The Independent and Joint Effects of Physical Activity and Sedentary Behavior on Dementia and Cognitive Function

by Laura Major

B.A. in Anthropology and Psychology, May 2008, Dickinson College
MPH in Health Behavior, May 2012, University of North Carolina-Chapel Hill

A Dissertation submitted to

The Faculty of
The Milken Institute School of Public Health
of The George Washington University
in partial fulfillment of the requirements
for the degree of Doctor of Public Health

August 31, 2022

Dissertation directed by

Loretta DiPietro
Professor of Exercise and Nutrition Sciences

Melissa Napolitano
Professor of Prevention and Community Health

The Milken Institute School of Public Health of The George Washington University certifies that Laura Major has passed the Final Examination for the degree of Doctor of Education as of July 25, 2022. This is the final and approved form of the dissertation.

The Independent and Joint Effects of Physical Activity and Sedentary Behavior on Dementia and Cognitive Decline

Laura Major

Dissertation Research Committee:

Loretta DiPietro, Professor of Exercise and Nutrition Sciences, Dissertation Co-Director

Melissa Napolitano, Professor of Prevention and Community Health, Dissertation Co-Director

Eleanor Simonsick, Epidemiologist and Staff Scientist in the Intramural Research Program of the National Institute on Aging, Committee Member

© Copyright 2022 by Laura Major
All rights reserved

Dedication

This dissertation is dedicated to James K. Major, Lucille E. Fino, and Sweet Pea. I love you and I miss you every day.

Acknowledgments

I could not have completed this dissertation without the help of many people. I want to start by thanking my dissertation committee. Their feedback, intellectual contributions, and encouragement over the past two years have improved the quality of this work in immeasurable ways and have been a wellspring of motivation when I needed it the most. My committee co-chairs, Drs. Loretta DiPietro and Melissa Napolitano, offered their valuable time to meet with me regularly to troubleshoot issues, provide suggestions, and keep me laughing when I wanted to cry. Dr. Eleanor Simonsick is a font of information about the Health ABC Study, particularly as it relates to movement and cognitive function, and helped me to understand the data and interpret the findings and challenged my thinking to help me grow as a researcher. I admire each of you and hope that we have the chance to work together many more times in the future. I would also like to thank my readers, Drs. Keith Cole and David Marquez, who did not hesitate to lend their time and expertise to reviewing this dissertation and providing me with feedback.

I would be remiss in not thanking the 2018 PCH DrPH and PhD cohorts. Your support helped me to not only keep going during challenging academic times, but also challenging societal times. Erin Wentzell was a rock and always on my wavelength, knowing the right thing to say when I needed support. When are we getting those milkshakes? Krishna Patel and Shaon Lahiri kept me going with both their smiles and their encouragement. I'm lucky to have met each of you and look forward to continuing our friendships in the future.

My colleagues at BSR have also contributed to my success in ways I can't even begin to count. Dr. Lis Nielsen was the first one to suggest that I go back to school and

wrote the recommendation letter to make it happen. She's an inspiring mentor and role model and I quite literally would not be where I am without her. Dr. Dana Plude consistently gives the best advice, including encouraging me to make this dissertation my number one priority when I needed to hear it the most. Dr. Janine Simmons shows me every day how to be a better team member and helps me deal with daily frustrations with a smile. Drs. Lisa Onken, Elena Fazio, Melissa Gerald, Partha Bhattacharyya, Jonathan King, Liz Necka, and John Phillips have been the best colleagues I could ask for and each has been an integral part of my career and academic journeys in so many different ways. Working at BSR with all of you has been one of the great privileges of my life.

Lastly, I owe a ton of gratitude to my friends and family who have all helped me in different ways. Nora West, to whom I can't go a day without talking, has always been there for me when I needed her both as a friend and as an inspiration for how to do good in the field of public health. Abby Youngblood is a constant source of joy and laughter in my life and has been present for all my highs and lows through almost 20 (!) years of friendship. I've known Katrine Herrick since we were 10 and I hope to know her when we're 100. Olivia Kent gets me like few other people and is a good enough friend and person to have even read a draft of this dissertation (I owe you one). Farheen Akbar, Jessica Boten, Prisca Fall, Amelia Karraker, Chandra Keller, Emerald Nguyen, Roxanne Semple, and Courtney Wallin have all provided support and laughter to help me through the tough times.

Mostly importantly, to my mom, Judy Major; my brothers, Thomas and Chris Major; my sister-in-law, Ashley Jucha; my niece, Lucy Major; my aunt, Susan Fino; and my dog, Wobee. Thank you for all you've done for me and continue to do – my successes are only possible because of you. I can't imagine a better support system – love you all.

Abstract of Dissertation

The Independent and Joint Effects of Physical Activity and Sedentary Behavior on Dementia and Cognitive Decline

Background: Cognitive impairment and dementia, which is cognitive impairment to the point that it interferes with daily function, are prevalent among older adults and are associated with serious health and socioeconomic consequences. Physical activity has been identified as a promising avenue for preventing or delaying cognitive decline, but only represents one component of an individual's daily movement. Sedentary behavior is another potential factor, but there is a dearth of evidence regarding the relationship between sedentary behavior and cognitive function and dementia in the literature. This is particularly true for different types of sedentary behavior, including both cognitively stimulating and non-cognitively stimulating activities performed while seated. The joint associations of physical activity and sedentary behavior with cognitive function and dementia have been even less studied.

Aims and Methods: This research employed secondary data analysis to examine whether and how sedentary behavior and physical activity were associated with dementia and cognitive function, as assessed by the Teng Min-Mental State (3MS), Digit Symbol Substitution Test (DSST), and CLOX 1, in participations responding to the Health, Aging and Body Composition (Health ABC) Study.

The first aim examined the independent and combined associations of physical activity and sitting time with future odds of dementia. Physical activity (kcal/week) and sitting time (hours/day) were self-reported in 1999-2000 and dementia status was evaluated from June 1, 2001 through September 30, 2014. Multivariable logistic regression evaluated the independent and joint associations of physical activity and

sitting time with odds of dementia.

The second aim examined the associations of different types of sedentary behavior and 3-year change in the time spent on those activities with cognitive function and dementia. Multivariable linear regressions was used to examine associations between baseline sitting, TV watching, and reading time – and change in those behaviors – with cognitive function test scores. Multivariable logistic regression evaluated associations between change in sitting, TV, and reading time with odds of dementia.

Results: For Aim 1, sedentary behavior and physical activity were not independently or jointly associated with odds of dementia. In the independent associations model, neither being in the high sitting group (9+ hours/day; OR=0.94, 95% CI=0.72, 1.23) nor being in the low physical activity group (<500 kcal/week; OR=1.06, 95% CI=0.79, 1.42) were associated with greater odds of dementia. In the joint associations model, participants in the high sitting and low physical activity group did not have a greater odds of dementia compared with participants in the low sitting and high physical activity group (OR=1.16, 95% CI=0.74, 1.82).

For Aim 2, more reading time at baseline was associated with a 0.09-point (SE=0.03, $p<0.05$) higher 3MS score and a 0.14-point (SE=0.04, $p<0.01$) higher DSST score. An increase in TV watching time between 1999-2000 and 2002-2003 was associated with a 1.53-point (SE=0.72, $p<0.05$) decrease in 3MS score.

Conclusion: This research adds to the evidence base related to daily movement and cognitive function and dementia among older adults. The relationship among these variables is complex and difficult to study, particularly because some types of sedentary behavior may have benefits for cognitive function in older adults, outweighing the

potential harms associated with lack of movement. More research is needed to explicate whether and how daily movement affects and/or reflects cognitive function, including dementia, among older adults.

Table of Contents

Acknowledgments ..... **iv**

Abstract of Dissertation ..... **vii**

Table of Contents ..... **x**

List of Figures ..... **xiii**

List of Tables ..... **xiv**

Chapter 1: Introduction 1

Statement of the Problem 1

Executive Function 2

Physical Activity, Cognitive Function, and Dementia 3

Sedentary Behavior, Cognitive Function, and Dementia 6

Sedentary Behavior as an Independent Behavior from Physical Activity 8

Joint Effects of Physical Activity and Sedentary Behavior 9

Theoretical Framework 11

Manuscript Aims 12

Chapter 2: Methods 15

The Health ABC Study 15

Protection of Human Subjects 15

Timeline of Assessments 16

Measures 17

Sedentary Behavior 17
Physical Activity 19
Joint Sedentary Behavior and Physical Activity Variables 21
Cognitive Function and Dementia 21
Covariables 23
Statistical Analysis Plan 25
Univariate Analyses 25
Manuscript 1 Analyses 25
Manuscript 2 Analyses 26
Chapter 3: Manuscript 1 27
Abstract 28
Introduction 29
Methods 31
Study Participants 31
Physical Activity and Sedentary Behavior 32
Dementia 33
Cognitive Function 33
Covariables 34
Statistical Analysis 35
Results 36

Discussion 46

Chapter 4: Manuscript 2 51

Abstract 52

Introduction 53

Methods 56

Study Participants 56

Sedentary Behavior 57

Cognitive Outcome Measures 58

Covariables 59

Statistical Analysis 60

Results 61

Discussion 71

Chapter 5: Conclusion 76

Overview 76

Limitations 77

Strengths 79

Implications for Future Research 80

Implications for Public Health Practice 82

Conclusion 83

References 84

List of Figures

Figure 1: 2018 Physical Activity Guidelines Scientific Report Heat Map of Relationship Among Moderate-to-Vigorous Physical Activity, Sitting Time, and Risk of All-Cause Mortality……..…9

Figure 2: Behavioral Psychosocial Model of Sedentary Behavior, Physical Activity, and Cognitive Function……...11

Figure 3: Aim 1 Timeline of Measurements…….....16

Figure 4: Aim 2 Timeline of Measurements…….....17

Figure 5: Manuscript 1 Participant Selection……. ..32

Figure 6: The Joint Associations of Sedentary Time and Physical Activity with Dementia……... ..40

Figure 7: The Joint Associations of Sedentary Time and Physical Activity Time with Dementia……...…..44

Figure 8: The Joint Associations of TV Time and Physical Activity with Dementia… ..46

Figure 9: Manuscript 2 Participant Selection……. ..57

List of Tables

Table 1: Domains and Subdomains of Cognitive Function…… …3

Table 2: Physical Activity Questionnaire Items...…….. ..19

Table 3: Joint Sedentary Behavior and Physical Activity Variables…….. ..21

Table 4: Manuscript 1 Descriptive Statistics…….. ..36

Table 5: Categories of Physical Activity and Sedentary Time According to Dementia Status……...… ..37

Table 6: Independent Associations of Sedentary Time and Physical Activity with Dementia…….. ..38

Table 7: Independent Associations of Sedentary Time and Physical Activity with 3MS, DSST, and CLOX 1 Scores……..39

Table 8: Joint Associations of Sedentary Time and Physical Activity with 3MS, DSST, and CLOX 1 Scores……. ..41

Table 9: Categories of Physical Activity Time and Sedentary Time According to Dementia Status……... ..42

Table 10: Independent Associations of Sedentary Time and Physical Activity Time with Dementia…… ..43

Table 11: Categories of Physical Activity and TV Time According to Dementia Status……..45

Table 12: Independent Associations of TV Time and Physical Activity with Dementia……..…..45

Table 13: Manuscript 2 Descriptive Statistics…… ..61

Table 14: Associations of Baseline Sitting Time with 3MS, DSST, and CLOX 1 Scores 7 Years Later…… ..63

Table 15: Associations of Baseline TV Watching with 3MS, DSST, and CLOX 1 Scores 7 Years Later…… ..64

Table 16: Associations of Baseline Reading with 3MS, DSST, and CLOX 1 Scores 7 Years Later…… ..65

Table 17: Associations of Change in Sitting Time with 3MS, DSST, and CLOX 1 Scores……..…..66

Table 18: Associations of Change in TV Watching Time with 3MS, DSST, and CLOX 1 Scores…… ..67

Table 19: Associations of Change in Reading Time with 3MS, DSST, and CLOX 1 Scores…….…..…..68

Table 20: Associations of Change in Sitting Time, TV Watching, and Reading with Dementia……..…..69

Chapter 1: Introduction

Statement of the Problem

Dementia, defined as cognitive decline to the point where it interferes with an individual's daily functioning, is a significant public health problem facing older adults (National Institute on Aging, 2017a). Dementia is common among older adults: for example, analysis of data from a nationally representative study of adults over 50 in 2016 found prevalence and incidence estimates of 7.7% and 3.8%, respectively (Farina, Zhang, Kim, Hayward, & Crimmins, 2022). Dementia represents the most severe form of cognitive decline; however, older adults frequently experience deficits in cognitive function that do not rise to the level of dementia. Recent estimates indicate that cognitive impairment occurs in 11.2% of adults aged 55-69 and 27.3% of adults aged 65 or older (Choi, Schoeni, Martin, & Langa, 2018; Rajan et al., 2021). Although studies have observed a slight decrease in prevalence in recent years (possibly due to greater population-level educational attainment), the number of individuals with dementia across the world is expected to grow as the population continues to age (Langa et al., 2017; Prince et al., 2016; Rajan et al., 2021). Projections indicate that, by 2035, there will be more older adults than children in the United States population for the first time in history, highlighting the scope of the issue (U.S. Census Bureau, 2018).

Dementia is not only pervasive, but also has serious consequences for health and wellbeing. Alzheimer's disease, one type of dementia, is the sixth leading cause of death for all age groups and the fourth leading cause of death for individuals 85 and older in the United States (Heron, 2019). The role of dementia in causing mortality may be even greater than these estimates indicate, as research shows that death certificates routinely

undercount dementia as a cause of death (Stokes et al., 2020). Death also occurs relatively quickly after developing dementia with a median survival time of 10.5 years after onset and 5.7 years after diagnosis (Waring, Doody, Pavlik, Massman, & Chan, 2005).

