognitive impairment. Assesses short-term memory, visuospatial abilities, executive function, attention, concentration and working memory, language and orientation to time and place.
Patient Reported Outcomes Measurement Information System (PROMIS) Applied Cognition Abilities[28]	16-item measure assessing self-impressions of cognitive function in the past 7 days.
Sleep Domain	
Pittsburgh Sleep Quality Index (PSQI)[39]	19-item instrument to estimate subjective sleep quality. Scores range from 0 to 21; higher scores indicate worse sleep quality.
Insomnia Severity Index[40]	7-item instrument that assesses severity of insomnia. Higher scores indicate worse insomnia symptoms.
Morningness- Eveningness[41]	19-item instrument that assesses preferred 'chronotype', or morningness vs eveningness. Higher scores indicate greater morningness.
Epworth Sleepiness Scale[42]	8-item questionnaire to estimate daytime sleepiness. Higher scores indicate greater sleepiness.
Brief Index of Sleep Control[43]	4-item instrument designed to quantify the degree to which someone has control over their sleep. Higher scores indicate greater control.
Health Domain	
Medication Use	This form collects details on prescription medication used in the past 4 weeks or over-the-counter medication used in the past 2 weeks.
Medical History	23-item questionnaire that records information about individuals' medical history. High scores indicate better health.
Short Form-36 Questionnaire[60]	36-item measure assessing health-related quality of life. Scores are summarised in a Physical Component Summary and Mental Component Summary. Higher scores indicate better health status.
Kansas City Cardiomyopathy Questionnaire[61]	23-Item measure examining heart failure symptoms, physical limitations and quality of life. Lower scores represent more severe symptoms/limitations.
PROMIS Global Health[62]	10-item scale that assesses physical, mental and social aspects of health. Higher scores indicate better health.
Time Use Questionnaire	7-item scale that assesses the frequency and duration of activities.
COVID-19 Questionnaire	15-item questionnaire that related to exposure to COVID-19.
Sociodemographic Domain	
Sociodemographic Information Questionnaire	38 items are collected to assess sociodemographic characteristics such as age, gender, ethnicity, education level, income, access to healthcare, perceived social standing, etc.
Lifestyle Behaviour Domain	
Global Physical Activity Questionnaire (GPAQ)[63]	13-item scale examining several components of physical activity including intensity, duration and frequency.
Tobacco History	Item questionnaire that determines when an individual began smoking and their current smoking habits.
Automated Self-Administered (ASA) 24-Hour Dietary Recall[64]	Automated self-administered 24-hour dietary assessment tool web-based tool(.
Substance Use	12-item questionnaire that determines the use of alcohol and marijuana.
Psychosocial Domain	
STRAIN[65]	The Stress and Adversity Inventory (STRAIN) is a secure, online stress assessment system that measures individuals' lifetime exposure to different types of acute and chronic stress that can affect mental and physical health. The system is intended to combine the reliability and sophistication of an interview-based measure of stress with the simplicity of a self-report instrument. To accomplish this goal, the STRAIN enquires about 75 different types of stressors (Adolescent STRAIN) or 55 different types of stressors (Adult STRAIN) that cover all major life domains (eg, health, intimate relationships, friendships, children, education, work, finances, housing, living conditions, crime) and several social-psychological characteristics (eg, interpersonal loss, physical danger, role change, entrapment).
PROMIS Social Isolation-Short Form 4 a[66]	6-item scale examining perceived social isolation. Higher scores indicate higher perceived isolation.
Quick Inventory of Depressive Symptomatology (QIDS-SR16)[67]	16-item scale examining endorsement of depressive symptoms. Higher scores indicate higher symptoms.
Perceived Stress Scale[68]	10-item scale assessing the degree to which situation in participant's life are appraised as stressful. Higher scores indicate higher levels of stress.
University of California, Los Angeles Loneliness Questionnaire[69]	8-item scale assessing perceived isolation from others. Higher scores indicate higher perceived loneliness.
Generalized Anxiety Disorder[70]	7-item questionnaire assessing self-reported anxiety symptoms in the past 2 weeks. Higher scores indicate higher anxiety symptoms.
Brief Resilience Scale[71]	6-item questionnaire used to assess the ability to bounce back. High score indicated high resilience,
Bereavement	1-item examining whether participants have lost a spouse/partner or loved one in the past 6 months.
United States Department of Agriculture Food insecurity[72]	Item questionnaire used to measure household food security and food insecurity. High score indicated extremely low food security.

Continued

Table 2 Continued

Instrument	Description
Social Support[73]	Item questionnaire indicated the no of people available for support and satisfaction of support.

