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Examination of Baseline Physical Activity and Cognitive Function Data in Middle-Aged and Older Adults

CAMRYN CHAFFEE
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Reviewed and approved* by the following:

David Conroy
Professor of Kinesiology and Human Development & Family Studies
Thesis Supervisor

Mark Dyreson
Professor of Kinesiology and Affiliate Professor of History
Honors Adviser

* Electronic approvals are on file.

ABSTRACT

Introduction. Alzheimer's Disease impacts over 6.5 million Americans and the estimated cost for caring for people with Alzheimer's disease in the United States is $321 billion. The overall objective of this honors thesis was to examine the relationship between physical activity and cognitive function as a method for determining further areas of Alzheimer's Disease research. As part of the DOSE Feasibility Trial, baseline data was collected and used for analysis. **Methods.** Participants from two age groups, middle-aged adults (40-59 years) and older adults (60-80 years), who owned an Apple Watch were enrolled in this study ($N = 13$). Participants wore an activPAL activity monitoring device for one week while also completing cognitive tests through an app four times daily. The devices were then returned to the study lab where the data was downloaded for each participant. The cognitive function app assessed data through the Mobile Monitoring of Cognitive Change (M2C2). **Results.** The majority of the sample was female (n = 13, 93%), White (n = 12, 86%), and had a bachelor's degree (n = 6, 43%) with a mean age of 52.4 years. Using a multiple regression analysis, it was found that physical activity variables did not statistically significantly predict processing speed, $F(3,9)$, $p = 0.351$, $R^2 = 0.30$ or predict Grid Memory accuracy, $F(3,9)$, $p = 0.964$, $R^2 = 0.029$. **Discussion.** The baseline results from this study showed that our study protocol was feasible for recruiting participants and having them complete baseline procedures. Although underpowered, a non-significant trend suggested that adults with higher step counts had superior accuracy in working memory. Overall, the findings support the hypotheses that increased physical activity through MVPA and daily step counts are associated with better cognitive function, and that sedentary time is correlated with worse cognitive function.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

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Chapter 1

Introduction

Alzheimer's Disease Overview

Over 6.9 million Americans are currently living with Alzheimer's disease, including 1 in 9 people over 65 years (2024 Alzheimer's Disease facts and figures, 2024). This is a continuing public health concern because of the prevalence of the disease, impacts on individuals and families, health burden, and the estimated cost of $321 billion for caring for people with Alzheimer's disease in the United States (Dhana et al., 2023). Alzheimer's disease is a brain disease caused by damage to neurons in the brain which are responsible for memory and language. (Dhana et al., 2023). Alzheimer's is a progressive disease that continues to worsen over time and is characterized by symptoms of forgetfulness, problems thinking, language troubles, changes in mood, wandering, and difficulty forming memories (2023 Alzheimer's Disease facts and figures, 2023). Once Alzheimer's disease develops further into an individual being unable to perform everyday activities, it is classified as Alzheimer's dementia. Alzheimer's disease is ultimately fatal as more neurons are damaged, including those responsible for swallowing, walking, and other essential functions. Although there are treatment options to manage and reduce symptoms, there is no current cure for Alzheimer's, thus early detection and prevention is essential. To reduce the future incidence of dementia and Alzheimer's disease, there is a need for interventions that focus on the disease process from its earliest stages. Midlife is a critical period for the beginning of dementia pathology, which makes research on interventions targeting this age group increasingly important (Irwin et al., 2018).

One of the earliest symptoms of Alzheimer's is the individual forgetting newly introduced information, repeating the same questions frequently, and a need for more memory reminders, such as notes, to remember daily tasks and activities. Another symptom is confusion around the time, place, or people around them. A dangerous activity that is common in Alzheimer's patients is known as wandering. This is when individuals walk away from a place, but they may forget where they are trying to go and do not know how to get back to where they came from, which can put them in danger. In addition to wandering, individuals may also misplace items and be unable to retrace their steps to find it. They may start placing items in unusual places and forget that they had moved it, which can lead to more confusion, or even thoughts that someone else has stolen the item, especially as the disease progresses. Patients may have difficulties performing everyday tasks such as cooking, playing a familiar game, or organizing a shopping list. Lastly, Alzheimer's disease patients may have difficulty solving problems, understanding visual images, and develop new issues with speaking, writing, and vocabulary (2024 Alzheimer's Disease facts and figures, 2024). Due to these symptoms, cognitive tests that measure processing speed and working memory can index key functions impacted by this disease.

Once Alzheimer's dementia develops further into the most severe form, individuals are at risk for many more severe complications. Their ability to communicate diminishes and individuals will need constant care in order to ensure their safety. Damage to neurons that are involved in movement will lead many patients with the inability to walk or maintain mobility, which can lead to physical complications such as blood clots, sepsis, or skin infections from increased time in sitting and laying positions (2024 Alzheimer's Disease facts and figures, 2024). Eventually, neurons that are responsible for swallowing can be damaged, which can cause individuals to swallow foods into their trachea instead of their esophagus, causing aspiration pneumonia and possibly death. In the United States, deaths from Alzheimer's disease have continued to rise and be a leading cause of disability, morbidity, and death in the population. Because of the detrimental effects of this disease, it is important for interventions to target middle-aged and older adults in an effort to prevent and reduce the incidence of Alzheimer's disease.

Global Impact of Alzheimer's Disease

Globally, more than 25 million people are affected by dementia and Alzheimer's disease, and it is projected that Alzheimer's disease will impact over 106 million people by the year 2050 (Qiu et al., 2009, Brookmeyer et al., 2007). This can be attributed to the ageing of the world's population, with the number of people over the age of 65 expected to increase from 420 million in 2000 to approximately 1 billion by the year 2030 (Qiu et al., 2009). Developing countries are also projected to experience an increased burden of an older population in comparison to already developed countries. Developing nations are seeing the largest increase in older persons, with their share of the worldwide ageing population increasing from 59% to 71% (Qiu et al., 2009).

Interventions aimed at delaying the onset of Alzheimer's could be an effective strategy for reducing the global disease of Alzheimer's. Prevention programs and therapeutic treatments that could delay disease onset by one to two years could reduce the worldwide prevalence of

Alzheimer's by about 22.8 million cases (Brookmeyer et al., 2007). Therefore, there has been an increase in efforts to find a cure for Alzheimer's disease or effective preventation strategies.

Preventing Alzheimer's Disease

In addition to possible medications and biological treatments for Alzheimer's disease, there is also ongoing research on risk factors that are modifiable through lifestyle changes. The first set of risk factors that have been investigated for its association with Alzheimer's disease involves vascular risk factors. The presence of hypertension, diabetes, smoking, obesity, stroke, or cardiovascular disease at midlife increases Alzheimer's risk (Sindi et al., 2015). One randomized control study, FINGER, aimed at preventing cognitive decline and dementia in community-dwelling older adults through modifiable lifestyle changes and monitoring vascular risk factors. They found a significant beneficial impact on the intervention group, with their cognition scores being 25% higher than their control group counterparts at the completion of the study (Sindi et al., 2015). Another study found a strong correlation between high systolic blood pressure and high serum cholesterol in midlife and the risk for Alzheimer's disease later in life. An even greater risk was found when there was a combination of these two risk factors, rather than either on its own. It was concluded that the treatment of hypertension and hypercholesterolemia may have implications for the prevention of Alzheimer's disease later in life (Kivipelto et al., 2001).