A dementia diagnosis has other wide-ranging impacts on both individuals and their families, including negative socioeconomic and psychosocial effects on care partners of a person living with dementia (Svanberg & Spector, 2011). For example, individuals who die with dementia experience enormous health care costs at the end of their lives, more so than those who die of heart disease or cancer (Kelley, McGarry, Gorges, & Skinner, 2015). At the societal level, estimates put the cost of dementia care at $604 billion worldwide, highlighting the significant burden of this disease (Wimo et al., 2013).

Currently no cure for dementia exists, thus it is imperative that we learn more about potentially modifiable risk factors for dementia to add to the science aimed at uncovering ways to mitigate the devastation of this debilitating disease.

Executive Function

Dementia and cognitive function are global terms that encompass multiple subdomains of cognitive function. The subdomains include sensation, perception, motor skills, attention and concentration, memory, speed of processing, language/verbal skills, and executive function (Harvey, 2019; **Table 1**).

Executive function refers to the higher-order, complex cognitive processes necessary for reasoning, problem solving, planning for the future, and flexibly adapting to changing situations (Harvey, 2019; Gilbert & Burgess, 2008). Executive function is a particularly important domain of cognitive function because it has demonstrated links

with multiple health and quality of life outcomes, including mental health and physical health, education and career success, social relationships, and others (Diamond, 2013). In addition, evidence suggests that declines in executive function may occur before declines in globally assessed cognitive function and that declines in executive function are predictive of dementia onset (Clark et al., 2012). This is significant because if changes in executive function predate decline in global cognitive function and dementia, such decline may be an indicator of future deficits among individuals who do not manifest other signs of cognitive decline or dementia.

Table 1. Domains and subdomains of cognitive function *Adapted from Harvey (2019).*

Domains	**Subdomains**
Sensation	Multisensory
Perception	Object recognition Organizational strategies
Motor skills	Copying Drawing Other praxic skills
Attention and concentration	Selective attention Sustained attention
Memory	Working memory Episodic memory Procedural memory Semantic memory Prospective memory
Speed of processing	Semantically relevant Coding and tracking
Language	Naming Fluency Reading and comprehension
Executive function	Reasoning Problem solving Planning Adapting to changing situations

Physical Activity, Cognitive Function, and Dementia

Evidence of the link between physical activity and cognitive outcomes is mixed. A Cochrane review of randomized control trials (RCT) evaluating the effect of physical activity interventions reported no benefit of physical activity for improving cognitive

function among older adults without cognitive complaints and a meta-analysis of studies testing this relationship also did not support a link between physical activity and cognitive function in older adults (Young, Angevaren, Rusted, & Tabet, 2015; Etnier, Nowell, Landers, & Sibley, 2006). Similarly, a 2-year moderate intensity physical activity intervention did not lead to improvements in cognitive function in a sample of sedentary older adults without preexisting cognitive impairment (Sink et al., 2015). Lastly, a prospective cohort study with a 28-year follow-up period found no relationship between engaging in recommended amounts of physical activity and dementia risk (Sabia et al., 2017).

However, an Agency for Healthcare Research and Quality (AHRQ) systematic review that examined the effectiveness of cognitive decline and dementia prevention interventions reported that, while the evidence was mixed and not altogether sufficient, physical activity is one promising avenue to continue exploring (Kane et al., 2017). This conclusion is borne out in other literature, including systematic reviews, meta-analyses, and randomized control trials, that demonstrates physical activity may lead to improved cognitive function (Bherer, Erickson, & Liu-Ambrose, 2013; Nagamatsu et al., 2013; Sofi et al., 2011; Zhu et al., 2017; Hamer, Terrera, & Demakakos, 2018; Zheng, Pleuss, Turner, Ducharme, & Aguiar, 2022). Furthermore, the 2018 Physical Activity Guidelines Advisory Committee Scientific Report determined that there was moderate evidence to support the existence of a benefit from engaging in long-term physical activity on cognitive function (PAGAC, 2018).

Regarding dementia, a 2014 meta-analysis of prospective cohort studies reported that physical activity was associated with an 18% reduction in dementia risk (Blondell,

Hammersley-Mather, & Veerman, 2014). In 2015, an evidence review concluded that there was strong evidence to support the role of physical activity in preventing dementia (Baumgart et al., 2015). A meta-analysis published in 2017 reported that physical activity was protective against Alzheimer's disease, but not dementia considered more broadly (Guure, Ibrahim, Adam, & Said, 2017). Finally, a 2018 systematic review of prospective observational studies found that regular physical activity was associated with lower risk of dementia (Lee, 2018).

Specific to executive function, a systematic review of six studies conducted in older adults with Alzheimer's disease revealed that physical activity was significantly associated with better executive function in four studies and trended in that direction in the other two studies (Guitar, Connelly, Nagamatsu, Orange, & Muir-Hunter, 2018). In another systematic review of physical activity interventions in older adults with mild cognitive impairment (MCI) or dementia, six studies among participants with MCI measured executive function, three of which noted a positive effect (the other three had no effect). Four of the studies among participants with dementia measured executive function, and three of those had a positive effect, while the remaining study reported no effect (Öhman, H., Savikko, N., Strandberg, T. E., & Pitkälä, 2014). Another systematic review of 23 studies of cognitively intact older adults reported that exercise improved executive function, although the effect sizes were small (Sanders, Hortobágyi, la Bastide-van Gemert, van der Zee, & van Heuvelen, 2019).

While the weight of the literature seems to support physical activity as an avenue for improving cognitive function and reducing dementia risk, it is clear that we do not yet have a full understanding of this relationship. There are multiple potential reasons for the

discrepant findings and poor evidence quality, including differences between observational and interventional studies, how physical activity is assessed, the length and frequency of engagement in the physical activity, how cognitive function is assessed, and the length of time between the exposure and the outcome variables. One possible explanation that will be explored here is the singular focus on physical activity or, in other words, failing to consider how another aspect of movement, sedentary behavior, may independently or jointly with physical activity affect cognitive function and dementia.

Sedentary Behavior, Cognitive Function, and Dementia

Sedentary behavior is a particularly significant public health concern for older adults. While prevalence estimates vary depending on how studies define and measure sedentary behavior, a 2015 systematic review found that adults 60 years and older are sedentary for up to 80% of the time that they are awake (Harvey, Chastin, & Skelton, 2015). A 2017 analysis of Reasons for Geographic and Racial Differences in Stroke study data corroborated this finding with objective measurements, determining that older adults spend 77% of waking time sedentary (Diaz et al., 2017). This is problematic for many health outcomes as the amount of time that older adults are sedentary is inversely associated with functional ability, quality of life and wellbeing, metabolic risk, and mortality (Copeland et al., 2017; Madden, Feldman, & Chase, 2021; Ekelund et al., 2019).

The link between sedentary behavior and cognitive function has yet to be fully examined, however. Some research indicates that reducing sedentary time could be beneficial for brain health and has even proposed potential mechanistic links to explain

the association, but studies in older adults to date have been largely cross-sectional in nature (Edwards & Loprinzi, 2017a; Edwards & Loprinzi, 2017b; Wheeler et al., 2017). One longitudinal study that examined the effect of sedentary behavior on cognitive function reported that more sedentary time was associated with declining cognitive function two years later (Ku, Liu, Lo, Chen, & Stubbs, 2017); however, another study that combined data across five cohorts of persons without dementia did not observe this relationship (Maasakkers et al., 2020). Regarding dementia specifically, a recent meta-analysis of data from 18 cohort studies concluded that being sedentary increases risk of dementia by 30 percent, although a critique of the article noted that the investigators may have conflated sedentary behavior with physical inactivity (Yan et al., 2020; Dillon & Gardiner, 2021). Relatedly, a pair of systematic reviews indicate that results from high quality cohort studies suggest an association between sedentary behavior and cognitive impairment, but inconsistent measurement across studies makes it difficult to determine the extent of the association (Falck et al., 2017; Olanrewaju, Stockwell, Stubbs, & Smith, 2020).

Other research suggests that certain types of sedentary behavior may benefit cognitive function whereas other types may have a negative effect (Bakrania et al., 2018; Kesse-Guyot et al., 2012), which could be another potential explanation for mixed findings across studies. For example, evidence shows that television (TV) watching is associated with worse cognitive function in older adults (Copeland et al., 2017; Fancourt & Steptoe, 2019; Fajersztajn, Di Rienzo, Nakamura, & Scazufca, 2021). However, reading and other cognitively stimulating activities performed while sedentary may be positively associated with cognitive function (Kurita et al., 2019; Nemoto et al., 2018).

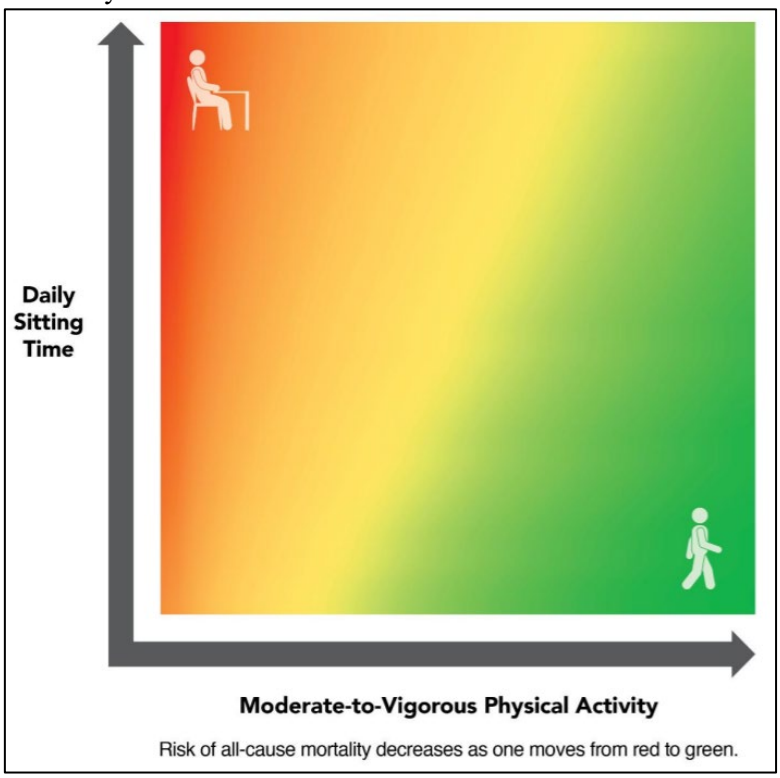
The lack of a well-developed evidence base regarding different types of sedentary behavior and their association with cognitive decline in older adults highlights the need for more research in this area.

Sedentary Behavior as an Independent Behavior from Physical Activity

In 2012, The Sedentary Behaviour Research Network proposed a standardized definition of sedentary behavior that is distinct from physical activity (or lack thereof): "any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalents [of task (METS)] while in a sitting or reclining posture" (p. 540). To put this in context, a MET is the ratio of the energy cost of performing a given activity relative to the resting metabolic rate (RMR = 1 MET). Thus, when performing an activity of 4 METs (say, brisk walking), one is working at 4 times their RMR (Jetté, Sidney, & Blümchen, 1990). While there remains some disagreement among researchers regarding how precisely to define sedentary behavior, the definition proposed by The Network has seen broad uptake in the field (Tremblay et al., 2017). Indeed, several studies suggest that sedentary behavior and lack of physical activity are independent behaviors with regard to their association with health and function and that performing minimal recommended levels of physical activity (i.e., 150 min/week of moderate-intensity activity) may not be enough to compensate for high levels of uninterrupted sedentary time (Katzmarzyk, 2010; Gennuso, Gangnon, Matthews, Thraen-Borowski, & Colbert, 2013). This paradigm shift is further demonstrated by the inclusion of sedentary behavior as independent from physical activity for the first time in the 2018 Physical Activity Guidelines for Americans (Physical Activity Guidelines Advisory Committee, 2018). To illustrate the combined effects of physical activity and sedentary behavior, the Guidelines Committee developed

a “heat map" (Figure 1) that depicts increasing risk of all-cause mortality with higher sedentary time and low moderate to vigorous physical activity (PAGAC, 2018).

Figure 1. 2018 Physical Activity Guidelines Scientific Report Heat Map of Relationship Among Moderate-to-Vigorous Physical Activity, Sitting Time, and Risk of All-Cause Mortality



Joint Effects of Physical Activity and Sedentary Behavior

Evidence suggests that sedentary behavior and physical activity are independent risk factors for health outcomes and that sedentary behavior is not simply the absence of physical activity (Physical Activity Guidelines Advisory Committee, 2018). However, the interaction of sedentary behavior and physical activity may be essential for influencing health in a way that cannot be understood by simply examining the effects of each independent of the other (Guallar-Castillón et al., 2019). This is particularly true as activity patterns tend to change with age, with levels of physical activity decreasing and sedentary time increasing (Evenson, Buchner, & Morland, 2012). Indeed, previous research has demonstrated that compensating for sedentary time with moderate to vigorous physical activity can reduce risk of all-cause mortality, indicating that, perhaps, enough or certain types of physical activity may reduce risk of sedentary time on health

outcomes (Ekelund et al., 2016). In addition, the negative outcomes associated with being sedentary are exacerbated among those with low levels of physical activity, suggesting that the pattern of interaction between the two behaviors may be essential for understanding the association between activity levels and health (Katzmarzyk et al., 2019). Similar findings have been demonstrated regarding physical function in older adults, wherein high levels of physical activity offset some of the risk of disability associated with being sedentary (DiPietro, Jin, Talegawkar, & Matthews, 2018).