MOCA, Montreal Cognitive Assessment.

Participants repeat these examination procedures 6–24 months after their baseline assessment.

All data are stored electronically via REDCap and on a secure, encrypted, password-protected server.

Assessment of cognitive function

A primary outcome in the study is cognitive function as determined using the NIH Toolbox cognition battery.[23 24] Participants whose preferred language is Spanish are administered the NIH Toolbox Spanish translation. DISCO participants complete the tests that assess attention,[25] executive and memory domains,[26] and episodic memory[27 28] because of the overlap between Alzheimer's disease and vascular cognitive impairment (cerebral small vessel disease) in this age group.[29]

A second measure of cognitive abilities is determined using the PROMIS Applied Cognition Abilities Instrument, which is a 16-item measure evaluating self-impressions of cognitive function in the previous 7 days in areas such as mental acuity, concentration and memory.[30]

Sleep assessment

We are using several methods to assess sleep health in the DISCO study that are consistent with gold-standard measures for in-home unattended assessments in observational population studies.

Wrist actigraphy

Sleep-wake activity is measured over 7–8 days using wrist activity monitors (Actiwatch Spectrum Plus or Pro, Philips Respironics). Wrist actigraphy has been validated against polysomnography (the gold standard of sleep measurements), demonstrating a high correlation for sleep duration among both people with insomnia (r=0.82) and in healthy people (r=0.97) with a discrepancy ranging from 12 to 25 min.[31] This method is thought to be a more accurate representation of habitual sleep patterns than polysomnography because it is less disruptive to sleep, can be carried out in the home, and is usually averaged over multiple days. Participants also complete a simple sleep diary and are asked to push the event marker button each time they try to go to sleep and when they wake up.

The actigraphy recordings are scored by a trained technician following specific study guidelines regarding the use of event markers, sleep diary and the activity and light data from the device. We document which method was used to determine the start and end of all rest intervals. All scored recordings are reviewed by PI and Sleep Specialist Dr. Knutson. We use the validated algorithms included in the Actiwatch software analysis system (Actiware) to calculate several measures for each rest interval. The primary actigraphic estimates of habitual sleep include: (1) sleep duration, (2) sleep percentage (%, the sleep period actually spent sleeping) and (3) sleep fragmentation (an index of restlessness). We also are calculating rest-activity rhythms and sleep regularity indices using previously published methods.[32 33]

Type 2 polysomnography

Attended, in-laboratory, full-polysomnography recordings are the gold-standard method to assess sleep architecture (ie, sleep stages) and respiratory events; however, this method is burdensome on the subject. Thus, we have selected an easy-to-use electroencephalography (EEG) monitor that can be self-applied and worn at home. We are using the Sleep Profiler system (Advanced Brain Monitoring, Carlsbad, California, USA) to assess sleep stages, spectral power and respiratory events. The system has configurable acquisition of up to six channels of electrophysiological signals to acquire EEG, electromyography, electrooculography and electrocardiography signals. The device also includes respiratory measures via airflow adapter, cannula, wireless WristOx, Thorax and Abdomen Piezo belts. Several validation studies have been performed comparing the Sleep Profiler to polysomnography and demonstrated strong agreement between these methods.[34 35] In addition, analysis of two nights of recording demonstrated stability in the measures of the sleep stages, indicating the Sleep Profiler provides valid measures of sleep stages with a single night.[36]

Participants are asked to wear the device for one night and are given detailed instructions and demonstrations, along with both videos and written instructions. The system firmware monitors signal quality to ensure that the sensors are properly applied and that high-quality signals are being acquired. Impedance checking is automatically initiated when acquisition begins. Voice messages are delivered to the patient if the impedances are too high or the sensors have become detached. We disable any voice messaging during sleep, however, because we do not want to impair the sleep of the participants. The acquired signals are saved in a universal data format (European Data Format) that can be analysed with third party software, if needed. For our primary analyses, we are using the Sleep Profiler cloud that includes automatic scoring and staging. The pulse rate is analysed to detect autonomic activation. Head movement is used to assist in detecting sleep/wake and to identify periods with gross movement which result in artefact or indicate behavioural arousals. The software provides visual presentation of the recordings and the ability to rescore by a technician.

All recordings are reviewed by a trained technician who modifies the analysis if needed.