Another modifiable factor that has been found to influence risk of Alzheimer's disease involves the amount of mental activities that an individual performs on a regular basis. Some activities that are labeled as mentally demanding and have shown a protective effect on developing Alzheimer's include knitting, dancing, playing board games or musical instruments, gardening, or reading. Multiple studies have found that more complex work and higher-level cognitive activities have shown to reduce the rate of hippocampal atrophy as well as the risk for vascular dementia (Qiu et al., 2009). Overall, current studies have shown that there are many modifiable risk factors that could decrease the risk of an individual developing Alzheimer's disease. Although current research is promising, there is still a need for further studies with an aim to prevent or treat Alzheimer's disease more effectively.

In addition to blood pressure management and cognitive training, many recent studies have indicated that physical activity could have an impact on cognition in older adults and be used as a prevention method for Alzheimer's. The 2018 Physical Activity Guidelines Advisory Committee conducted a systematic review and concluded that moderately strong evidence has indicates that long-term moderate-to-vigorous physical activity has a positive effect on cognitive outcomes in older adults over the age of 50 years (Erickson et al., 2019). In cognitively healthy adults, studies have shown that regular physical activity is associated with a delay in the onset of dementia or Alzheimer's disease (Qiu et al., 2009).

Pozo Cruz and colleagues found that increasing steps per day as well as participating in intensive exercise are associated with lower risks of dementia (2022). One method for increasing daily step counts involves the use of momentary feedback prompts to self-monitor (i.e., recall and record) physical activity. Studies have shown that having a step goal is a key predictor of physical activity (Vetrovsky et al., 2022). It was found that there is a dose-response relationship between the frequency of self-monitoring and physical activity, possibly due to the cognitive task of recalling and encoding physical activity from memory to create a behavioral change (Conroy et al., 2023). The daily frequency of smartwatch-based self-reporting prompts was associated with increased physical activity, with the largest effect seen at three self-monitoring prompts, which guided our use of three prompts daily in this study (Conroy et al., 2023). Self-monitoring may be a helpful method in increasing physical activity in older adults to preserve their cognitive function. The significance of these findings has led to further research investigating the impact of self-monitored exercise on cognitive function.

Future Alzheimer's Disease Research

This study aims to research the effects of physical activity on cognitive function and if modifying activity habits can improve cognitive function outcomes. For the purpose of this thesis, only baseline data will be used for data analysis and conclusions, however this data is from a pilot 6-month randomized controlled trial. This research is aiming to advance on the previous research on physical activity and cognitive function by determining both the feasibility and effectiveness of smartwatch prompts to increase physical activity. The trial aimed to recruit a diverse study population to support research on health disparities in both physical activity and cognitive function and to accurately measure the future burden of disease, determine differences in risk for Alzheimer's between races, and understand how risk factors and interventions work on different populations (2023 Alzheimer's Disease facts and figures, 2023). We hypothesized that participants will enroll in the study and complete baseline measures. Additionally, we hypothesize that participants accumulating more physical activity at baseline will exhibit faster processing speed and fewer working memory errors than participants accumulating less physical activity (either daily step counts or moderate-to-vigorous physical activity duration). Lastly, we hypothesized that participants with higher amounts of daily sedentary behavior at baseline will have less accurate working memory than participants with less daily sedentary behavior time. This research study can add to the field of Alzheimer's disease research by determining the feasibility of trial recruitment and baseline measurement completion and validating physical activity to increase physical activity in older adults, and whether that is associated with an improvement in cognitive function.

Purpose of Study

Alzheimer's disease is a global health problem that is continuously growing. It is characterized by complex biological mechanisms for disease and minimal methods of treatment or prevention. To reduce the global impact of Alzheimer's disease and cognitive decline, we investigated the feasibility of recruitment and assessment procedures for a trial evaluating a physical activity intervention to promote cognitive function in midlife and older adults. The results from the parent trial could be an important step in determining an effective strategy for delaying the onset or preventing Alzheimer's disease and reducing the global burden of disease. Data from the baseline assessment will be used to evaluate the feasibility of recruitment and assessment procedures and to evaluate descriptive relations between physical activity, sedentary behavior, processing speed, and working memory. I hypothesized that individuals with higher baseline moderate-to-vigorous physical activity levels, step counts, and lower amounts of sedentary time will have higher cognitive function scores than those with lower amounts of physical activity or more sedentary behavior.

Chapter 2

Methods

Participants

This observational study used baseline data from a two-arm parallel group randomized controlled trial, involving midlife and older adults. Participants range in age from 40 to 80 years and recruitment was stratified between middle-aged adults (40-59 years) and older adults (60-80 years). Participants were eligible if they owned an Apple iPhone and Apple Watch, were proficient in English, were capable of providing informed consent, and were willing to complete full six-month study protocol. Participants were excluded if they live outside the continental United States, self-reported more than 90 minutes per week of moderate-to-vigorous physical activity, have any mobility restrictions that do not allow them to exercise unassisted, are pregnant or planning to become pregnant, are planning to have surgery during the study duration, concurrently participating in another study involving physical activity or weight loss, or if they already have an Alzheimer's disease or other cognitive impairment diagnosis. Recruitment of participants was completed through a Facebook advertisement, which was promoted on the website to increase enrollment of participants, as well as through Research Match. This study was conducted with Institutional Review Board approval.

Measures

Physical activity was assessed by activPAL activity monitors (PAL Technologies, Glasgow, Scotland). This device logs minute-level step counts, duration of time with a step cadence of at least 100 steps per minute, and sedentary time. Daily sedentary time is measured through recorded sitting time and moderate-to-vigorous physical activity (MVPA) was calculated using the variable of stepping time with a cadence greater than or equal to 100 steps per minute.

The baseline questionnaire and demographic data was collected using REDCap (Research Electronic Data Capture) project database. Once verbal consent was obtained from the participants, REDCap automatically emailed the questionnaire to the participants, including questions on demographic data (Harris et al., 2009).

Cognitive function was assessed using the Mobile Monitoring of Cognitive Change framework implemented in a mobile application called Catalyst by MetricWire (Sliwinski et al., 2018). Assessments were distributed four times daily, and each assessment incorporated 18 Symbol Search trials to measure processing speed, and 4 Grid Memory trials to measure working memory. The first cognitive test, Symbol Search, gave the participants a set of three flashcards at the top of their screen and then another set of two flashcards at the bottom. Each flashcard has two symbols, and the participants needed to match a flashcard from the bottom of the screen to a flashcard at the top with the same symbols. Processing speed was assessed using the average reaction time on correctly-matched trials in the Symbol Search task. The second cognitive test, Grid Memory, gave the participants a 5x5 grid with three red dots placed among the boxes. They are asked to memorize where the dots are located. Another screen then appears with a grid of letter “E”s and letter “F”s and the participants needed to click on each “F” to turn it into an “E”.