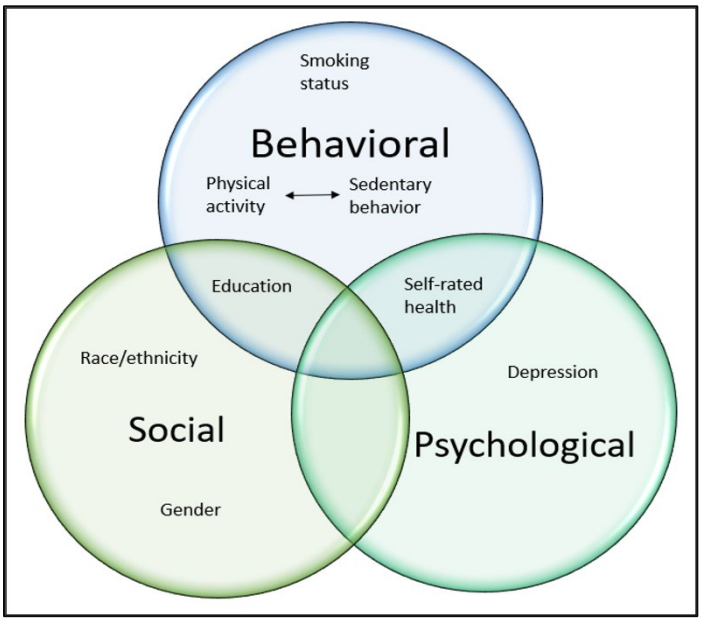
Recently, investigators examined data from the English Longitudinal Study on Ageing (N=12,099) and reported that participants who were sedentary at baseline but active 15 years later had lower risk of dementia than those who remained sedentary over the study period (Feter, Leite, Smith, Coombes, Rombaldi, 2020). However, this study examined replacing sedentary behavior with physical activity sequentially and still operationalized sedentary behavior as the absence of physical activity, rather than as an independent risk factor, and thus, did not evaluate their joint association with cognitive function. A small-scale experimental study among young adults did not find a relationship between the joint effects of sedentary behavior and physical activity and cognitive function (Blough & Loprinzi, 2019). However, participants had a mean age of 20 years old and thus may not experience detectable changes in cognitive function in the same way as older adults. Beyond these studies, a model of joint effects of sedentary behavior and physical activity has not been rigorously applied to cognitive decline in older adults. As a result, it is unknown whether sedentary behavior and physical activity combine to influence cognitive outcomes in older age. Understanding how the interplay of sedentary behavior and physical activity can increase or attenuate risk of dementia at

different activity levels could have important implications for the evidence base around primary prevention or reduction of dementia and cognitive deficits in old age.

Theoretical Framework

This study used a biopsychosocial model to contextualize how sedentary behavior and physical activity might independently and jointly influence cognitive function and dementia. The biopsychosocial model was developed by George Engel in 1977 as a response to traditional medical models that did not consider psychosocial factors that also influence disease and health outcomes. Since then, the framework has gained widespread recognition and remains relevant today in providing a more holistic conceptualization of disease (Wade & Halligan, 2017). For this research, Engel's biopsychosocial model was adapted to create a behavioral psychosocial model of cognitive function, due to the primary focus on health behaviors as predictors of cognitive function. Because cognitive function is complex, it is likely that a variety and confluence of behavioral, psychological, and social factors affect the outcome (Spector & Orrell, 2010). For that reason, while sedentary behavior and physical activity are the main predictors of interest, they are situated within a constellation of other possible behavioral, social, and psychological predictors of cognitive function (**Figure 2**).

Figure 2. Behavioral Psychosocial Model of Sedentary Behavior, Physical Activity, and Cognitive Function



In this framework, health behaviors (including physical activity, sedentary behavior, and smoking) are one major component thought to influence cognitive function. Education is noted in the overlap between behavioral and social factors because, while it is a behavior, it also represents opportunities for social interactions as well as position in the social hierarchy. Race/ethnicity and gender are included in the framework as social constructs. Depression is included as the only purely psychological factor. Lastly, self-rated health is in the overlap between psychological and biological components because while health is influenced by an individual's behaviors, one's perception of health is affected by their psychology.

Manuscript Aims

Manuscript 1: Examine the joint associations of sedentary behavior and physical activity in 1999-2000 on odds of dementia from June 1, 2001 to September 30, 2014 in participants responding to the Health, Aging and Body Composition (Health ABC) study. Examine the joint associations of sedentary behavior and physical activity in 1999-2000 on cognitive function and executive function in 2006-2007 in in the same population.

Hypothesis 1a: Health ABC participants who exhibit high sedentary time and low physical activity in 1999-2000 will have higher odds of dementia across 13 years of follow-up relative to older adults with low sedentary time and high physical activity, independent of key sociodemographic, health, and behavioral covariables.

Hypothesis 1b: Odds of dementia will be accelerated among those who sit the most and who are the least active, independent of key sociodemographic, health, and behavioral covariables.

Hypothesis 1c: Health ABC participants who exhibit high sedentary time and low

physical activity in 1999-2000 will have lower cognitive and executive function scores in 2006-2007 relative to participants with low sedentary time and high physical activity, independent of key sociodemographic, health, and behavioral covariables.

Manuscript 2: Examine the effects of 3-year change (1999-2000 to 2002-2003) in different types of sedentary behavior on cognitive function and executive function in 2006-2007 in participants responding to the Health ABC study. Determine the effects of 3-year change in different types of sedentary behavior on odds of dementia from June 1, 2004 to September 30, 2014 in the same population.

Hypothesis 2a: Sedentary time, including time spent sitting upright, watching TV, and reading, in 1999-2000 will predict global cognitive function (assessed by the Teng Mini-Mental State; 3MS) and executive function (assessed by the CLOX 1) in 2006-2007, independent of key sociodemographic, mental and physical health, and behavior covariables. Sedentary time in 1999-2000 will also predict cognitive function, as assessed by the Digit Symbol Substitution Test (DSST), in 2006-2007, independent of key sociodemographic, mental and physical health, and behavior covariables.

Hypothesis 2b: Increased sitting and TV time over 3 years (from 1999-2000 to 2002-2003) will predict worse cognitive function (assessed by 3MS and DSST) and executive function (assessed by CLOX 1) in 2006-2007, independent of key sociodemographic, mental and physical health, and behavior covariables. Increased reading time over 3 years (from 1999-2000 to 2002-2003) will predict higher cognitive function (assessed by 3MS and DSST) and executive function (assessed by CLOX 1) in 2006-2007, independent of key sociodemographic, mental and physical health, and behavior covariables.

Hypothesis 2c: Those participants who increase sitting and TV time between 1999-2000 and 2002-2003 will have higher odds of dementia across 10 years of follow-up (June 1, 2004 to September 30, 2014) relative to participants who maintained or decreased sedentary and TV time. Those participants who increased reading time between 1999-2000 and 2002-2003 will have lower odds of dementia, compared with participants who maintained or decreased reading time.

Chapter 2: Methods

The Health ABC Study

Secondary analyses of data from Health ABC were used to test these hypotheses. The National Institute on Aging conducted Health ABC, a prospective cohort study of older adults who were aged 70-79 when recruitment began in 1997-1998 (National Institute on Aging, n.d.). The participants were followed for 16 years, and data collection occurred through both questionnaires and clinical examinations. The goal of the study was to examine the role of body composition as a potential mechanism whereby behavioral and health factors lead to decreases in independence and function in old age.

Participants were a random sample of Medicare beneficiaries living in pre-selected zip code areas in Memphis, Tennessee and Pittsburgh, Pennsylvania at the time of recruitment (Peninx et al., 2003). To be eligible for recruitment, participants had to report ability to walk a quarter of a mile, climb ten steps, not use equipment for walking, and report no difficulties with activities of daily living (Colbert et al., 2004). In addition, the participants could not have been treated for cancer within three years prior to recruitment or have plans to leave the area for three years. At least one-third of the 3,075 participants were Black/African American (National Institute on Aging, n.d.).

Protection of Human Subjects

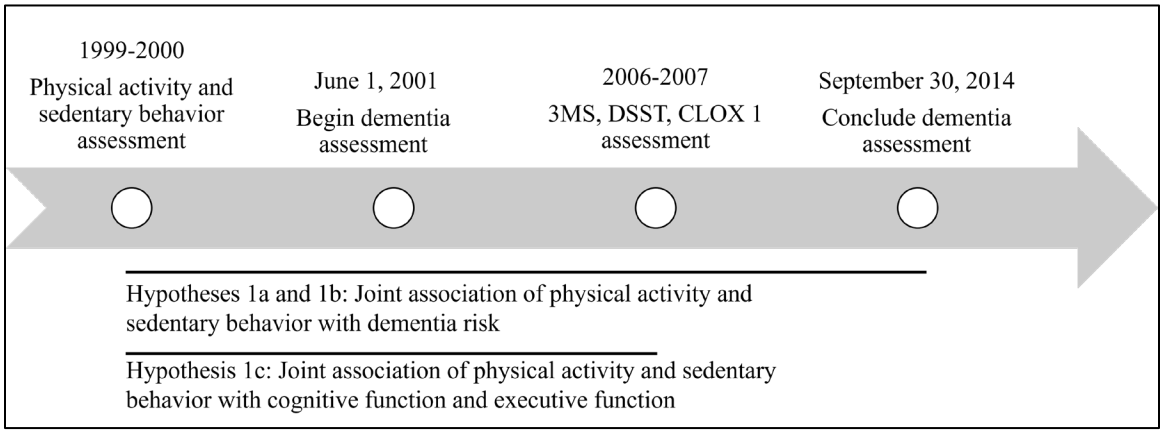
This dissertation research was performed through secondary data analysis and did not pose greater than minimal risk to human subjects. Regardless, this study received a determination from The George Washington University Institutional Review Board (IRB) that the project was exempt from IRB review. In addition, a Data Management Plan approved by The George Washington University documented how data were securely

handled and protected. Lastly, to access the data, an authorized representative of The George Washington University and the author entered into a data use agreement with The National Institute on Aging to ensure that the data were handled appropriately.

Timeline of Assessments

Both manuscripts used 1999-2000 data for the independent variables and 2006-2007 data for the cognitive function dependent variables. Since 1999-2000 was the first wave in which both physical activity and sedentary behavior were assessed in Health ABC, those data were used as baseline data even though the study began in 1997-1998. The CLOX 1 was last administered to the full sample in 2006-2007, which also included the 3MS and DSST assessments. For Manuscript 1, dementia status was cumulatively assessed from June 1, 2001 through September 30, 2014, allowing for dementia cases to be pooled across 13 years of follow-up. **Figure 3** depicts the timeline of assessments for each of the hypotheses tested in Manuscript 1.

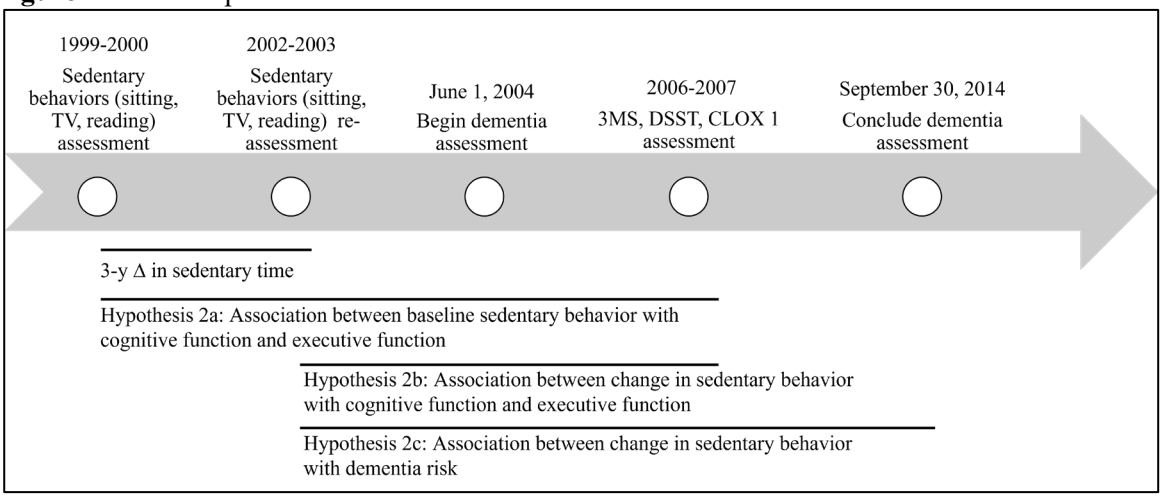
Figure 3. Manuscript 1 Timeline of Assessments



Manuscript 2 also used sedentary behavior data from 2002-2003, which was the final time that these data were collected from the full sample, to model 3-year change in sedentary behavior. Manuscript 2 included dementia cases pooled across June 1, 2004 through September 30, 2014, allowing for 10 years of follow-up. **Figure 4** depicts the

timeline of assessments for each of the hypotheses tested in Manuscript 2.

Figure 4. Manuscript 2 Timeline of Assessments



Measures

Sedentary Behavior

Health ABC measured sedentary behavior with three questions that were used across the two manuscripts in this dissertation research. The first question is: "During an average 24-hour day, about how many hours do you usually spend sitting upright? Be sure to include time sitting at the table eating, driving or riding in a car or bus, sitting watching T.V. or talking, etc." This item was the primary measure of interest for sedentary time in Manuscript 1. The variable was used as a continuous measure for Manuscript 2 baseline associations with cognitive function and dementia and as a categorical measure for Manuscript 1, with two levels: eight hours or less per day and greater than nine hours per day.

Analyses for both manuscripts were repeated using an individual item that assessed TV watching: "About how many hours per week do you spend watching television?". The inclusion of the TV item in Manuscript 1was based on findings from

DiPietro and colleagues' (2018) study, in which associations were stronger when time spent watching TV was used in the models instead of total sedentary time. The authors posit that possible reasons for these findings are that TV time is easier to recall because it is more structured and/or that individuals may be more likely to sit uninterrupted while watching TV. This variable was divided into two categories for both manuscripts: zero to twenty-seven hours and twenty-eight or greater hours per week. These groupings are based on research by Fancourt and Steptoe (2019), which found a threshold effect wherein 3.5 hours or more of TV watching per day was associated with poorer cognitive function, but there was no observed detriment from watching three hours or fewer.

Manuscript 2 also included analyses that used time spent reading as a third measure of sedentary behavior based on findings from the literature that reading, even when performed in a sitting or reclined position, may be cognitively beneficial (Kurita et al., 2019; Nemoto et al., 2018). The question in Health ABC asked, "About how many hours per week do you spend reading, including books, newspapers, and magazines?". This variable was left continuous to preserve variation.