The Sleep Profiler System provides the following measures: minutes and percentage of stages of rapid eye movement (REM) sleep, non-REM sleep (N1, N2, N3), sleep latency, wake after sleep onset (WASO), sleep efficiency, arousals, pulse rate and average power spectra, including delta (or slow-wave activity). The software also detects apnoeas and hypopnoeas based on either 3% or 4% desaturation. We are using the American Academy of Sleep Medicine definition of hypopnoea when there is a ≥3% oxygen desaturation from pre-event baseline and/or the event is associated with an arousal.[37] We then calculate the Apneoa–Hypopnoea index (AHI; events/hour).

Sleep questionnaires

Participants complete several questionnaires to assess subjective sleep quality and chronotype preferences.[38] The following validated instruments are collected at both time points: the Pittsburgh Sleep Quality Index,[39] Insomnia Severity Index,[40] Morningness-Eveningness Questionnaire,[41] Epworth Sleepiness Scale[42] and the Brief Index of Sleep Control.[43] See table 2 for a description of each instrument.

Other measurements

Cerebral blood flow velocity is assessed via transcranial Doppler (TCD) ultrasound measurements.[44] TCD provides a powerful tool for non-invasive assessment of cerebral vascular responses to various physiological challenges such as motor or cognitive activation or change in blood pressure and end-tidal carbon dioxide, which we know are regulated at the level of arterioles or resistance vessels of the brain (cerebral small vessels). After 10 min of resting data are recorded, participants perform cognitive tasks and then perform the cerebral vasoreactivity test, which is assessed using the CO2 breathing and hyperventilation method. The resting data are used to calculate cerebral autoregulation and pulsatility index, the cognitive trial will be used to calculate neurovascular coupling and the breathing trial will be used to measure vasoreactivity. These cognitive tests are completed only at baseline for all but a small proportion of participants (<5%).

Table 2 lists the remaining domains that are assessed in the study. We selected these domains with the goal of capturing the multidimensional factors that could influence sleep or cognitive function. We assessed a broad set of social determinants of health that we know underlie disparities in health behaviours and disease outcomes by race and ethnicity. All questionnaires that did not have Spanish language translations available were translated by our study team or professional translation company and reviewed by two additional Spanish-speaking coinvestigators.

Sociodemographic characteristics including race, ethnicity, age and educational level were determined based on self-report from the participants. Wherever possible, validated questionnaires were used to assess covariates that we hypothesised were associated with sleep, cognitive function or both.

Participants are also asked to walk across a 25 ft mat (ZenoMat, Protokinetics, Pennsylvania, USA) and their walking speed is measured during two trials in order to measure gait speed, which has been strongly associated with blood pressure, cardiovascular disease and stroke.[45–48]

DATA MANAGEMENT

Sample size and power calculation

Analyses in both aims will include the entire proposed sample of 495 recruited participants. Power to detect clinically meaningful effect sizes were calculated conservatively assuming 9% (n=450) and 18% (n=405) of participants would have missing data for primary analyses or would be lost to attrition. A study that examined sleep quality, including percentage of WASO,[49] found that sleep after days with lower subjective stress had a lower percentage of WASO than sleep after days with higher stress (mean WASO%=12.2% vs 16.4%, SD=12.1% vs 14.9%). We have 91% power to detect these differences with the proposed sample of 450 participants and 87% power to detect this difference assuming 10% attrition (n=405) in aim 1 analyses. For power analyses using the structural equation modelling approach in aim 2, we calculate the power to detect both unacceptable model-fit using root mean square error of approximation (RMSEA) and effect sizes. With a sample size of n=450, we achieve 92% power to detect an RMSEA of 0.1 (unacceptable model fit) against the null hypothesis of RMSEA=0.5 (good model fit). With a sample size of n=450 participants and using RMSEA=0.05 under the null hypothesis of a good model fit and RMSEA=0.1 under the alternative hypothesis of unacceptable model fit, we can achieve a power of 92% by observing 5 variables of interest. Assuming 10% are lost to follow-up after baseline, with the sample size of n=405 we can achieve a power of 89%.[50] With the proposed sample size, we can achieve an effect size of 0.2 (small-moderate effect size) with five observed variables and five latent variables.[51 52] Furthermore, with n=405, we achieve 87% power to detect an OR of 3:1 in cognitive decline for the group with adequate sleep compared with the group with inadequate sleep.

The definition of 'inadequate sleep' will vary based on the hypotheses under study. We are capturing a comprehensive set of measures of sleep health including habitual sleep as well as sleep architecture. We plan to examine multiple dimensions of sleep health, including sleep duration and wake after sleep onset (WASO), but in secondary analyses we can explore the wealth other measurements that we collected and develop a composite 'sleep health' score as has been proposed in the literature. We have the flexibility to generate composite sleep health scores so that we can produce research that is aligned with contemporary research objectives.