A blank grid then pops up and the participants were asked to place the three red dots where they remembered them being located. Working memory was assessed using the proportion of correctly-placed dots on the Grid Memory trials (as opposed to the Euclidian distance measure often used). These mobile cognition tests have shown validity in detecting mild cognitive impairment through processing speeds and short-term memory binding. Findings from previous studies have shown that cognitive test results are consistent between laboratory testing and smartphone assessments (Cerino et al., 2021).

Procedures

Participants who saw a study ad expressed interest by completing an online screening questionnaire via a link in the study ad. Once the participants filled out the initial eligibility questionnaire, those eligible were contacted via phone call to schedule their first Zoom visit if they were still interested in participating. Contact information and mailing addresses were confirmed for the mailing of the activity monitors. After scheduling the initial Zoom visit with the participant, the date and time were entered into a REDCap project database, which automatically sent an email to the participant confirming their meeting date and time with the consent form attached, as well as reminders before the meeting occurred (Harris et al., 2009). Prior to the initial Zoom meeting, the activPAL device's serial number was recorded with the participant's study ID number and placed in a package along with a printout of the study overview packet, alcohol wipes, medical adhesives, and a pre-paid and labeled return envelope. This was mailed to participants approximately one week before their initial Zoom meeting.

During the first Zoom visit, participants were given an overview of the study and verbal consent was obtained. They then filled out a baseline questionnaire distributed through REDCap while on the call, which asked them about their physical activity, cognition, and attitudes towards both. Next, they were given instructions on how to use the necessary study materials. The participants were informed that the device is secured on the midline of the thigh with medical tape after the area has been cleaned with an alcohol wipe. They were instructed to apply the device later on the same day as the meeting and to wear the device for one week to obtain baseline measurements. After the one week of wear, they were asked to remove the device and place it in the mailing envelope to send back to the lab for data collection.

Next, the participants were shown how to download the Catalyst application on their phone and login successfully. After installation, they were asked to take the one-time survey available that allowed them to input their start day as the following day, as well as their average wake-up time to avoid notifications occurring during sleep. Next, the participants were educated on the cognitive tests that they would be asked to complete. They were given directions on how to complete the Symbol Search and Grid Memory cognitive tests, as well as on how many times daily they would complete these tasks, and to perform these tasks as quickly and as accurately as possible. Lastly, the app gave the participants a survey asking if they were distracted during the tests, how distracted they were, and what distracted them. Participants received notifications to complete these cognitive tests four times daily during the study period that they wore the activPAL device.

Chapter 3

Data Collection and Analysis

The cognitive tasks were completed using a mobile app-based cognitive testing platform called Mobile Monitoring of Cognitive Change (M2C2). This program allowed us to monitor participant adherence, as well as when cognitive tests were administered and completed. Additionally, data from each participant could be downloaded, including their average completion time and accuracy for each trial on each cognitive test. Response time for the symbol search test was calculated only using response time for correct trials.

The activPAL device was used to measure physical activity of the participants and provided an output that was used for interpretation. After receiving the device back in the mail, it is plugged into the PALconnect base, where the data are uploaded to the computer. The computer software, PALanalysis, displays all participant data through both numerical and graphical outputs. This data was downloaded into Microsoft Excel format where the data was cleaned. A valid day of activPAL data is classified as a day in which the participant wore the device for 20 hours or more. Only valid days were used for the analysis of activPAL data and participants with less than four valid days were treated as missing. PALanalysis version v8.11.8.75 was used.

Lastly, the responses for each baseline questionnaire were downloaded into Microsoft Excel from RedCap. The data was cleaned in Excel and recoded for specific variables. To evaluate the impact that physical activity has on cognitive function, both sets of data were uploaded into the Statistical Package for Social Sciences (SPSS) software for data analysis. Demographic data was analyzed in SPSS using descriptive statistic frequencies and descriptives. A table was created through the SPSS software and displays the demographic data in Table 1.

Next, multiple regressions were run to show the impact of the physical activity variables on the four cognitive function outcome variables. Both tables and scatterplots were generated and are shown in Table 4 and Figures 2 – 6. Lastly, a correlation test was run to determine the association between MVPA, daily step counts, sedentary time, and cognitive function outcomes. This yielded coefficient values, significance values, standard deviations, and 95% confidence intervals. All tables and outputs were created using version 29.02 SPSS software.

Chapter 4

Results

A sample of 14 middle-aged and older adults were eligible, enrolled, and completed all study activities through baseline (Figure 2). We received activPAL devices back from 13 of the 14 participants in time for data analysis (93%). The majority of the sample was female (n = 13, 93%), White (n = 12, 86%), and had a bachelor's degree (n = 6, 43%) (Table 1). The mean age of participants was 52.4 years (SD = 7.861), with a minimum of 40 years and maximum of 62 years. All 13 participants had valid activPAL data from wearing the device for at least 20 hours per day, each with a varying number of valid days (mean = 6.5).

Table 1. Demographics

		Frequency	Percent
Sex	Female	13	92.9
	Male	1	7.1
Ethnicity	Hispanic/Latino	1	7.1
	Not Hispanic/Latino	13	92.9
	Total	14	100.0
Race	Asian	2	14.3
	White	12	85.7
	Black/African American	0	0.0
	American Indian/Alaska Native	0	0.0
	Native Hawaiian/Pacific Islander	0	0.0
	Two or More Races	0	0.0
	Total	14	100.0
Education	Associate’s degree: Academic Program	1	7.1
	Bachelor's Degree, ex: BS, BA, AB, BBA	6	42.9
	Doctoral Degree, ex: PhD, EdD	2	14.3
	High school graduate	1	7.1
	Professional school degree, ex: MD, DDS, DVM, JD	1	7.1
	Master’s Program, ex: MA, MS, MEng, Med, MBA	1	7.1
	Some college, no degree	2	14.3
	Total	14	100.0