Changes in sitting and reading time between 1999-2000 and 2002-2003 were operationalized by creating categorical change variables that represented whether participants decreased, maintained, or increased time spent sitting or reading (0=decreased time, 1=maintenance, 2=increased time). For TV watching, the change variable was created with four categories: 1=maintaining a low level (0-27 hours/week), 2=maintaining a high level (28+ hours/week), 3=increasing from low to high, or 4=decreasing from high to low.

Physical Activity

The physical activity questionnaire used in Health ABC was designed specifically for the study, and was modeled after other validated scales, primarily the Minnesota Leisure Time Physical Activity Questionnaire (Lange-Maia et al., 2015). In the questionnaire, participants were first asked whether they have performed a specific activity at least 10 times in the past year. If they indicated that they had, participants were then asked whether they had performed the activity or exercise in the last 7 days. If the answer to that question was yes, the participants were next asked questions about the amount of time spent doing the activity, as well as the intensity level. **Table 2** lists each question asked in the physical activity scale, along with the response options.

Table 2. Physical activity questionnaire items

The first question in each section is denoted by italics.

Item	**Response Options**
In the past 12 months, did you go walking for exercise, at least 10 times?	*Yes* *No* *Don't know*
In the past 7 days, did you go walking for exercise?	Yes No
How many times did you go walking for exercise in the past 7 days?	Open-ended (number of times)
About how much time, on average, did you spend walking each time you walked (excluding rest periods)?	Open-ended (hours and minutes)
When you walk for exercise, do you usually walk at a brisk pace (as fast as you can), a moderate pace, or at a leisurely stroll?	Brisk Moderate Stroll Don't now
About how many blocks, on average, did you walk each time?	Open-ended (number of blocks)
In the past 12 months, did you do any other type of walking, such as walking to work, the store, to church, or walking the dog, at least 10 times?	*Yes* *No* *Don't know*
In the past 7 days, did you do other walking?	Yes No
How many times did you do other walking in the past 7 days?	Open-ended (number of times)
About how much time, on average, did you spend doing other walking each time you walked (excluding rest periods)?	Open-ended (hours and minutes)

When you do other walking, do you usually walk at a brisk pace (as fast as you can), a moderate pace, or at a leisurely stroll?	Brisk Moderate Stroll Don't know
About how many blocks, on average, did you walk each time?	Open-ended (number of blocks)
In the past 12 months, did you walk up a flight of stairs (a flight is about 10 steps), at least 10 times?	*Yes* *No* *Don't know*
In the past 7 days, did you walk up a flight of stairs?	Yes No
About how many flights did you walk up in the past 7 days? If you are unsure, please make your best guess.	Open-ended (number of flights)
About how many of these flights did you walk up carrying a small load like laundry, groceries, or an infant?	Open-ended (number of flights)
In the past 12 months, did you do any high intensity exercise such as bicycling, swimming, jogging, racquet sports or using a stair-stepping, rowing or cross country ski machine or exercycle, at least 10 times?	*Yes* *No* *Don't know*
In the past 7 days, did you do high intensity exercise activities?	Yes No
What activity(ies) did you do?	Bicycling/exercycle Swimming Jogging Aerobics Stair-stepping Racquet sports Rowing machine Cross country ski machine Other (specify)
In the past 7 days, about how much time did you spend doing (each activity)?	Open-ended (hours and minutes)

Previous studies using the physical activity data from Health ABC have converted the responses to the questions into energy costs, measured in kilocalories per week (kcal/week), to create a summary variable that encompasses weekly energy expenditures across activity types (Koster et al., 2008; Brach et al., 2004; Havlik et al., 2003; Peterson et al., 2009; Visser et al., 2005; Lange-Maia et al., 2015). This process entails assigning a metabolic equivalent to each activity based on the intensity of the activity. The metabolic equivalents are derived from a compendium that quantifies the energy costs of a wide

variety of physical activity types and that is standard in the field of physical activity research (Ainsworth et al., 2011). After the metabolic equivalents have been determined, they are multiplied by the amount of time spent doing the activity per week and by the participant's body weight to obtain the kcal/week values. The summary variable includes the kcal/week measurements for all the tasks reported by the participant. Based on the summary variable, participants were then divided into three different activity level categories: 0-499 kcal/week, 500-1,999 kcal/week, and 2000+ kcal/week.

Joint Sedentary Behavior and Physical Activity Variables

The joint associations of sedentary behavior and physical activity with cognitive function and dementia were determined by nesting the two sitting time categories into each of the three physical activity categories. In other words, within each level of physical activity, there were two levels of sedentary behavior. Indicator variables were created for each possible combination, for a total of six indicator variables. The indicator variables are displayed in **Table 4**. The same process was completed for the two categories of hours spent watching TV per day and the three physical activity categories.

Table 4. Joint sedentary behavior and physical activity variables.

Variable Label	Description
Low PA, low sedentary	0-499 kcal/week PA, 0-8 hrs sitting
Low PA, high sedentary	0-499 kcal/week PA, 9+ hrs sitting
Medium PA, low sedentary	500-1,999 kcal/week PA, 0-8 hrs sitting
Medium PA, high sedentary	500-1,999 kcal/week PA, 9+ hrs sitting
High PA, low sedentary	2,000+ kcal/week PA, 0-8 hrs sitting
High PA, high sedentary	2,000+ kcal/week PA, 9+ hrs sitting

Cognitive Function and Dementia

Global cognitive function in Health ABC was assessed using the 3MS. The 3MS measures cognitive function across a range of domains, including orientation, attention,

and recall, among others (Yaffe et al., 2009). Example questions from the 3MS include asking the participant where and when they were born, how to spell words, to count from 1 to 5, to recall words, where they are in space (i.e., city, county, state) and time (i.e., date, day of the week, season), and others. Possible scores range from 0-100, with higher scores indicating better cognitive function. The 3MS is an enhanced version of the more commonly employed Mini-Mental State Examination (MMSE), offering better sensitivity and specificity in screening for dementia (Health ABC, n.d.).

Health ABC also included the Digit Symbol Substitution Test (DSST), which is a polyfactorial measure of cognitive function, but is not considered a measure of global cognitive function. In other words, the DSST assesses several subdomains of cognitive function, but not all of them. While there is some debate about the specific subdomains measured by DSST, most researchers coalesce around the DSST as an assessment of motor skills, attention, and executive function (Jaeger, 2018; Lambiase, Kuller, & Matthews, 2014; Yaffe et al., 2008; Lin et al., 2014). Notwithstanding this lack of specificity, one of the strengths of the DSST is that it is very sensitive to cognitive impairment, which is why it was included in the present research – the DSST may identify deficits in cognitive function that the 3MS may not (Jaeger, 2018).

The DSST is a paper and pencil test, which has a key at the top that matches symbols with digits from one to nine. Below the key are four rows of 25 sets of double boxes with a digit in the top box and the bottom box empty. The participant is asked to draw the symbol in the bottom box that matches the number in the top box. The score is the number of correct symbols provided in 90 seconds. Higher scores indicate better performance (Rosano, Newman, Katz, Hirsch, & Kuller, 2008; Lambiase et al., 2014).

Executive function in Health ABC was measured with the CLOX 1. The CLOX 1 is a clock drawing task wherein participants are asked to draw a clock that shows 1:45. Various elements of the clock drawing (e.g., whether the clock is a circle, whether the numbering and spacing are correct, whether the hands are in the correct positions, etc.) are then assessed by a rater. Possible scores range from zero to fifteen, with higher scores indicating better executive function. The CLOX 1 has been determined to be reliable and valid as a measure of cognitive function (Royall, Cordes, & Polk, 1998).

Dementia in Health ABC was assessed using a binary indicator variable (0=no dementia, 1=dementia) derived from multiple sources of data, including whether the participant has been prescribed a medication used to treat dementia specifically (e.g., galantamine, rivastigmine, memantine, donepezil, or tacrine); received a dementia diagnosis; or demonstrated a race-adjusted decline in 3MS score of 1.5 or more standard deviations. Participants were considered to have dementia if they met one or more of these criteria. Dementia cases for Manuscript 1 were pooled across 13 years of follow-up, starting on June 1, 2001 (one year after baseline data collection concluded in 2000) and ending on September 30, 2014. Dementia cases for Manuscript 2 were pooled across 10 years of follow-up, starting on June 1, 2004 (one year after data collection for the second year used to create the change variables concluded in 2003) and ending on September 30, 2014.

Covariables

Race/ethnicity. Health ABC included a race variable that allows for comparisons between Black/African American individuals and White individuals. The data were coded such that White=1 and Black=2. By design, other races were not identified in the

dataset.

Demographics. Age, education, and gender were statistical controls in the models. Education in Health ABC was measured as 1=less than high school education, 2=high school graduate, and 3=postsecondary. Age (measured continuously) was assessed at each wave. Gender was a dichotomous variable, coded as Male=1 and Female=2.

Physical function. The Health ABC investigators created a walking ability index as an indicator of physical function (Simonsick et al., 2009). The index was constructed from a series of questions that ask participants whether they have any difficulty walking a quarter of a mile. Those who reported difficulty were asked the extent of difficulty (i.e., a little, some, or unable to walk). Those who did not report difficulty were asked how easy it was for them to walk, with possible response options of very, somewhat, or not so easy. This set of questions was repeated for walking a full mile. Scores on the index range from zero to nine, with zero indicating inability to walk a quarter of a mile and nine indicating walking a mile is very easy.

Self-rated health. Self-rated health is a single item measure: "In general, how would you say your health is? Would you say it is excellent, very good, good, fair, or poor?" The data were scored as 1=excellent, 2=very good, 3=good, 4=fair, and 5=poor.

BMI. Body mass index (kg/m^2) was calculated based on measured height and weight.

Smoking status. The Health ABC dataset included a calculated smoking status variable with categories of 0=never smoker, 1=current smoker, and 2=former smoker

Depressive Symptoms. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression (CES-D 10) short form scale (Williams et al., 2015).

Possible scores range from 0-30, with higher scores indicating more depressive symptoms. Scores on the CES-D were left continuous to preserve variation.

Statistical Analysis Plan

Univariate Analyses

Univariate analyses were conducted for all variables to derive measures of central tendency (mean±SD) and frequencies (%). These analyses helped inform descriptive statistics to characterize the study samples. Analyses were conducted using participants with non-missing data for the independent and dependent variables.

Manuscript 1 Analyses

Logistic regression tested Hypothesis 1a (Health ABC participants who exhibit high sedentary time and low physical activity in 1999-2000 will have a higher risk of dementia across 13 years of follow-up, compared with older adults with low sedentary time and high physical activity) by modeling the relationship between joint associations of sedentary behavior and physical activity in 1999-2000 and cumulative odds of dementia across June 1, 2001 to September 30, 2014.

For Hypothesis 1b (odds of dementia will be accelerated among those who sit the most and who are the least active), odds ratios for each of the joint associations indicator variables were then plotted to determine visually whether the odds ratios increased in a dose-response manner as physical activity decreased and sedentary time increased.

To test Hypothesis 1c (Health ABC participants who exhibit high sedentary time and low physical activity in 1999-2000 will have lower cognitive and executive function scores in 2006-2007), multivariable linear regression was used to model the relationships between the joint associations of sedentary behavior and physical activity in 1999-2000

and 3MS, CLOX 1, and DSST scores in 2006-2007.

Manuscript 2 Analyses

Linear regression was used to test Hypothesis 2a (time spent sitting upright, watching TV, and reading in 1999-2000 will predict global cognitive function and executive function in 2006-2007). The regressions modeled the relationships between sedentary behavior (time spent sitting upright, watching TV, and reading) in 1999-2000 and 3MS, CLOX 1, and DSST scores in 2006-2007.

Similarly, linear regression was used to test Hypothesis 2b (increased sitting and TV time between 1999-2000 and 2002-2003 will predict lower cognitive function and executive function in 2006-2007 while increased reading time over the same 3-year period will predict higher cognitive function and executive function in 2006-2007). The regressions modeled the relationships between change in sedentary time between 1999-2000 and 2002-2003 (operationalized with previously described categorical change variables) and 3MS, CLOX 1, and DSST scores in 2006-2007.

Lasty, logistic regression tested Hypothesis 2c (participants who increased sitting and TV time between 1999-2000 and 2002-2003 will have higher odds of dementia across 10 years of follow-up while those who increased reading time will have lower odds of dementia across the same time period) by modeling the relationship between change in sedentary time and odds of dementia.

Chapter 3: Manuscript 1

Joint associations of physical activity and sitting time on 7-year odds of dementia: The Health ABC Study

Laura Major[1], Eleanor M. Simonsick[2], Melissa A. Napolitano[1,3], and Loretta DiPietro[3]

Departments of [1]Prevention & Community Health and [3]Exercise & Nutrition Sciences, Milken Institute School of Public Health, The George Washington University, Washington, DC and [2]Intramural Research Program, Translational Gerontology Branch, National Institute on Aging, Baltimore, MD

Running title: Physical activity, sitting, and dementia

Word count: Abstract 232; Manuscript 3,925

Author contact: Loretta DiPietro, PhD, MPH
Department of Exercise and Nutrition Sciences
Milken Institute School of Public Health
The George Washington University
950 New Hampshire Ave
Washington, DC 20052
ldp1@gwu.edu

Abstract

Background: Physical activity represents one component of daily movement. This study aims to examine the combined associations of physical activity and sitting time, as a more complete representation of movement, with future odds of dementia. **Methods:** We analyzed prospective data from 1,988 men and women (52%) aged 72-81 years at baseline participating in the Health Aging and Body Composition (Health ABC) Study between baseline (1999-2000) and study conclusion (2014). Physical activity (kcal/week) and sitting time (hours/day) were self-reported in 1999-2000 and dementia status was evaluated from June 1, 2001 through September 30, 2014. Multivariable logistic regression determined the independent and joint associations of physical activity and sitting time with odds of dementia. **Results:** In the independent associations model, neither being in the high sitting group (9+ hours/day; OR=0.94, 95% CI=0.72, 1.23) nor being in the low physical activity group (<500 kcal/week; OR=1.06, 95% CI=0.79, 1.42) were associated with greater odds of dementia. In the joint associations model, participants in the high sitting and low physical activity group did not have a greater odds of dementia, compared with participants in the low sitting and high physical activity group (OR=1.16, 95% CI=0.74, 1.82). **Conclusion:** We did not observe a relationship between physical activity and sitting time and incident dementia either independently or jointly. More research is needed to explicate whether and how daily movement affects and/or reflects cognitive decline, including dementia, among older adults.