Quality control and quality assurance

Study data are collected using electronic methods that constrain response ranges to plausible ranges. Participants either enter responses directly into the REDCap system or data are entered by study staff members who interviewed study participants. The analytical team meets monthly to review data regarding data completeness, data quality and additional data topics as needed. This process will ensure proper data management, scoring of questionnaires and completion of study procedures in a timely manner.

Data analysis plan

General considerations

In all analyses, distributional characteristics of each measure and residual diagnostics will be used to assess modelling assumptions. As needed, transformations, non-parametric methods and/or inclusion of higher-order (quadratic, cubic, interaction, etc) terms may be considered in analytic models. Statistical estimates (eg, regression coefficients) will be reported with accompanying 95% CIs and p values as applicable. We will use type I error rate of 0.05 to assess statistical significance, while also qualitatively determining if the effect magnitude is clinically meaningful.

Missing data

The multilevel models planned for analysis of longitudinal data are generally robust for unbalanced data across study time points. Nonetheless, multiple imputation with chained equations will then be used to examine the sensitivity of findings to missing data.[53] For non-ignorable missing data, we will conduct sensitivity analyses using non-ignorable pattern-mixture and selection models to investigate the robustness of our conclusions across the different models for missing data.

Analyses for aim 1

To evaluate the contribution of psychosocial characteristics to sleep disparities, we will compare the coefficient estimate for race in models including vs excluding each characteristic of interest. The base model for the primary analyses will be a linear regression model with WASO duration as the outcome and race, sex and age as explanatory variables. Each subsequent model will add a psychosocial characteristic (eg, depressive symptoms) to the base model and calculate the percentage reduction in the estimated coefficient for race in the expanded model compared with the base model. This same modelling strategy will be used to evaluate the contribution of characteristics to disparities in self-reported sleep quality (eg, PSQI) or sleep disorders. Secondary analyses will examine the cross-sectional associations between measured psychosocial variables and objective and subjective measures of sleep. We will fit regularised regression models (eg, LASSO, elastic net) for each sleep outcome (eg, WASO, PSQI) that include interaction terms between race and psychosocial characteristics to assess effect modification by race.[54] These models will be adjusted for sociodemographic characteristics and comorbidities measured at the baseline visit. The final models will identify the psychosocial variables that best explain each sleep outcome. Additional analyses will stratify by obstructive sleep apnea (OSA, ie, AHI<or≥15) and by sex. OSA is not an exclusion.

Analyses for aim 2

We will assess whether WASO is associated with greater cognitive decline over 24 months via mixed-effects models for change in continuously determined cognitive function score, with a random intercept for participant to account for the correlation that arises from measuring multiple time points from an individual.[55] The mixed-effects models will be adjusted for time-invariant (eg, sex) and time-varying (eg, body mass index, comorbid disease) covariates. Results from this analysis will inform whether baseline sleep measurements or change in sleep measurements will be used in subsequent analyses. To assess whether WASO mediates racial/ethnic differences in change in cognitive function over 24 months, we will use two approaches to mediation analysis: the Baron and Kenny mediation method and Vanderweele's causal mediation method, which allows for interactions between the independent and mediator variable.[56–58] Furthermore, we will test for interactions between the sleep variables and race/ethnicity to determine if different aspects of sleep vary by race. We will use the same analytic approach to test to what extent cerebral vascular blood flow or insulin resistance mediate the association between WASO and other sleep metrics and cognitive function.

ETHICS AND DISSEMINATION

The DISCO study is approved by the Northwestern University Feinberg School of Medicine Institutional Review Board. As stated above, informed consent is obtained in writing from participants and stored in Study Tracker. All data will be deidentified before sharing the results, posing no risk to participant confidentiality.

Deidentified datasets will be shared via the BioLINCC repository following the completion of the study. In addition to the ongoing processing of biospecimens during the study, study investigators are banking serum, plasma and buffy coat. Samples that are not being analysed can be made available to qualified investigators with a materials transfer agreement and/or data use agreement as applicable. The study investigators will review and consider all requests that do not lead to participant burden nor conflict with the primary aims of the study.

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Contributors All authors have contributed to the design of this protocol. AG, DC, FS, KH, KK, MC, PCZ, SA and T-HV initiated and conceptually designed the project. SC is acquiring data. This protocol was drafted by KH, KK, MLP, MC, MW, SC, SJA and SSR, and was refined for critically important content by DC, SSR and T-HV. Statistical advice was provided by MW and SJA. KK and MC obtained funding for the study. All authors approved the final manuscript.

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Competing interests None declared.

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