Figure 1. Participant Flow Diagram

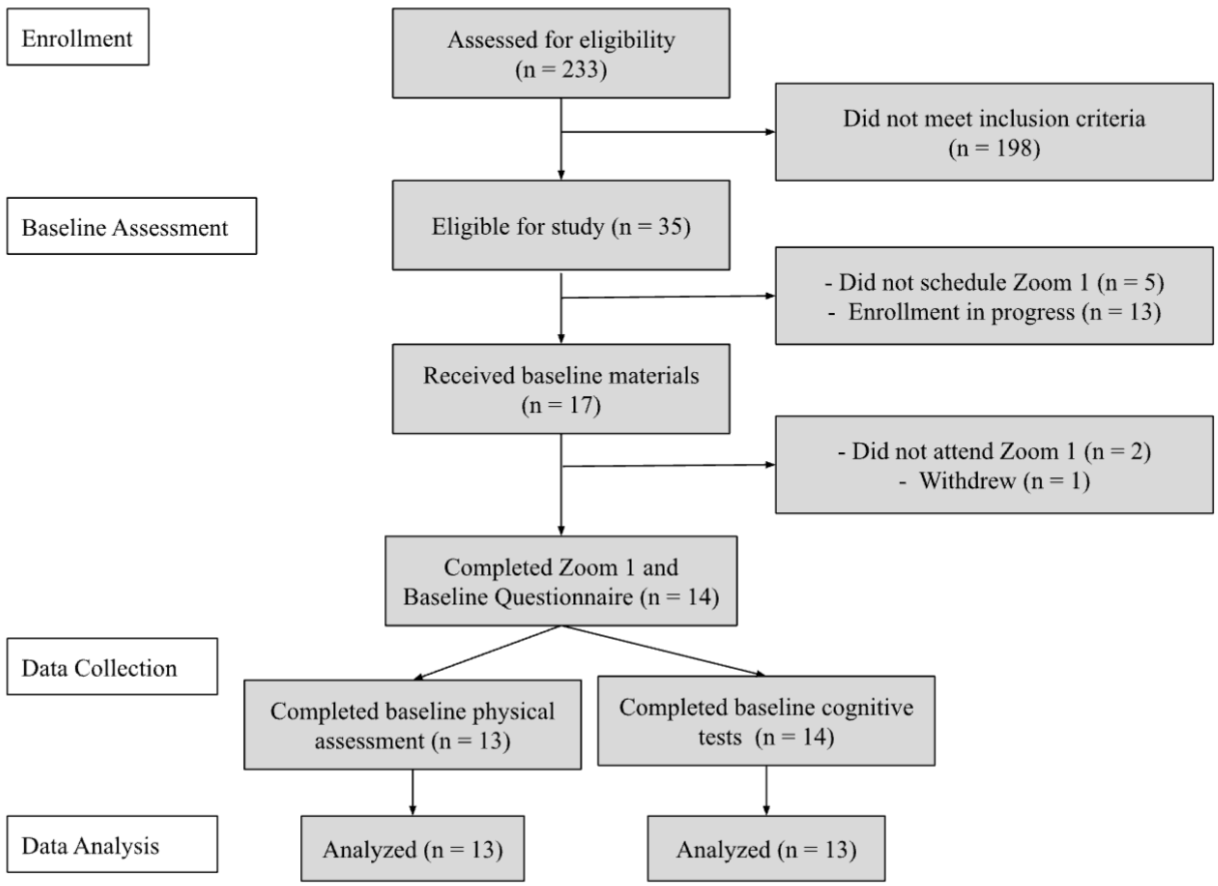


Table 2 shows the baseline activPAL data collected from the participants for average daily duration of MVPA, average daily step count, and average daily sedentary time. Participants took an average of 6,485 steps per day, had an average sedentary time of 515 minutes each day (about 8.6 hours), and an average moderate-to-vigorous physical activity time of 18 minutes per day.

Table 2. activPAL Activity Data at Baseline

	N	Minimum	Maximum	Mean	Std. Deviation
Average steps per day	13	3587.43	10855.43	6485.24	2257.54
Sedentary time per day (in minutes)	13	295.28	855.25	515.64	145.81
MVPA (in minutes)	13	1.04	67.71	17.93	17.42

Table 3 presents descriptive statistics for cognitive tests at baseline. The average time to complete correct trials on the Symbol Search cognitive test was 1,970 milliseconds (SD = 294.76) and average accuracy was 97.25% (SD = 2.45). On the Grid Memory cognitive test, participants had an average of 1.9108 dots correct out of 3 possible (64%).

Table 3. M2C2 Cognitive Data at Baseline

	N	Minimum	Maximum	Mean	Std. Deviation
Symbol Search response time (ms)	13	1569.80	2544.22	1970.07	294.76
Grid response time (ms)	13	3650.84	7554.67	5254.0	1281.78
Symbol Search accuracy %	13	91.56	99.41	97.25	2.45
Grid accuracy (# correct dots out of 3)	13	0.81	2.86	1.91	0.56

Additionally, Table 4 summarizes the results of three multiple regression analyses that regressed processing speed on step count, moderate-to-vigorous physical activity, and sedentary time on cognition using a multiple regression analysis. A multiple regression was run to predict processing speed from step count, MVPA, and sedentary time (Figure 2). These variables did not statistically significantly predict Symbol Search response time, $F(3,9)$, $p = 0.351$, $R^2 = 0.30$, and only average daily step count added statistically significantly ($p = 0.04$). Table 5 summarizes coefficients from a model that regressed working memory on step count, moderate-to-vigorous physical activity, and sedentary time. The physical activity variables did not statistically significantly predict Grid Memory accuracy, *F*(3,9), $p = 0.964$, $R^2 = 0.029$, and no variables added statistically significantly at the $p < 0.05$ level to the prediction (Figure 3).

Table 6 shows the correlation between all physical activity and cognitive function variables. A positive relationship was found between step count and working memory, with the higher the step count, the higher the accuracy for the working memory cognitive tests. A positive correlation was found between steps and response time for Symbol Search. Sedentary time was negatively correlated with Symbol Search response time and Grid Memory accuracy, but not at a statistically significant level. A positive correlation was found between MVPA and processing speed, and a negative correlation was found between MVPA and working memory, although not at a statistically significant level.

Table 4. Multiple Regression of Processing Speed (Symbol Search Response Time)

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	2237.19	552.82		4.05	.003
Average Steps	-.006	.04	-.04	-.13	.902
Sedentary Time	-.72	.67	-.357	-1.07	.314
MVPA Duration	7.34	4.81	.436	1.53	.161