Introduction

Aging is the primary risk factor for most types of dementia (Wahl et al., 2019). Thus, due to aging demographics, the global prevalence of dementia is expected to nearly double from 36 million cases in 2010 to 66 million cases in 2030 (Prince et al., 2016; Langa et al., 2017). Approximately 7.7% of adults 50 years and older in the United States have dementia (Farina et al., 2022). These estimates of dementia are expected to increase by 2050 (Hebert et al., 2013; Friedman et al., 2013) and have significant implications for the health and function of older adults, as well as for their families, and the healthcare system (Hurd et al., 2013). Currently, there is no cure for dementia (Centers for Disease Control and Prevention, 2019), which underscores the importance of examining potentially modifiable behaviors that can mitigate both the development and progression of this disease.

A growing body of literature suggests that physical activity may protect against dementia (Blondell, Hammersley-Mather, & Veerman, 2014; Baumgart et al., 2015; Guure, Ibrahim, Adam, & Said, 2017), with evidence from a meta-analysis of a dose-response relationship between increasing levels of leisure time physical activity and decreasing risk of dementia and Alzheimer's disease (Xu, Wang, Wan, Tan, Yu, & Tan, 2017). Recently, the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (PAGAC, 2018) concluded that moderate evidence supports the benefit of regular physical activity to brain health – even among older people with existing dementia and Alzheimer's disease (Groot et al., 2016). In contrast, a recent review of intervention and observational studies in people with mild cognitive impairment or dementia (Demurtas et al., 2020) highlighted substantial bias among these studies, which diminishes the

certainty of the evidence on the effectiveness of physical activity for altering the trajectory of cognitive decline. Among the reasons for the disparate findings were numerous methodological issues, including differences between observational and intervention studies, in the assessment of physical activity and cognitive function, in the dose and timing of physical activity, and in the length of follow-up. It is possible that one reason it has been difficult to establish a relationship between physical activity and dementia is that physical activity is only one component of daily movement and that the joint associations of physical activity and sedentary behavior, as a more complete representation of movement, may be more informative.

Although the existing evidence suggests that physical activity and sedentary behavior are independent risk factors for health outcomes (USDHHS, 2018), conceivably the interaction of these two behaviors may affect health and function in a way that cannot be understood by simply examining each independently from the other (Guallar-Castillón et al., 2014). In fact, the 2020 WHO Physical Activity and Sedentary Behavior Guidelines Development Group identified the lack of information on the joint association between physical activity and sedentary time with health outcomes across the life-course as an evidence gap (DiPietro et al., 2020). Although several studies have examined these joint associations in older adults (DiPietro, Jin, Talegawkar, & Matthews, 2018; Feter, Leite, Smith, Coombes, & Rombaldi, 2020; Blough & Loprinzi, 2019; Yerramalla et al., 2021), to our knowledge, this study is among the first to consider them with respect to cognitive function and dementia.

Therefore, the purpose of this study was to examine the combined associations of physical activity and sitting time with the likelihood of developing dementia over a

period of 13 years. The study sample consists of older people participating in the Health, Aging and Body Composition (Health ABC) Study. Similar to other studies examining these joint effects (Katzmarzyk et al., 2019; DiPietro et al., 2018; Ekelund et al., 2016), we hypothesized that the odds of dementia would increase in a dose-response manner with decreasing levels of physical activity combined with increasing sedentary behavior. We also examined whether physical activity and sedentary behavior were jointly associated with scores on cognitive function tests that would indicate cognitive impairment below the threshold for dementia.

Methods

Study Participants

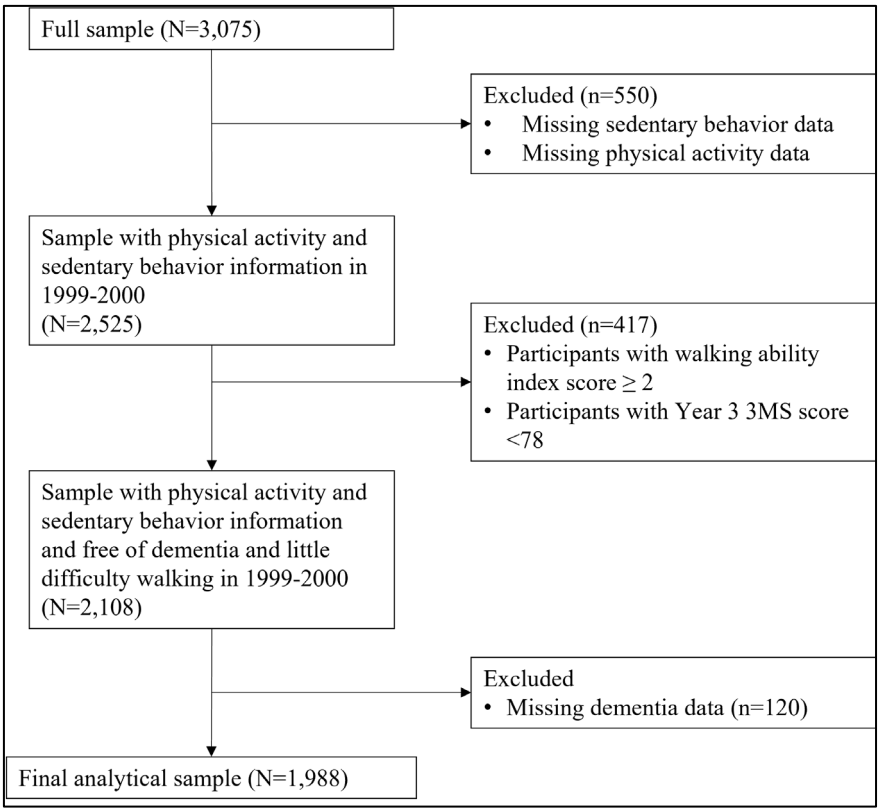
Health ABC is a longitudinal cohort study that was conducted by the National Institute on Aging between 1997 and 2014. The cohort comprised 3,075 community-dwelling older adults, 70-79 years of age, living in designated zip code areas in Memphis, Tennessee and Pittsburgh, Pennsylvania at the time of recruitment (Penninx et al., 2003). Details of the study design, sampling scheme, and recruitment have been described previously (National Institute on Aging, n.d.). To be eligible for the study, participants had to report no difficulty in walking ¼ mile, climbing 10 steps, or performing any basic activity of daily living. In addition, they had to be free of any life-threatening cancers and plan to remain in the study area for at least three years. Respondents who were free of dementia and who had complete data on physical activity and sedentary behavior in 1999-2000 (the first year in which both physical activity and sedentary behavior were assessed) were eligible to be included in the current analysis. In addition, only those who reported being able to walk ¼ mile with no more than some difficulty and who were free

of dementia in 1999-2000 were included to ensure the healthiest baseline sample possible and rule out potential confounding effects of functional limitations (N=1,988; **Figure 5**).

Physical Activity and Sedentary Behavior

Regular physical activity over the past week was assessed by self-report using an adapted version of the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ; Taylor et al., 1978; Lange-Maia et al., 2015).

Figure 5. Participant selection from the Health ABC cohort. Those respondents who provided complete data on physical activity, sedentary behavior, and dementia and who were free of dementia and had limited difficult walking in 1999-2000 were eligible to be included in the analysis (N=1,988).



Participants were first asked whether they had performed a specific activity at least 10 times in the past year. If they indicated that they had, participants were then asked whether they had performed that activity in the last 7 days. If the response was yes, participants were asked about the frequency, intensity, and duration of the activity. Each activity then was assigned a metabolic equivalent of task (MET) value based on its intensity (Ainsworth et al., 2011) and converted into energy costs (kcal) by multiplying

the MET value by duration (hours/week) by body weight (kg). The energy costs for each reported activity were then summed over all activities for the week to derive a summary physical activity variable expressed as kcal/week. This summary variable was next divided into three categories (0=≥2000; 1= 1,999-500; and 2=<500 kcal/week) similar to those used in other Health ABC analyses to facilitate cross-comparisons (e.g., Beavers et al., 2013). Sitting time was assessed by asking respondents how many hours they typically spend sitting upright over a 24-h period and was dichotomized (0=0-8 and 1=9-18 h/day).

Dementia

Dementia was assessed using a binary indicator variable that combined multiple sources of data, including whether the participant was prescribed medication used to treat dementia (galantamine, rivastigmine, memantine, donepezil, or tacrine), received a dementia diagnosis from a health care provider, or exhibited race-adjusted decline in Teng Mini-Mental State (3MS) score of 1.5 or more standard deviations. An individual was determined to have dementia if they met one or more of these criteria. Dementia data were pooled across June 1, 2001 to September 30, 2014, representing 13 years of cumulative follow-up.

Cognitive Function

Cognitive function was measured using the 3MS, the Digit Symbol Substitution Test (DSST), and the CLOX 1 in 2006-2007, the last year in which cognitive function was assessed on the full sample in Health ABC. The 3MS is a measure of global cognitive function, assessing cognitive function across all domains, including orientation, attention, and recall, among others (Yaffe et al., 2009). Possible scores range from 0-100,

with higher scores indicating better cognitive function. The DSST assesses multiple subdomains of cognitive function, including motor skills, attention, and executive function (Jaeger, 2018; Lambiase, Kuller, & Matthews, 2014; Yaffe et al., 2008; Lin et al., 2014). Notwithstanding this lack of specificity, one strength of the DSST is its high sensitivity to cognitive impairment, which is why it was included in the present research – the DSST could identify deficits in cognitive function that the 3MS may not (Jaeger, 2018). The CLOX 1 is a measure of executive function, the cognitive subdomain associated with planning and decision-making, and was included because declines in executive function may occur before declines in globally assessed cognitive function and declines in executive function are predictive of dementia onset (Clark et al., 2012). Possible scores range from zero to fifteen, with higher scores indicating better executive function. The CLOX 1 has been determined to be reliable and valid as a measure of cognitive function (Royall, Cordes, & Polk, 1998).

Covariables

Several covariables were included in this analysis, based on their demonstrated relationships with physical activity, sedentary behavior, or dementia (Peterson et al., 2009; Yaffe et al., 2009). These variables include age, sex, race (white vs. black/African American), education level (<HS, HS grad, post-secondary), smoking status (never, former, current smoker), body mass index (BMI: kg/m^2), self-rated health (excellent, very good, good, fair, poor), and depressive symptoms. Depressive symptoms were measured using the Centers for Epidemiologic Studies Depression (CES-D 10) short form scale (Andresen et al. 1994). Possible scores range from 0-30, with higher scores indicating more depressive symptoms.

Statistical Analysis

Univariate statistics [mean±SD; frequencies (%)] first were generated on all variables to determine their distributions within the study population. Unadjusted relationships between each study variable and dementia status were tested using independent *t*-tests and chi-square tests. Multivariable logistic regression was used to examine the independent relationship between physical activity, sedentary behavior, and the odds of dementia, while adjusting for the covariables of interest. Multivariable linear regression was used to model the independent associations between physical activity, sedentary behavior, and 3MS, DSST, and CLOX 1 scores.

To examine the joint associations between physical activity and sitting time with dementia risk, we nested the two categories of sedentary behavior within each physical activity category to create six indicator variables. This allowed us to compare directly groups with varying amounts of physical activity and sedentary time against those who had the most physical activity and also sat the least (referent group). Multivariable logistic regression models included these indicator variables, as well as the covariables that were statistically significant in the unadjusted analyses. Odds ratios (OR) and 95% confidence intervals (CI) are reported from the final logistic regression model to describe the odds of dementia within each level of sitting time and physical activity relative to the referent group. Multivariable linear regression models also included these indicator variables, along with the same set of covariables, to evaluate the association between physical activity and sitting time with 3MS, DSST, and CLOX 1 scores. Parameter estimates, standard errors, and *p* values are reported for each level of sitting time and physical activity.

Results

The cumulative incidence of dementia over the follow-up period was 19%. On average, participants were 75.4±2.8 years of age and overweight (27.1±4.5 kg/m^2; **Table 4**). Approximately 52% were women and 66% were white. The majority of the study population were fairly well-educated, with 49% reporting some post-secondary level of educational attainment. Most participants rated their health as good or very good, and there was a low prevalence of current smoking. The mean score from the CES-D 10 was 4.1±3.8 indicating low levels of depressive symptomology. **Table 4** also displays results from the simple analysis. As indicated, age, education level, self-rated health, CES-D 10 score and BMI score at baseline were each significantly associated with dementia at

Table 4. Descriptive statistics (N=1,988).

