ARIC Manuscript Proposal #4336

PC Reviewed: 10/10/23	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Associations of Accelerometry-Derived Sleep, Sedentary Behavior, and Physical Activity with Cognitive Outcomes: A Compositional Data Analysis Approach

b. Abbreviated Title (Length 26 characters): Compositional Analyses & Cognition

2. Writing Group [please provide a middle name if available; EX: Adam Lee Williams]:

Writing group members (order TBD):
Jill A Rabinowitz, PhD (first and corresponding author)
Lin Yee Chen, MD
Josef Coresh, MD, PhD
Ciprian Crainiceanu, PhD
Anis Davoudi, PhD
Ryan Dougherty, PhD
Lacey Etzkorn, PhD
Rebecca F. Gottesman, MD, PhD
Pamela Lutsey, PhD
Francesca R. Marino, BS
Priya Palta, PhD
Jennifer A. Schrack, PhD
Adam P. Spira, PhD
Amal A. Wanigatunga, PhD, MPH
Sarah K. Wanigatunga, BS
Hau-Tieng Wu, PhD
Vadim Zipunnikov, PhD

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _JR____ **[please confirm with your initials electronically or in writing]**

First author [please provide a middle name if available; EX: Adam Lee Williams]:
Address: 624 N. Broadway
Hampton House, Rm. 880
Baltimore, MD 21205

Phone: 410-955-1906
E-mail: jrabino3@jhmi.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

Name: Adam P. Spira, PhD
Address: 624 N. Broadway
Hampton House, Rm. 794
Baltimore, MD 21205

Phone: 650-575-9927 Fax: 410-614-9498
E-mail: aspira@jhu.edu

3. Timeline:

We expect that data cleaning and analyses will take 3 to 6 months, and manuscript writing and submission should take another 9-12 months.

4. Rationale:

The benefits of physical activity in reducing risk for cognitive impairment, dementia, and Alzheimer's disease (AD) and related dementias (ADRD) have been well established.[1-8] Excessive sedentary behavior and both short and long sleep duration have also been linked to poorer cognitive outcomes and an increased likelihood of dementia and ADRD.[9-12] Moreover, sleep, sedentary behaviors, and physical activity are all modifiable,[1, 13, 14] and may represent important intervention and treatment targets to reduce risk for cognitive impairment, dementia, and ADRD.

There are important limitations to extant work examining associations of sleep, sedentary behaviors and physical activity with cognition and brain health. First, most of the available research on this topic has assessed sleep, sedentary behaviors, and physical activity via self-report.[9, 15-17] Self-reports of these behaviors may be influenced by social desirability and recall biases, as well as cognitive impairment. Wearable technologies, such as accelerometers, can provide objective measures of activity and sleep and more detailed information that may not be captured through subjective reports.[18, 19] Second, traditional approaches to analyzing sleep, sedentary behavior, and physical activity have focused on individual domains and have often studied these constructs independently of each other.[20, 21] Approaches that focus on one domain (i.e., that are domain-specific) do not take into account the fact that these behaviors are compositional in nature.[20, 22] Stated another way, time spent in these behaviors creates a composite of a 24-hour period and modifying the time spent in one behavior simultaneously changes the amount of time available to spend on the other two behaviors.

Compositional data analysis can be used to model individual differences in the distribution of time spent in sleep, sedentary behavior, and physical activity in relation to cognition and brain health.[21] Numerous studies have used compositional data analysis approaches to examine the impact of self-reported sleep, sedentary behavior and physical activity on obesity and cardio-metabolic health outcomes,[23-25] mental health,[26] and mortality.[24, 25] However, few studies have used a compositional data analysis approach to study objectively measured activity/sedentary behavior/sleep in relation to cognitive outcomes. Available work has shown that redistributing time from sedentary behavior to moderate to vigorous physical activity

is linked to better cognitive outcomes among adults.[27, 28] Other work has shown that substituting 30 min/day of sleep with 30 min/day of sedentary activity, walking/bicycling, or moderate-to-vigorous physical activity is linked with better cognitive performance among individuals with excessive sleep (i.e., > 7 hours).[28]

Leveraging a compositional data analysis framework, the current study will examine the effect of 24-hour temporal compositions including time spent in accelerometry-derived sleep, sedentary behaviors, and physical activity on cognitive outcomes, including cognitive performance and mild cognitive impairment (MCI) or dementia.

5. Main Hypothesis/Study Questions:

Using compositional data analysis, the proposed analyses will investigate the association of accelerometry-derived times spent in sleep (SL), sedentary behavior (SB), and physical activity across consecutive 24-hour periods on cognitive performance and mild cognitive impairment (MCI)/dementia among adults. Considering all pairs from the three types of behaviors (i.e., SL, SB, and PA), we will study the association between daily compositions of time and cognitive performance, MCI, and dementia risk. We will further investigate the association of the (1) relative compositions of SL and wake behaviors (i.e., SB, PA), and (2) relative compositions of movement behaviors (SB, PA) with cognitive outcomes. Given no prior research has used compositional data analysis to examine individual differences in SL, SB, and PA in relation to cognitive outcomes -and that sleep and cognition have a u-shaped association- we do not have a priori hypotheses.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

We will study participants who completed wrist actigraphy and had available data on cognitive performance, and MCI/dementia at Visit 9. Actigraphy data were collected using the Actigraph Link (GT9x) (Actigraph, Pensacola, FL) wrist worn accelerometer from 1329 participants. While wearing the actigraph, participants were requested to fill out a sleep log and record the time they got into bed with the intention of sleeping, got out of bed or no longer intended to sleep, and took off the device. All data will be scored by two staff members, using the times listed on the diaries along with activity counts to identify in-bed intervals. A validated algorithm was applied to identify "in-bed" intervals (Ancoli-Israel et al., 2003). We will include observations with ≥3 days of actigraphy data.

Of the 1329 participants with actigraphy data, ~1,300 were also adjudicated for MCI and dementia and completed a cognitive battery, which consisted of tests that assessed executive function/processing speed, language, memory, and global cognition and a shorter subset of tests ("Block A").[29] In terms of cognitive outcomes, we will use domain-specific factor scores for executive function/processing speed, language, memory, and global cognition.

The proportion of time spent engaging in sedentary or active behaviors will be calculated using minute level activity data (raw counts) across all the valid days. For each subject, the log ratios of the compositions log will be obtained as compositional metrics, which will represent the proportion of time spent in one activity relative to another. Cognitive outcomes will be modelled using cross-sectional regression models with log-ratios of time spent within each behavior pair

(i.e., SL, SB, and PA) as key predictors, while adjusting for participant demographics (e.g., age, sex, race), education, BMI, and physical health comorbidities.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes _X___ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes _X___ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.
ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

4253: Association of Circadian Rest/Activity Rhythms with MRI Measures of Brain Health in ARIC (Spira)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _X___ Yes ____ No

11.b. If yes, is the proposal

__X_ A. primarily the result of an ancillary study (list number* 2014.18 & 2021.01)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

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