a. Dependent Variable: Symbol Search Response Time

Figure 2. Regression Plots – Processing Speed

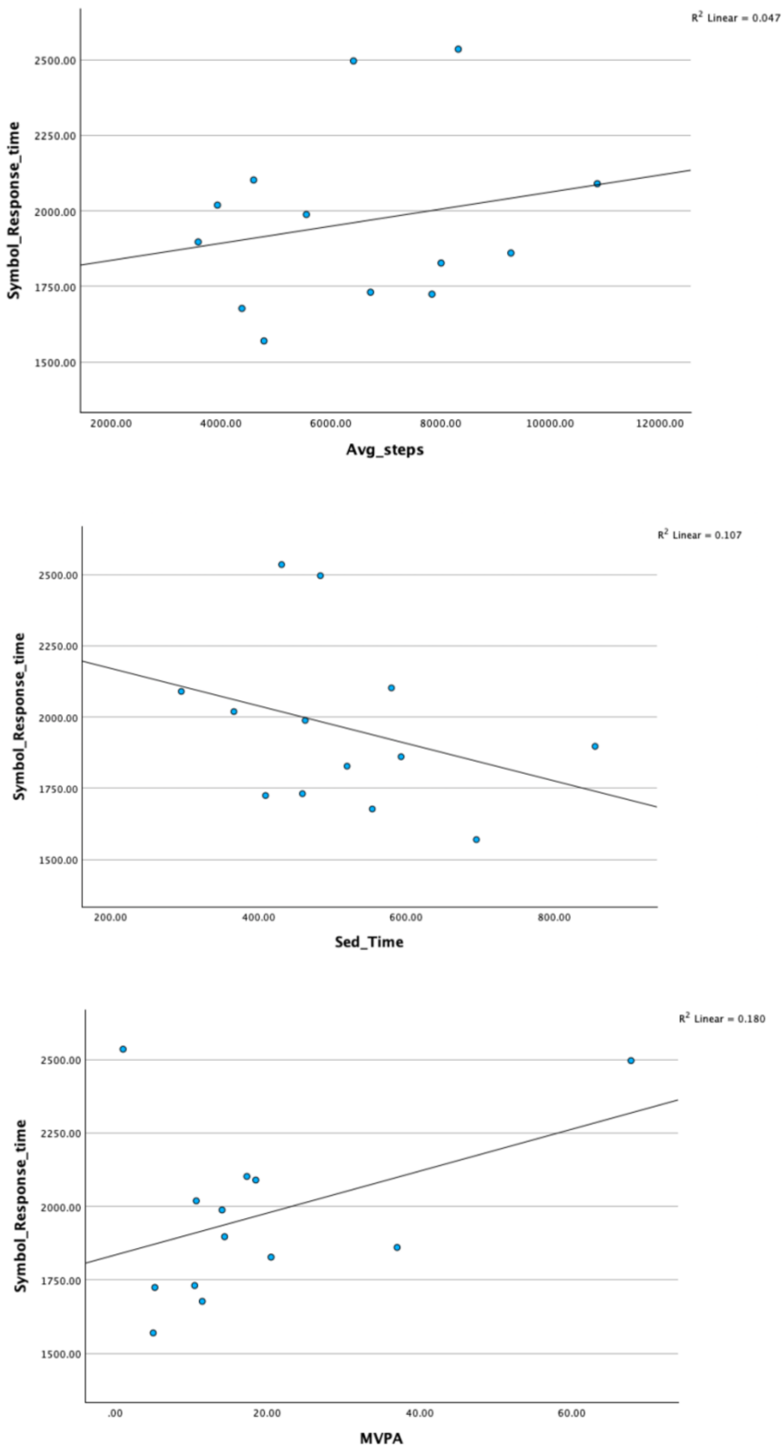


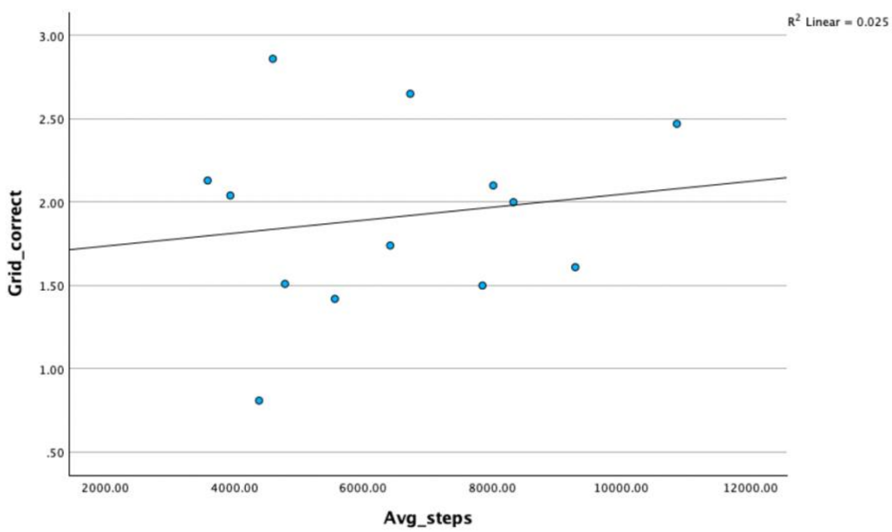
Table 5. Multiple Regression of Working Memory

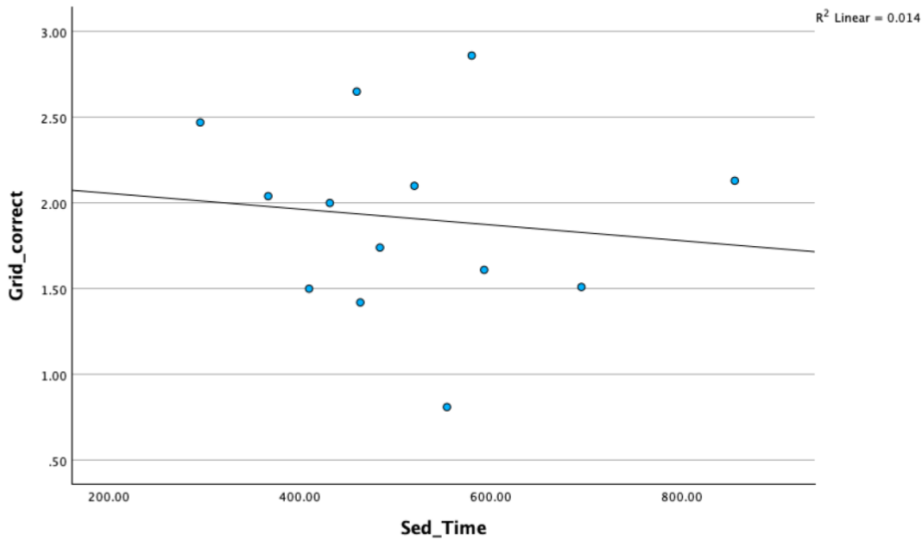
Coefficients[a]

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	1.80	1.24		1.45	.18
Average Steps	.00	.000	.14	.36	.73
Sedentary Time	.00	.002	-.04	-.11	.91
MVPA Duration	-.002	.01	-.05	-.15	.88

a. Dependent Variable: Grid Memory Accuracy

Figure 3. Regression Plots – Grid Accuracy

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2.50
2.00
1.50
1.00
.50
Grid_correct
200.00
400.00
600.00
800.00
Sed_Time

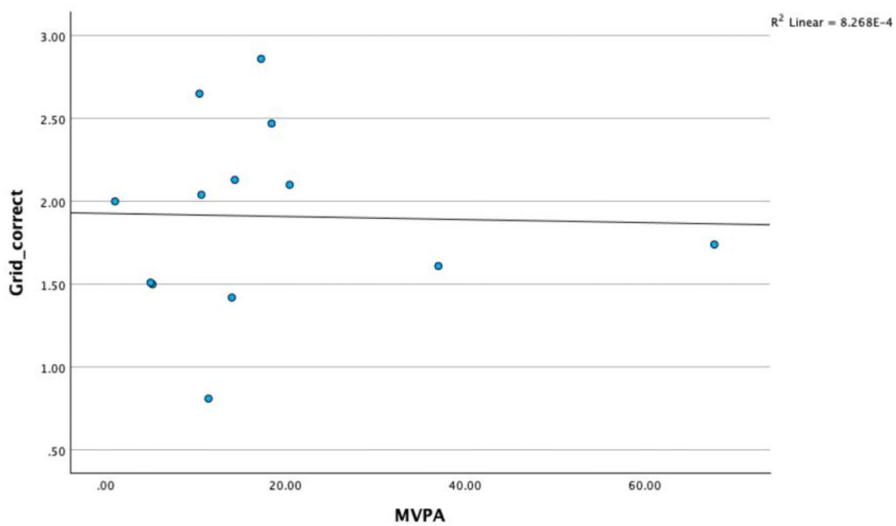

R2 Linear = 8.268E-4
3.00
2.50
2.00
1.50
1.00
.50
Grid_correct
.00
20.00
40.00
60.00
MVPA