		Dementia		
		Yes (n=383)	**No (n=1,605)**	***p***
Mean age (SD)	75.43 (2.82)	76.16 (2.90)	75.25 (2.77)	<0.0001
Female, n (%)	1,036 (52.11)	206 (53.79)	830 (51.71)	0.82
Race, n (%)				0.47
Black	645 (32.44)	131 (34.20)	514 (32.02)	
White	1,343 (67.56)	252 (65.80)	1.091 (67.98)	
Educational attainment, n (%)				<0.05
Less than high school	320 (16.10)	76 (19.84)	244 (15.20)	
High school graduate	687 (34.56)	136 (35.51)	551 (34.33)	
Postsecondary	981 (49.35)	171 (44.65)	810 (50.47)	
Self-rated health, n (%)				<0.001
Excellent	260 (13.08)	52 (13.58)	208 (12.96)	
Very good	711 (35.76)	122 (31.85)	589 (36.70)	
Good	752 (37.83)	138 (36.03)	614 (38.26)	
Fair	246 (12.37)	61 (15.93)	185 (11.53)	
Poor	19 (0.96)	10 (2.61)	9 (0.56)	
Smoking status, n (%)				0.21
Never smoker	910 (45.77)	189 (49.35)	721 (44.92)	
Current smoker	124 (6.24)	19 (4.96)	105 (6.54)	
Former smoker	954 (47.99)	175 (45.69)	779 (48.54)	
Mean CES-D 10 score (SD)	4.13 (3.79)	4.72 (4.16)	3.99 (3.69)	<0.001
Mean BMI (SD)	27.11 (4.55)	26.68 (4.83)	27.22 (4.48)	<0.05

follow-up, whereas sex, race, and smoking status were not. The sample comprised physically active individuals, as more than 2/3 of participants were classified in either the high (2000+ kcal/week) or medium (500-1,999 kcal/week) physical activity groups and about 75% of participants reported sitting 8 hours or fewer per day (**Table 5**). Neither physical activity level nor sitting time were significantly associated with dementia in the unadjusted analysis (**Table 5**).

Table 5. Categories of physical activity and sedentary time according to dementia status (N=1,988).

		Dementia		
		Yes (n=383)	No (n=1,605)	*p*
Hours sitting per day, n (%)				0.64
0-8 hours	1,487 (74.80)	290 (75.72)	1,197 (74.58)	
9+ hours	501 (25.20)	93 (24.28)	408 (25.42)	
Physical activity, n (%)				0.14
2,000+ kcal/week	766 (38.53)	131 (34.20)	635 (39.56)	
500-1,999 kcal/week	672 (33.80)	136 (35.51)	536 (33.40)	
0-499 kcal/week	550 (27.67)	116 (30.29)	434 (27.04)	

Multivariable parameter estimates for the independent associations of physical activity and sitting time with the odds of dementia are reported in **Table 6**. Smoking status was excluded from the model due to its negligible association with dementia in the simple analysis. The relationships between physical activity and dementia and sitting time and dementia remained not significant in the presence of the other covariables. The only independent predictors of dementia at follow-up were age and poor health.

Table 7 displays the results of the analyses of the independent associations of physical activity and sitting time with 3MS, DSST, and CLOX 1 scores, respectively. Each model was statistically significant and explained 17% of the variance in 3MS score,

26% of the variance in DSST score, and 7% of the variance in CLOX 1 score. Physical activity and sedentary behavior were not independently associated with 3MS, DSST, or CLOX 1 scores, with one exception. Reporting low physical activity (<500 kcal/week) at baseline was associated with a 1.18-point lower (p<0.05) 3MS score at follow-up, compared to reporting high physical activity (>2,000 kcal/week). In each of the models, older age, racial identity of black, lower educational attainment, and poorer self-rated health were associated with lower 3MS, DSST, and CLOX 1 scores, while female sex was associated with higher scores. Depressive symptoms were also associated with a lower 3MS score, such that each 1-point higher score on the CES-D was associated with a 0.15-point (p<0.05) lower 3MS score.

Table 6. Independent associations of sedentary time and physical activity with dementia (N=1,988).

	OR	95% CI	*p*
Hours sitting per day			
0-8 hours	1.00		
9+ hours	0.94	0.72, 1.23	0.66
Physical activity			
2,000+ kcal/week	1.00		
500-1,999 kcal/week	1.18	0.89, 1.54	0.26
0-499 kcal/week	1.06	0.79, 1.42	0.72
Age	1.11	1.07, 1.16	<0.0001
Female	1.07	0.85, 1.42	0.56
Black race	1.09	0.84, 1.42	0.53
Educational attainment			
Postsecondary	1.00		
High school graduate	1.13	0.87, 1.47	0.31
Less than high school	1.34	0.96, 1.87	0.09
Self-rated health			
Excellent	1.00		
Very good	0.77	0.53, 1.11	0.16
Good	0.78	0.54, 1.11	0.20
Fair	1.01	0.63, 1.60	0.98
Poor	3.08	1.13, 8.44	<0.05
CES-D 10 score	1.02	0.99, 1.06	0.17
BMI	0.98	0.95, 1.00	0.16

Table 7. Independent associations of sedentary time and physical activity with 3MS, DSST, and CLOX1 scores.

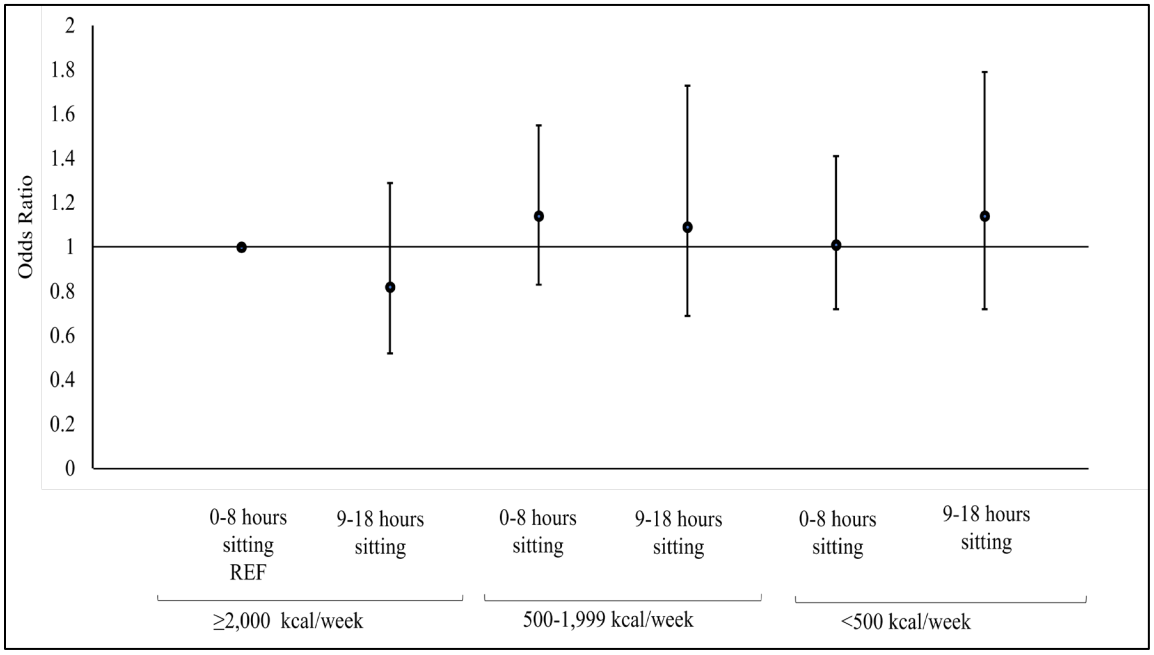
	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Hours sitting per day									
0-8 hours	REF			REF			REF		
9+ hours	0.34	0.54		1.27	0.75		-0.02	0.15	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.22	0.54		0.58	0.75		0.18	0.15	
0-499 kcal/week	-1.18	0.61	*	-0.36	0.84		0.25	0.17	
Age	-.044	0.08	**	-0.83	0.12	**	-0.10	0.02	**
Female	1.64	0.48	*	4.44	0.66	*	0.52	0.13	**
Black race	-3.46	0.55	**	-6.66	0.77	**	-0.30	0.15	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.70	0.72	**	-3.03	0.73	**	-0.59	0.15	**
Less than high school	-6.78	0.72	**	-10.61	1.00	**	-1.06	0.20	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.94	0.71		-2.45	0.98	*	-0.19	0.20	
Good	-1.44	0.74	*	-4.69	1.02	**	-0.30	0.21	
Fair	-1.69	0.99		-5.96	1.38	**	-0.57	0.28	*
Poor	-2.87	3.24		-10.92	4.49	*	-1.05	0.91	
CES-D 10 score	-0.15	0.07	*	-0.17	0.09		-0.03	0.02	
BMI	0.07	0.05		0.09	0.07		0.01	0.01	
	N=1,328 R^2=0.17 F(14, 1313)=19.20 Model *p*<.0001			N=1,308 R^2=0.26 F(14, 1293)=32.66 Model *p*<.0001			N=1,325 R^2=0.07 F(14, 1310)=7.07 Model *p*<.0001		

**p<.01. *p<.05

The odds ratios for the joint associations of physical activity and sitting time with dementia are shown in **Figure 6**. None of the activity categories carried greater odds of dementia when compared to the most active group, those who sat 8 hours or fewer per day and who expended 2,000 or more kcal/week. Older age (OR=1.12, 95% CI=1.07, 1.16), higher CES-D score (OR=1.04, 95% CI=1.01, 1.07), and having less than a high

school education (OR=1.39, 95% CI=1.00, 1.94) were associated with greater odds of dementia.

Figure 6. The joint associations of sedentary time and physical activity with dementia (N=1,988). Odds ratios (OR) represent the increased odds of dementia relative to the referent group. Multivariable logistic regression model adjusted for age, sex, race, BMI, self-rated health, and depressive symptoms.



The parameter estimates for the joint associations of physical activity and sitting time with 3MS, DSST, and CLOX 1 scores are shown in **Table 8**. Similar to the dementia logistic regression model, none of the activity categories were associated with 3MS, DSST, or CLOX 1 performance. In these models, compared with the dementia logistic regression model, more of the covariables were significantly associated with cognitive function score, with older age, black race, less education, and worse health associated with lower scores and female sex associated with higher scores.

Table 8. Joint associations of sedentary time and physical activity with 3MS, DSST, and CLOX 1 scores.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Joint sedentary time and physical activity									
≥2,000+ kcal/week PA and 0-8 hours sitting	REF			REF			REF		
≥2,000+ kcal/week PA and 9+ hours sitting	0.84	0.81		2.07	1.13		0.02	0.23	
500-1,999 kcal/week PA and 0-8 hours sitting	0.24	0.61		0.77	0.86		0.20	0.17	
500-1,999 kcal/week PA and 9+ hours sitting	1.04	0.94		2.13	1.31		0.15	0.26	
0-499 kcal/week PA and 0-8 hours sitting	-0.69	0.69		0.23	0.97		0.27	0.19	
0-499 kcal/week PA and 9+ hours sitting	-1.85	1.04		-0.08	1.46		0.22	0.29	
Age	-0.44	0.84	**	-0.83	0.12	**	-0.10	0.02	**
Female	1.63	0.48	*	4.41	0.67	**	0.52	0.13	**
Black race	-3.43	0.55	**	-6.64	0.76	**	-0.30	0.15	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.64	0.52	**	-2.96	0.73	**	-0.59	0.15	**
Less than high school	-6.82	0.72	**	-10.65	1.00	**	-1.06	0.20	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.07	0.71		-2.43	0.98	*	-0.19	0.20	
Good	-1.40	0.74		-4.67	1.02	**	-0.30	0.21	
Fair	-1.63	0.99		-5.92	1.38	**	-0.57	0.28	*
Poor	-2.81	3.24		-10.85	4.49	*	-1.04	0.91	
CES-D 10 score	-0.15	0.07	*	-0.18	0.09		-0.03	0.02	
BMI	0.07	0.05		0.10	0.07		0.01	0.01	
	N=1,328 R^2=0.17 F(16, 1311)=16.97 Model *p*<.0001			N=1,308 R^2=0.26 F(16, 1291)=28.66 Model *p*<.0001			N=1,325 R^2=0.07 F(16, 1308)=6.18 Model *p*<.0001		

**p<.01. *p<.05

Post hoc statistical power analyses for all models were conducted used G*Power 3.1.9.7. The analytic sample for the logistic regression modeling the joint associations of physical activity and sedentary behavior with odds of dementia was 1,988. A post hoc power analysis revealed at least 82.9% power to detect an odds ratio of 1.16, which represented the odds of dementia associated with being in the low physical activity and high sitting time group compared with being in the high physical activity and low sitting

time group.

The linear regression modeling the joint associations of physical activity and sedentary behavior with 3MS score had 14 predictors and R^2=0.17. The sample size needed to achieve 95% power in this model was N=146, which was surpassed by the actual analytical sample size (N=1,328). The linear regression modeling the joint associations of physical activity and sedentary behavior with DSST score had 14 predictors and R^2=0.26. The sample size needed to achieve 95% power in this model was N=91, which was surpassed by the actual analytical sample size (N=1,308). The linear regression modeling the joint associations of physical activity and sedentary behavior with CLOX 1 score had 14 predictors and R^2=0.07. The sample size needed to achieve 95% power in this model was N=374, which was surpassed by the actual analytical sample size (N=1,325).

To confirm our findings, we ran a set of robustness checks. The first (**Tables 9-10, Figure 7**) coded physical activity in units of time rather than energy expenditure because energy expenditure is derived by multiplying METs by body weight, meaning

Table 9. Categories of physical activity time and sedentary time according to dementia status (N=1,988).