Table 6. Correlation Between Physical Activity and Cognitive Function Variables

Correlations

		Average Daily Steps	Sedentary Time	MVPA
Symbol Search Response Time	Pearson Correlation	.217	-.327	.424
Grid Memory Accuracy	Pearson Correlation	.157	-.120	-.029

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Chapter 5

Discussion

The goal of this study was to evaluate the feasibility of a study protocol for testing relations between physical activity, sedentary time, and two key cognitive functions: processing speed and working memory. The baseline results from this study showed that there is a small significant association between average daily steps and cognitive processing speed. It was also found that as step counts increased, accuracy for working memory improved, with a non-significant trend between steps and accuracy. Sedentary behavior showed a decrease in accuracy for both working memory tests. Overall, the findings support the hypotheses that increased physical activity through MVPA and daily step counts are associated with better cognitive function, and that increased bouts of sedentary behaviors are correlated with worse cognitive function in observational baseline data.

The baseline data from this study shows promise for the rest of the larger DOSE Feasibility Study. The feasibility of this study was demonstrated with the recruitment goal being met within 2 months and 82% of enrolled participants completing study protocol. This shows that both middle-aged and older adults are interested in volunteering for this type of research. More substantial conclusions and associations can be drawn from the experimental phase of this study where retention and study completion rates will be analyzed. The results from this study could highlight benefits of using intervention methods to increase physical activity in older adults as a method of improving cognitive function or delaying declines in cognitive speed or accuracy. As this is a feasibility study, our study team has plans for a larger study if our protocol is found feasible.

Another implication from this study is the feasibility of using wearable devices, even those that do not provide feedback, for the collection of detailed activity data on middle-aged and older adults. Based on these results, future research could market fitness or activity apps as intervention methods for populations that are at high risk for developing Alzheimer's disease. Mobile apps have been proven feasible in providing square-stepping exercise (SSE) as a method of increasing physical activity in older adults as a method of improving cognitive function (Shellington et al., 2017). The Health*e*Brain study found that the utilization of this app in older populations to guide SSE could improve cognitive function and memory. This research, along with the results from this study, combine to show the possibilities for future research on the use of physical activity devices and mobile application use as a method of increasing physical activity in at-risk adults.

In addition to showing the feasibility of this study protocol, this study also highlighted the difficulties in recruiting a diverse sample that is representative of a broader population. Currently in the study, 85.7% of the sample is White, while the population of the United States is 75.5% White (United States Census Bureau, 2023). It is important to include racially diverse samples in Alzheimer's research due to the differences in risk factors by race and ethnicity. One study found that the population-attributable risk (PAR) for various modifiable risk factors for Alzheimer's disease differed by race and ethnicity. Compared to white individuals, combined PAR was higher in black, American Indian and Alaskan Native, and Hispanic individuals (Nianogo et al., 2022). Our goal was to obtain a sample that was made up of at least 50% minority populations. Recruitment and enrollment are still ongoing for the rest of the study, however that milestone has not been met. Despite efforts to recruit a racially diverse sample, there are many barriers that researchers face in recruiting these representative samples. This study shows the need for racially diverse Alzheimer's disease research in order to research interventions that can be effective in addressing health disparities and generalized for a broader population.

Due to this study focusing on the pre-experimental observational data and having a small sample size, the analyses of the results are underpowered. Despite the difficulty obtaining significant associations between variables, patterns of associations can be determined, and the results can guide future studies. The larger DOSE Feasibility study will include 30 participants, which at the conclusion of the study, will provide more data for analyses and conclusions to be drawn. However, this is still a small sample size that could be expanded on in the future. Since our study protocol was found to be feasible so far, a much larger study could be launched with many more participants, which would allow stronger and more accurate association data to be found.

Average sedentary time for participants in this study was about 515 minutes per day, which indicates that there is also a need for studies that investigate the best methods to reduce sedentary time in older age groups, especially those that no longer work during the day. One study found that older adults average 9.4 hours per day in sedentary behavior, which is comparable to our sample (Shrestha et al., 2019). Studies have shown that sedentary behavior may be associated with cardiovascular disease, type 2 diabetes, and some forms of cancers, which means that any reduction in time watching TV or participating in other sedentary behaviors could greatly improve public health outcomes (Shrestha et al., 2019). In addition to being detrimental to physical health, increased bouts of sedentary behavior can increase depressive symptoms, decrease overall mental health, and lower the odds for successful ageing (Gardiner et al., 2021). Current research on the associations between sedentary behavior and neurodegenerative diseases is mixed, and the role of sedentary behavior is still not well-understood. One sample of about 50,000 UK participants who spent 10 hours or more per day in sedentary behaviors were found to be associated with a higher risk for dementia (Zou et al., 2024). Additionally, other meta-analysis studies have shown that the more time spent in sedentary behavior was associated with a higher incidence of dementia in older adults (Zou et al., 2024). These studies, along with the results from this study, exemplify the importance of reducing sedentary time in older adults and researching effective methods to do so in order to improve their physical and cognitive health.

In addition to sedentary time, moderate-to-vigorous physical activity (MVPA) has been found to be associated with cognitive function. Other studies have found that after being physically active, or with a higher intensity than normal, participants have had better cognitive processing speeds. Our study aligns with these findings that physical activity can be used to boost performance on cognitive tasks that require processing speed, as MVPA was found to be positively correlated with response time (Kekäläinen et al., 2023).

In addition to MVPA and sedentary time, daily step count has been found to be associated with cognitive function. Contrary to our hypothesis, no significant relationship was found between average daily step count and processing speed. In contrast to self-reported physical activity data, step counts are an objective and reliable measure of physical activity that can be used to investigate impact on cognitive function. Another study that has focused on the impact of step count on cognitive function in middle-aged adults has found similar associations. They found that there was a positive association between average 7-day step count at baseline and Cognitive Abilities Screening Instrument (CASI) score in male adults ranging from 40-79 years. Their results also showed that higher average 7-day step count was associated with significantly higher cognitive function at follow-up five years later (Shibukawa et al., 2024). The findings from both studies may suggest an association between higher average daily step count and better cognitive function outcomes.

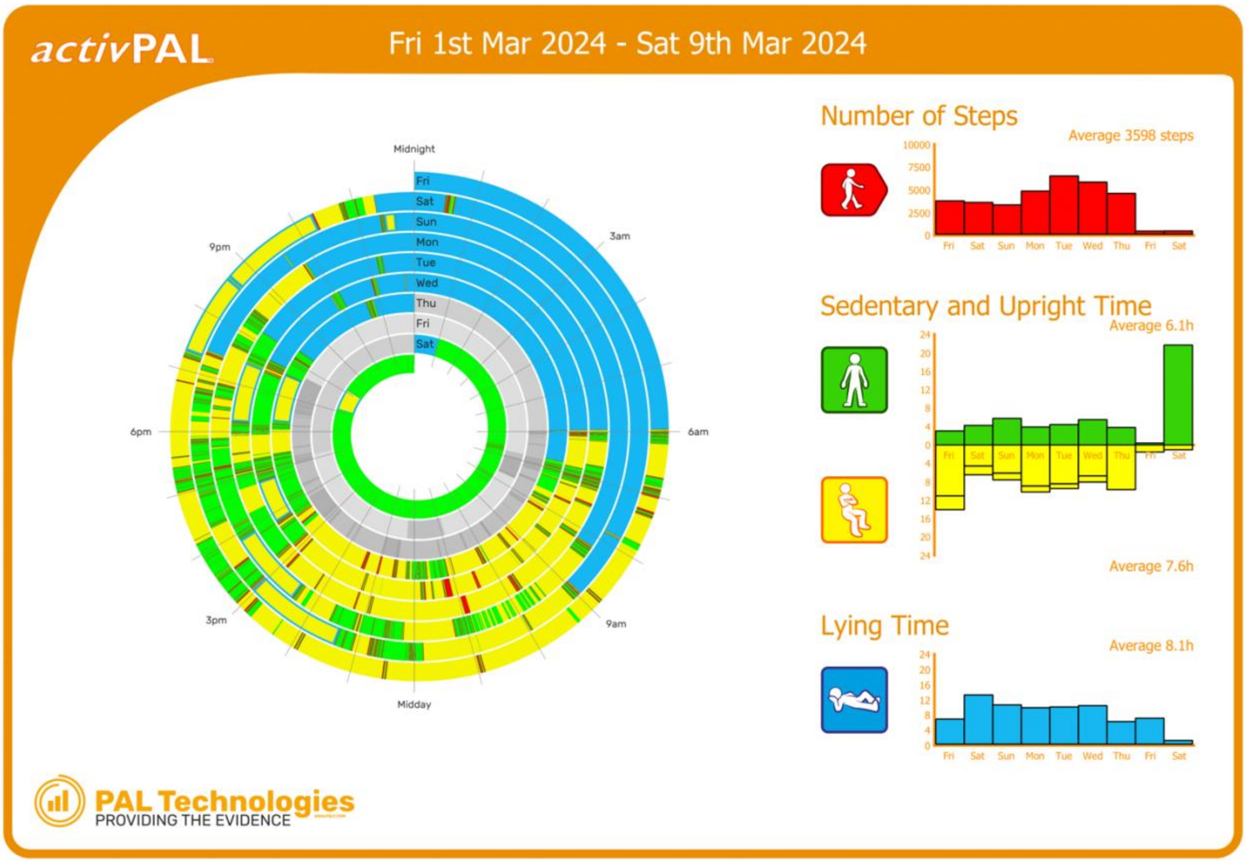
This study utilized ambulatory cognitive assessments through the MetricWire application. Traditional approaches to assessing cognition usually take place in unfamiliar physical and social environments that do not emulate the environments in which individuals perform cognitively demanding tasks in their daily life (Sliwinski et al., 2016). The use of ambulatory cognitive assessments was found to be both effective and feasible in this study. All participants were able to complete their cognitive tests and data was effectively collected for analysis. Other studies have shown that the grid-memory and symbol search ambulatory tasks were correlated with age and fluid-intelligence similarly to the in-lab assessments (Sliwinski et al., 2016). This study contributes to the research of ambulatory cognitive assessment measures in middle-age and older adult populations by showing feasibility in observational research studies on cognitive function.

One strength of this study is its use of the activPAL device for collection of physical activity data. The feasibility was shown of using this device in middle-aged and older adult populations to collect physical activity data. Additionally, this study focused on middle-age and older adult populations between 40 and 80 years; the midlife subgroup of this sample has often been neglected in Alzheimer’s disease research. It is important to research the associations between physical activity and cognition in midlife in order to find preventative measures for Alzheimer’s disease before clinical symptoms or biological changes arise. Preventing cognitive decline requires targeted interventions to this middle-aged adult population. One limitation of this study that needs to be discussed is the eligibility criteria. The participants needed to own both an Apple iPhone and Apple Watch to participate in this study, which could have eliminated some participants due to economic status or access to devices. Although it may be more difficult to recruit and retain lower-SES participants due to a lack of trust and accessibility, there are methods to improve socioeconomic diversity in research and science (Emery et al., 2023). Another limitation of this study is the small sample size. The speed at which participants were recruited and enrolled led to an even smaller sample size than originally desired. Only 13 participants were able to be enrolled and complete the baseline portion of the study during the timeframe for this analysis. This small sample size limits its application of the results to a larger population. This study is observational, as pre-experimental data was used, which limits the analyses due to the observational data in which causations cannot be drawn. Lastly, a limitation in the measures was that collecting physical activity data for one week may not be representative of average physical activity for participants across longer periods of time. In future studies, physical activity data could be collected over a longer period of time to gather more representative data.

In conclusion, this study found that our study protocol is feasible for recruiting and enrolling participants between the ages of 40 and 80 years and having them successfully complete baseline procedures. It was feasible to collect accurate physical activity data using the activPAL device as well as cognitive function data on processing speeds and working memory using ambulatory cognitive assessments through a smartphone app. This study also showed the difficulty of recruiting a diverse and widely representative sample that can be generalized to a broader population. Additionally, it was found that moderate-to-vigorous physical activity and average daily step counts were correlated with improved cognitive processing speed using baseline observational data. Lastly, this study provides a foundation for future research on daily step count, moderate-to-vigorous physical activity, sedentary behavior, and cognitive function that could lead to effective prevention methods for dementia and Alzheimer's disease in middle-aged and older adults.

Appendix

Participant Example activPAL Data



BIBLIOGRAPHY

2023 Alzheimer's disease facts and figures. (2023). *Alzheimer's & Dementia*, *19*(4), 1598–1695. https://doi.org/10.1002/alz.13016

Alzheimer's Association. (2024). (rep.). *2024 Alzheimer's Disease Facts and Figures*. Retrieved from https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf.