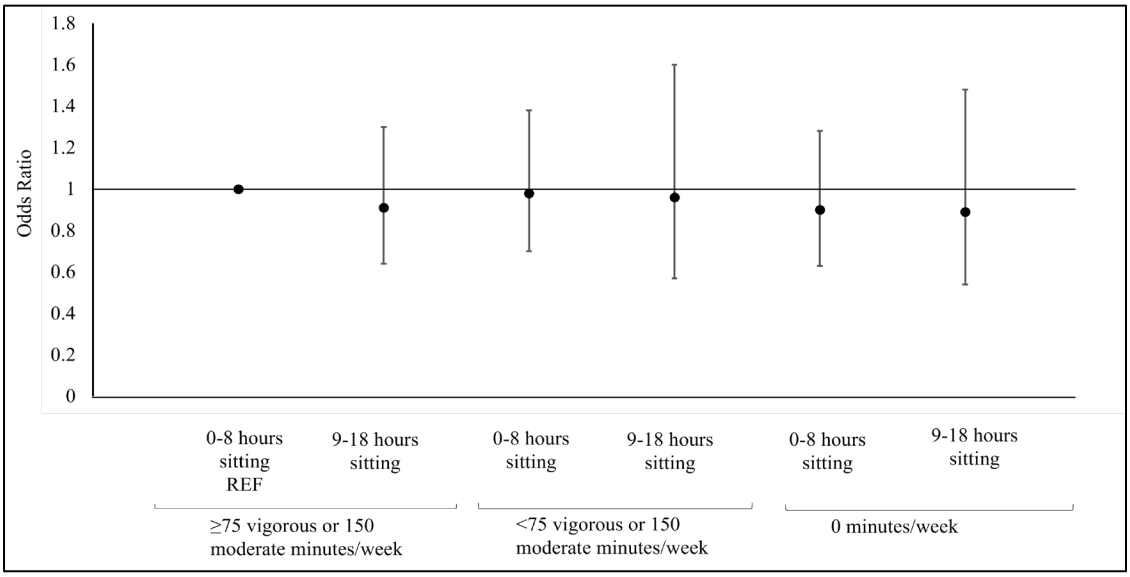
		Dementia		
		Yes (n=383)	**No (n=1,605)**	***p***
Hours sitting per day, n (%)				0.64
0-8 hours	1,487 (74.80)	290 (75.72)	1,197 (74.58)	
9+ hours	501 (25.20)	93 (24.28)	408 (25.42)	
Physical activity, n (%)				0.89
≥75 vigorous minutes or 150 moderate minutes	1,204 (60.56)	228 (59.53)	976 (60.81)	
<75 vigorous minutes or 150 moderate minutes	399 (20.07)	78 (20.37)	321 (20.00)	
0 minutes/week	385 (19.37)	77 (20.10)	308 (19.19)	

that people who weigh more will have a greater energy expenditure value for the same activity performed by someone who weighs less. Participants were divided into three groups based on current physical activity guidelines: 0 minutes of physical activity, some amount of activity but not meeting the guideline of 75 vigorous or 150 moderate minutes, and meeting or exceeding the guideline in the last 7 days. Operationalizing physical activity this way led to more participants (61%) being included in the high physical activity group (meeting or exceeding 75 vigorous or 150 moderate minutes) than when physical activity was classified by energy expenditure (39%), further indicating that Health ABC participants were a highly active sample. In these models, physical activity and sedentary behavior were neither independently nor jointly associated with odds of dementia.

Table 10. Independent associations of sedentary time and physical activity time with dementia (N=1,988).

	OR	95% CI	*p*
Hours sitting per day			
0-8 hours	1.00		
0+ hours	0.94	0.72, 1.23	0.67
Physical activity			
≥75 vigorous minutes or 150 moderate minutes	1.00		
<75 vigorous minutes or 150 moderate minutes	1.00	0.74, 1.34	0.98
0 minutes/week	0.92	0.68, 1.25	0.59
Age	1.12	1.07, 1.16	<0.0001
Female	1.09	0.86, 1.38	0.47
Black race	1.07	0.83, 1.40	0.59
Educational attainment			
Postsecondary	1.00		
High school graduate	1.14	0.88, 1.47	0.34
Less than high school	1.34	0.96, 1.87	0.09
Self-rated health			
Excellent	1.00		
Very good	0.77	0.54, 1.12	0.17
Good	0.79	0.55, 1.15	0.22
Fair	1.03	0.65, 1.63	0.92
Poor	3.15	1.16, 8.59	<0.05
CES-D 10 score	1.04	1.01, 1.07	<0.05
BMI	0.98	0.95, 1.00	0.06

Figure 7. The joint associations of sedentary time and physical activity time with dementia (N=1,988). Odds ratios (OR) represent the increased odds of dementia relative to the referent group. Multivariable logistic regression model adjusted for age, sex, race, BMI, self-rated health, and depressive symptoms.



The second robustness check (**Tables 11-12. Figure 8**) used time spent watching TV as a proxy for sedentary behavior, based on findings that individuals may be able to better recall TV time than time spent sitting, meaning that it may be a more accurate indicator (DiPietro et al., 2018). We created a dichotomous TV variable, with the low TV group defined as watching <27 hours of TV per week (or <4 hours/day) and the high group defined was watching 28 hours or more per week. Most participants (81%) were in the low group and there were no statistically significant relationships between TV watching and physical activity, either independently or jointly, and odds of dementia.

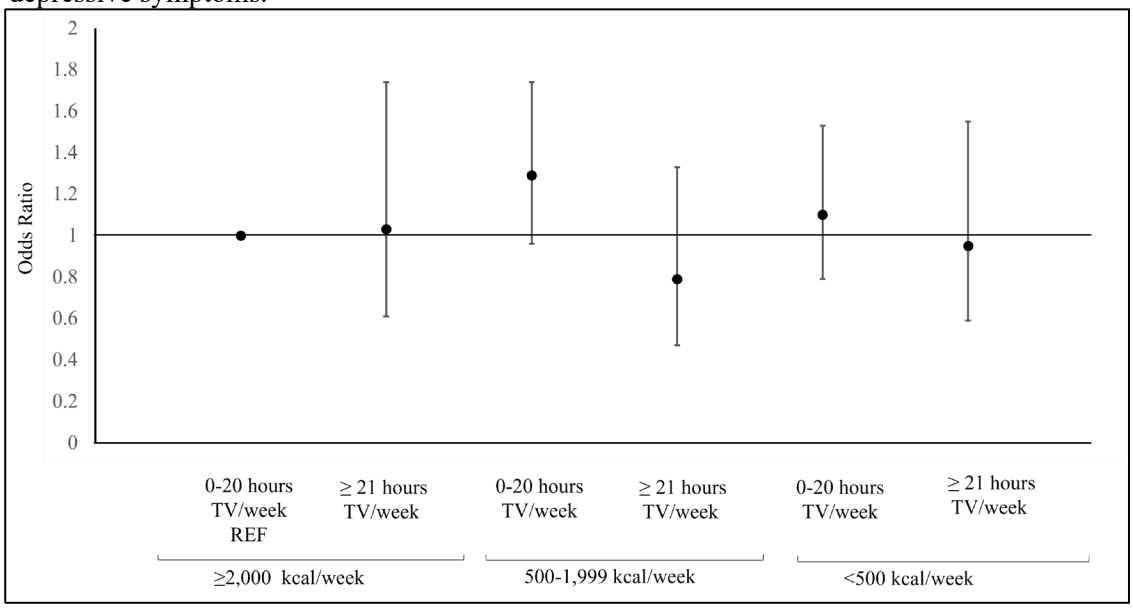
Table 11. Categories of physical activity and TV time according to dementia status (N=1,994).

		Dementia		
		Yes (n=386)	No (n=1,608)	*p*
Hours watching TV, n (%)				0.23
0-27 hours/week	1,599 (80.91)	318 (82.38)	1,281 (79.66)	
28+ hours/week	395 (19.81)	68 (17.62)	327 (20.34)	
Physical activity, n (%)				0.14
2,000+ kcal/week	1,204 (38.52)	132 (34.20)	636 (39.55)	
500-1,999 kcal/week	674 (33.80)	137 (35.49)	537 (33.40)	
0-499 kcal/week	552 (27.68)	117 (30.31)	435 (27.05)	

Table 12. Independent associations of TV time and physical activity with dementia (N=1,994).

	OR	95% CI	*p*
Hours watching TV			
0-27 hours/week	1.00		
28+ hours/week	0.81	0.60, 1.10	0.17
Physical activity			
2,000+ kcal/week	1.00		
500-1,999 kcal/week	1.19	0.90, 1.56	0.22
0-499 kcal/week	1.08	0.80, 1.45	0.61
Age	1.11	1.07, 1.16	<0.0001
Female	1.05	0.83, 1.33	0.66
Black race	1.10	0.84, 1.43	0.48
Educational attainment			
Postsecondary	1.00		
High school graduate	1.14	0.89, 1.48	0.31
Less than high school	1.34	0.96, 1.88	0.08
Self-rated health			
Excellent	1.00		
Very good	0.77	0.53, 1.12	0.17
Good	0.80	0.55, 1.17	0.25
Fair	1.02	0.64, 1.62	0.93
Poor	3.01	1.10, 8.27	<0.05
CES-D 10 score	1.04	1.01, 1.07	<0.05
BMI	0.98	0.95, 1.00	0.08

Figure 8. The joint associations of TV time and physical activity with dementia (N=1,994). Odds ratios (OR) represent the increased odds of dementia relative to the referent group. Multivariable logistic regression model adjusted for age, sex, race, BMI, self-rated health, and depressive symptoms.



Discussion

Our findings indicate that neither sedentary behavior nor physical activity were independently associated with dementia or cognitive function, except for individuals in the low physical activity group having worse scores on the 3MS compared to individuals in the high physical activity group. Furthermore, our hypothesis that odds of dementia would increase in a dose-response manner with decreasing levels of physical activity combined with increasing sedentary behavior was not supported. The same held true for the analyses that used cognitive function as the outcome variable, wherein physical activity and sedentary behavior were not jointly associated 3MS, DSST, or CLOX 1 scores. Lastly, our robustness checks, which used different operationalizations of physical activity and sedentary behavior indicated that, indeed, there is no relationship between sedentary time, physical activity, and dementia in the Health ABC sample analyzed in this study.

These findings are not well-aligned with literature that finds physical activity is associated with better cognitive function and thereby identifies physical activity to be a potentially promising intervention to prevent or slow the progression of dementia (Blondell et al., 2014; Baumgart et al., 2015; Guure et al., 2017; Xu et al., 2017). However, our findings are aligned with other research that has found no benefit of engaging in physical activity for cognitive function and dementia (Young, Angevaren, Rusted, & Tabet, 2015; Etnier, Nowell, Landers, & Sibley, 2006; Sink et al., 2015). One study that examined the association of physical activity and dementia risk over a 28-year follow-up period found no association, except as the length of follow-up decreased, suggesting that reverse causation may play a role in other studies that have found a relationship (Sabia et al., 2017). In other words, physical activity may not necessarily be protective in later life; rather, the capacity to be active is indicative of retained cognitive function.

One potential reason for the lack of relationship found in this study is that Health ABC participants constitute a healthy subset of the population (baseline inclusion criteria included reporting no difficulty in walking ¼ mile, climbing ten steps, or performing any basic activity of daily living). In addition, we further restricted the sample in this study to those who reported little or no difficulty walking and those who were free of dementia using a cutoff score of 77/78 on the 3MS at baseline to limit the confounding effects of some unmeasured health or social factor related to physical activity, sitting, and dementia. The good health of the sample is evidenced by how active participants in the study were, with most reporting low levels of sitting and medium or high levels of physical activity (e.g., N=148 in the low physical activity and high sitting group

compared to N=567 in the high physical activity and low sitting group). Relatedly, some research indicates that poor cognitive function is associated with greater risk of death and conversely, engaging in healthy behaviors is associated with a longer life expectancy free of dementia, meaning that the participants with worse health and/or cognitive function who otherwise may have developed dementia would be lost to follow-up and thus excluded from the study (Perls, Morris, Ooi, & Lipsitz, 1993; Stewart, Zelinski, & Wallace, 2000; Dhana et al., 2022). This selective survival, along with the overall health and high activity levels of the participants, may have limited our ability to detect independent and/or joint associations between physical activity and sitting time and dementia.

Another potential explanation for our null findings relates to measurement. For example, the physical activity questionnaire assesses only the past seven days of physical activity. While this may improve recall of activities among older people, it may not be representative of typical activity patterns occurring over several years that may affect cognitive function. Additionally, the sedentary behavior question specifically asked about sitting upright and did not include time spent reclining or lying down, which may have led to lower estimates of sedentary time. For example, a systematic review of objectively measured sedentary behavior found that older adults are sedentary for an average of 9.4 hours per day (Harvey et al., 2015), while in this study, only a quarter of individuals reported spending at least 9 hours sitting.

The results of this study indicate that more research is needed to examine the relationships between movement and risk of dementia or cognitive decline. While Health ABC was one of a few studies to prospectively measure physical activity, sedentary time,

and cognitive function, future studies should consider using objective measures of movement, as self-report measures are prone to bias. Indeed, ample evidence exists that people tend to over-report their physical activity and under-report their sitting behavior (Sallis & Saelens, 2000; Banda et al., 2010). Individuals typically engage in many cognitively stimulating activities (e.g., reading, board/card games, playing a musical instrument, crossword puzzles) while seated, which complicates our ability to evaluate the effects of sitting on dementia and cognitive function if the benefits of these activities to cognitive function outweighs any detrimental effects from lack of movement. Future research should aim disentangle whether lack of movement itself may increase risk or whether more cognitively demanding sedentary activities positively contribute to brain health.

Studies should also consider using continuous of measures of cognitive function. We included three of these measures (3MS, DSST, CLOX 1) to examine whether physical activity and sedentary behavior were associated with cognitive impairment that does not reach the threshold of dementia. We found an independent association between low physical activity and lower 3MS score, suggesting that physical activity may be associated with impairment in global cognitive function. The linear regression models also indicated that physical activity and sedentary behavior are not jointly associated with cognitive function, supporting our findings in the dementia odds model. Our analyses all indicate that continuous measures of cognitive function may be particularly useful among healthy older adults who are already in their mid-70s and subject to selective survival.

Although, our findings did not support our hypothesis, we believe that the relationship between movement, including sedentary time, and cognitive function

remains a topic that should be investigated further. Given aging demographics and the global economic burden associated with dementia-related disability, there is substantial public health benefit to understanding how physical activity and sedentary time interact to promote brain health in older age. This type of research is particularly timely, as public health recommendations move toward holistic considerations of daily movement, with physical activity representing one piece of the whole picture (PAGAC, 2018; Ross et al., 2020).