Brookmeyer, R., Johnson, E., Ziegler-Graham, K., & Arrighi, H. M. (2007). Forecasting the global burden of Alzheimer's disease. *Alzheimer's & Dementia*, *3*(3), 186–191. https://alz-journals-onlinelibrary-wiley-com.ezaccess.libraries.psu.edu/doi/10.1016/j.jalz.2007.04.381

Cerino, E. S., Katz, M. J., Wang, C., Qin, J., Gao, Q., Hyun, J., Hakun, J. G., Roque, N. A., Derby, C. A., Lipton, R. B., & Sliwinski, M. J. (2021). Variability in cognitive performance on mobile devices is sensitive to mild cognitive impairment: Results from the Einstein Aging Study. *Frontiers in Digital Health*, *3*. https://doi.org/10.3389/fdgth.2021.758031

Chastin, S., Gardiner, P. A., Harvey, J. A., Leask, C. F., Jerez-Roig, J., Rosenberg, D., Ashe, M. C., Helbostad, J. L., & Skelton, D. A. (2021). Interventions for reducing sedentary behaviour in community-dwelling older adults. *Cochrane Database of Systematic Reviews*, *2021*(6). https://doi.org/10.1002/14651858.cd012784.pub2

Conroy, D. E., Wu, J., Lee, A. M., Brunke-Reese, D., & Lagoa, C. M. (2023). Dose–response relations between the frequency of two types of momentary feedback prompts and daily physical activity. *Health Psychology*, *42*(3), 151–160. https://doi.org/10.1037/hea0001271 del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and intensity with incident dementia in 78430 adults living in the UK. *JAMA Neurology*, *79*(10), 1059. https://doi.org/10.1001/jamaneurol.2022.2672

Dhana, K., Beck, T., Desai, P., Wilson, R. S., Evans, D. A., & Rajan, K. B. (2023). Prevalence of Alzheimer's Disease dementia in the 50 US states and 3142 counties: A population estimate using the 2020 bridged-race postcensal from the National Center for Health Statistics. *Alzheimer's & Dementia*, *19*(10), 4388–4395. https://doi.org/10.1002/alz.13081

Emery, L. F., Silverman, D. M., & Carey, R. M. (2023). Conducting research with people in lower-socioeconomic-status contexts. *Advances in Methods and Practices in Psychological Science*, *6*(4). https://doi.org/10.1177/25152459231193044/v2/review2

Erickson, K. I., Hillman, C., Stillman, C. M., Ballard, R. M., Bloodgood, B., Conroy, D. E., Macko, R., Marquez, D. X., Petruzzello, S. J., & Powell, K. E. (2019). Physical activity, cognition, and Brain Outcomes: A review of the 2018 physical activity guidelines. *Medicine & Science in Sports & Exercise*, *51*(6), 1242–1251. https://doi.org/10.1249/mss.0000000000001936

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research Electronic Data Capture (redcap)—a metadata-driven methodology and workflow process for providing Translational Research Informatics Support. *Journal of Biomedical Informatics*, *42*(2), 377–381. https://doi.org/10.1016/j.jbi.2008.08.010

Irwin, K., Sexton, C., Daniel, T., Lawlor, B., & Naci, L. (2018). Healthy aging and dementia: Two roads diverging in midlife? *Frontiers in Aging Neuroscience*, *10*. https://doi.org/10.3389/fnagi.2018.00275

Kekäläinen, T., Luchetti, M., Terracciano, A., Gamaldo, A. A., Mogle, J., Lovett, H. H., Brown, J., Rantalainen, T., Sliwinski, M. J., & Sutin, A. R. (2023). Physical activity and cognitive function: Moment-to-moment and day-to-day associations. *International Journal of Behavioral Nutrition and Physical Activity*, *20*(1). https://doi.org/10.1186/s12966-023-01536-9

Kivipelto, M., Helkala, E.-L., Laakso, M. P., Hänninen, T., Hallikainen, M., Alhainen, K., Soininen, H., Tuomilehto, J., & Nissinen, A. (2001). Midlife vascular risk factors and alzheimer's disease in later life: Longitudinal, population based study. *BMJ*, *322*(7300), 1447–1451. https://doi.org/10.1136/bmj.322.7300.1447

Nianogo, R. A., Rosenwohl-Mack, A., Yaffe, K., Carrasco, A., Hoffmann, C. M., & Barnes, D. E. (2022). Risk factors associated with alzheimer disease and related dementias by sex and race and ethnicity in the US. *JAMA Neurology*, *79*(6), 584. https://doi.org/10.1001/jamaneurol.2022.0976

Qiu, C., Kivipelto, M., & von Strauss, E. (2009). Epidemiology of Alzheimer's disease: Occurrence, determinants, and strategies toward intervention. *Dialogues in Clinical Neuroscience*, *11*(2), 111–128. https://doi.org/10.31887/dcns.2009.11.2/cqiu

Shellington, E. M., Felfeli, T., Shigematsu, R., Gill, D. P., & Petrella, R. J. (2017). HealtheBrain: An innovative smartphone application to improve cognitive function in older adults. *mHealth*, *3*, 17–17. https://doi.org/10.21037/mhealth.2017.04.05

Shibukawa, T., Fujiyoshi, A., Moniruzzaman, M., Miyagawa, N., Kadota, A., Kondo, K., Saito, Y., Kadowaki, S., Hisamatsu, T., Yano, Y., Arima, H., Tooyama, I., Ueshima, H., & Miura, K. (2024). Association of step counts with cognitive function in apparently healthy middle-aged and older Japanese men. *Preventive Medicine Reports*, *38*, 102615. https://doi.org/10.1016/j.pmedr.2024.102615

Sindi, S., Mangialasche, F., & Kivipelto, M. (2015). Advances in the prevention of Alzheimer's Disease. *F1000 Prime Reports*, 7–50. https://doi.org/10.12703/P7-50

Shrestha, N., Grgic, J., Wiesner, G., Parker, A., Podnar, H., Bennie, J. A., Biddle, S. J., & Pedisic, Z. (2019). Effectiveness of interventions for reducing non-occupational sedentary behaviour in adults and older adults: A systematic review and meta-analysis. *British Journal of Sports Medicine*, *53*(19), 1206–1213. https://doi.org/10.1136/bjsports-2017-098270

Sliwinski, M. J., Mogle, J. A., Hyun, J., Munoz, E., Smyth, J. M., & Lipton, R. B. (2016). Reliability and validity of ambulatory cognitive assessments. *Assessment*, *25*(1), 14–30. https://doi.org/10.1177/1073191116643164

U.S. Census Bureau quickfacts: United States. United States Census Bureau. (2023). https://www.census.gov/quickfacts/fact/table/US/PST045223

Vetrovsky, T., Borowiec, A., Juřík, R., Wahlich, C., Śmigielski, W., Steffl, M., Tufano, J. J., Drygas, W., Stastny, P., Harris, T., & Małek, Ł. (2022). Do physical activity interventions combining self-monitoring with other components provide an additional benefit compared with self-monitoring alone? A systematic review and meta-analysis. *British Journal of Sports Medicine*, *56*(23), 1366–1374. https://doi.org/10.1136/bjsports-2021-105198

Zou, L., Herold, F., Cheval, B., Wheeler, M. J., Pindus, D. M., Erickson, K. I., Raichlen, D. A., Alexander, G. E., Müller, N. G., Dunstan, D. W., Kramer, A. F., Hillman, C. H., Hallgren, M., Ekelund, U., Maltagliati, S., & Owen, N. (2024). Sedentary behavior and Lifespan Brain Health. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2024.02.003