Chapter 4: Manuscript 2

Longitudinal associations between change in different sedentary behaviors over time with cognitive function: The Health ABC Study

Laura Major[1], Eleanor M. Simonsick[2], Melissa A. Napolitano[1,3], and Loretta DiPietro[3]

Departments of [1]Prevention & Community Health and [3]Exercise & Nutrition Sciences, Milken Institute School of Public Health, The George Washington University, Washington, DC and [2]Intramural Research Program, Translational Gerontology Branch, National Institute on Aging, Baltimore, MD

Running title: Sitting, television, reading, cognitive function, and dementia

Word count: Abstract 238; Manuscript 4,365

Author contact: Loretta DiPietro, PhD, MPH
Department of Exercise and Nutrition Sciences
Milken Institute School of Public Health
The George Washington University
950 New Hampshire Ave
Washington, DC 20052
ldp1@gwu.edu

Abstract

Background: This study aims to examine the associations of different types of sedentary behavior and 3-year change in the time spent on those activities with cognitive function and dementia. **Methods:** We analyzed prospective data from 1,677 women (52%) and men with a mean baseline age of 75±2.8 participating in the Health Aging and Body Composition (Health ABC) Study between 1999-2000 (baseline) and 2014 (study conclusion). Sitting time (hours/day), TV time (hours/week), and reading time (hours/week) were self-reported at baseline and change in sitting, TV, and reading time was measured between 1999-2000 and 2002-2003. Cognitive function (using the Teng Min-Mental State [3MS], Digit Symbol Substitution Test [DSST], and CLOX 1) was assessed in 2006-2007 and dementia status was cumulatively categorized from June 1, 2004 through September 30, 2014. Multivariable linear regressions was used to examine associations between baseline sitting, TV, and reading time and change in those behaviors with cognitive function test scores. Multivariable logistic regression evaluated associations between change in sitting, TV, and reading time with odds of dementia. **Results:** More reading time at baseline was associated with a 0.09-point (SE=0.03, $p<0.05$) higher 3MS score and a 0.14-point (SE=0.04, $p<0.01$) higher DSST score. An increase in TV watching time between 1999-2000 and 2002-2003 was associated with a 1.53-point (SE=0.72, $p<0.05$) decrease in 3MS score. **Conclusion:** Some types of sedentary behavior may have benefits for cognitive function in older adults, outweighing the potential harms associated with lack of movement.

Introduction

Dementia, defined as cognitive decline to the point where it interferes with an individual's daily functioning, is a significant public health problem facing older adults (National Institute on Aging, 2017a). Dementia is common among older adults: for example, analysis of data from a nationally representative study of adults over 50 in 2016 found prevalence and incidence estimates of 7.7% and 3.8%, respectively (Farina, Zhang, Kim, Hayward, & Crimmins, 2022). Projections indicate that, by 2035, there will be more older adults than children in the United States population for the first time in history, highlighting the scope of the issue (U.S. Census Bureau, 2018). Dementia represents the most severe form of cognitive decline; however, older adults frequently experience deficits in cognitive function that do not rise to the level of dementia. Recent estimates indicate that cognitive impairment occurs in 11.2% of adults aged 55-69 and 27.3% of adults aged 65 or older (Choi, Schoeni, Martin, & Langa, 2018; Rajan et al., 2021).

Currently no cures for dementia or cognitive impairment exist, thus it is imperative that we learn more about potentially modifiable risk factors for these conditions and add to the science aimed at uncovering ways to mitigate their impacts on health and wellbeing. One such potential risk factor is sedentary behavior, which heretofore has been understudied as a predictor of and/or contributor to cognitive decline and dementia. Sedentary behavior is defined as energy expenditure less than or equal to 1.5 metabolic equivalents (METs) while seated, reclined, or lying down (The Sedentary Behaviour Research Network, 2012).

Sedentary behavior is common among older adults. While prevalence estimates

vary, depending on how studies define and measure sedentary behavior, a 2015 systematic review found that adults 60 years and older adults are sedentary for up to 80% of the time that they are awake (Harvey, Chastin, & Skelton, 2015). A 2017 analysis of Reasons for Geographic and Racial Differences in Stroke study data corroborated this finding with objective measurement, determining that older adults spend 77% of waking time sedentary (Diaz et al., 2017). This is problematic for many health outcomes as the amount of time that older adults are sedentary is inversely associated with functional ability, quality of life and wellbeing, metabolic risk, and mortality (Copeland et al., 2017; Madden, Feldman, & Chase, 2021; Ekelund et al., 2019).

The link between sedentary behavior and cognitive function has yet to be fully examined, however. Some research indicates that reducing sedentary time could be beneficial for brain health and have even proposed potential mechanistic links to explain the association, but studies in older adults to date have been largely cross-sectional (Edwards & Loprinzi, 2017a; Edwards & Loprinzi, 2017b; Wheeler et al., 2017). One longitudinal study that examined the association between sedentary behavior and cognitive function reported that higher amounts of sedentary time were associated with declining cognitive function two years later (Ku, Liu, Lo, Chen, & Stubbs, 2017); however, another study that combined data across five cohorts of persons without dementia did not observe this relationship (Maasakkers et al., 2020). Regarding dementia, specifically, a recent meta-analysis of data from 18 cohort studies concluded that being sedentary increases risk of dementia by 30 percent, although a critique of the article noted that the investigators may have conflated sedentary behavior with physical inactivity (Yan et al., 2020; Dillon & Gardiner, 2021). Relatedly, a pair of systematic reviews

concluded that results from high quality cohort studies suggest an association between sedentary behavior and cognitive impairment, but inconsistent measurement across studies makes it difficult to determine the extent of the association (Falck et al., 2017; Olanrewaju, Stockwell, Stubbs, & Smith, 2020).

Some research suggests that certain types of sedentary behavior may benefit cognitive function whereas others may have a negative effect (Bakrania et al., 2018; Kesse-Guyot et al., 2012), which could possibly or partially explain mixed findings across studies. For example, evidence shows that television (TV) watching is associated with poor cognitive function in older adults (Copeland et al., 2017; Fancourt & Steptoe, 2019; Fajersztajn, Di Rienzo, Nakamura, & Scazufca, 2021). However, reading and other cognitively stimulating activities performed while sedentary may be positively associated with cognitive function (Kurita et al., 2019; Nemoto et al., 2018). The lack of a well-developed evidence base regarding different types of sedentary behavior and their association with cognitive decline in older adults highlights the need for more research in this area.

The study aims were to 1) investigate whether different types of sedentary behavior, including sitting time, TV watching, and reading, in 1999-2000 were associated with cognitive test performance seven years later (2006-2007) among participants of the Health Aging and Body Composition (Health ABC) Study and to 2) examine whether 3-year change (1999-2000 to 2002-2003) in the sedentary behaviors was associated with performance on the same cognitive tests as well as 10-year odds of dementia. We hypothesized that participants with the highest duration of sitting and TV time would have poorer cognitive test performance than participants with lower amounts of sitting

and TV time. Conversely, those with the highest amounts of reading time would have better cognitive function than those with less reading time. We also proposed that increased sitting and TV time over 3 years would be associated with higher 10-year odds of dementia, while increased reading time over that same period would be associated with lower odds.

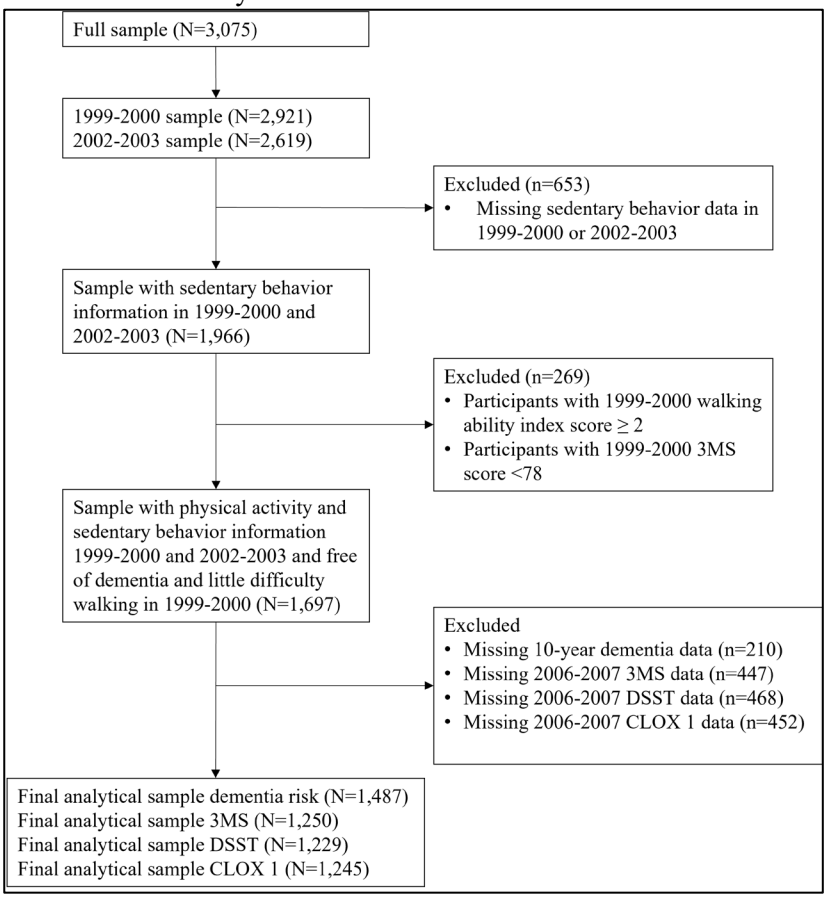
Methods

Study Participants

Health ABC was conducted by the National Institute on Aging Intramural Research Program and was a prospective cohort study of older adults aged 70-79 when recruitment began in 1997-98 (National Institute on Aging, n.d.). The participants were followed for 16 years with data collection occurring through both questionnaires and clinical examinations. Potential participants were identified from a random sample of white Medicare beneficiaries and all age-eligible community dwelling black residents in designated zip code areas surrounding the Pittsburgh, Pennsylvania, and Memphis, Tennessee field centers. To be eligible for recruitment, participants had to have been able to walk a quarter of a mile, climb ten steps, not use equipment for walking, and report no difficulties with activities of daily living (Colbert et al., 2004). In addition, the participants could not have been treated for cancer in three years prior to recruitment or have plans to leave the area within three years. At least one-third of the 3,075 participants were Black/African American (National Institute on Aging, n.d.). The final analytic sample for this study was 1,487, after excluding participants with missing data and after limiting the sample to individuals free of dementia and with limited or no difficulty

walking (≥ score of 2 on a walking ability index) at baseline (1999-2000) to ensure that participants were not sedentary due to some functional limitation (**Figure 9**).

Figure 9. Participant selection from the Health ABC cohort. Those respondents who provided complete data on sedentary behavior and cognitive function or dementia and who were free of dementia and had limited difficult walking in 1999-2000 were eligible to be included in the analysis.



Sedentary Behavior

Single item measures were used to assess sitting time, TV time, and reading time in Health ABC. For sitting time, participants were asked how many hours they typically spend sitting upright over a 24-hour period. TV time was assessed by asking participants how many hours per week they spent watching TV. Reading time was assessed by asking participants how many hours per week they spent reading, including books, newspapers, and magazines. For the baseline associations, sitting time and reading time were left continuous. TV time was divided into two categories: 0-27 hours and 28+ hours per week. These groupings are based on research by Fancourt and Steptoe (2019), which found a threshold effect wherein 3.5 hours or more of TV watching per day was associated with poorer cognitive

function, but there was no detriment from watching three hours or fewer.

Change in sitting and reading time between 1999-2000 and 2002-2003 was operationalized by creating categorical change variables that represented whether participants maintained, increased, or decreased time spent sitting or reading. For TV watching, the change variable was created with four categories: maintaining a low level (0-27 hours/week), maintaining a high level (28+ hours/week), decreasing from high to low, or increasing from low to high.

Cognitive Outcome Measures

Cognitive function measures occurred in 2006-2007. Global cognitive function in Health ABC was assessed using the Teng Mini-Mental State Exam (3MS). The 3MS measures cognitive function across a range of domains, including orientation, attention, and recall, among others (Yaffe et al., 2009). Possible scores range from 0-100, with higher scores indicating better cognitive function.

The Digit Symbol Substitution Test (DSST) is a polyfactorial measure of cognitive function that assesses motor skills, attention, and executive function (Jaeger, 2018; Lambiase, Kuller, & Matthews, 2014; Yaffe et al., 2008; Lin et al., 2014). The DSST is a paper and pencil test, which has a key at the top that matches symbols with digits from one to nine. Below the key are four rows of 25 sets of double boxes with a digit in the top box and the bottom box empty. The participant is asked to draw the symbol in the bottom box that matches the number in the top box. The score is the number of correct symbols provided in 90 seconds. Higher scores indicate better performance (Rosano, Newman, Katz, Hirsch, & Kuller, 2008; Lambiase et al., 2014).

The CLOX 1 is a clock drawing task wherein participants are asked to draw a

clock that shows 1:45. Various elements of the clock drawing (e.g., whether the clock is a circle, whether the numbering and spacing are correct, whether the hands are in the correct positions, etc.) are then assessed by a rater. Possible scores range from zero to fifteen, with higher scores indicating better executive function. The CLOX 1 has been determined to be reliable and valid as a measure of cognitive function (Royall, Cordes, & Polk, 1998).

Dementia in Health ABC is coded as a binary indicator variable (0=no dementia, 1=dementia) derived from multiple sources of data, including whether the participant took prescribed medication used to treat dementia (galantamine, rivastigmine, memantine, donepezil, or tacrine); received a dementia diagnosis, or experienced a race-adjusted decline in Teng Mini-Mental State (3MS) score of 1.5 or more standard deviations. Participants were considered to have dementia if they met one or more of these criteria. Dementia cases were pooled across ten years of follow-up, starting on June 1, 2004 (one year after data collection for the second year used to create the change variables concluded in 2003) and ending on September 30, 2014.

Covariables

Covariables were selected based on their relationship to sedentary behavior or cognitive function in the literature (Kesse-Guyot et al., 2012; Kurita et al., 2018). Sociodemographic variables included age, sex, race (white, black), and education level (<HS, HS grad, post-secondary) and health-related variables included smoking status (never, former, current smoker), body mass index (BMI: kg/m^2), self-rated health (excellent, very good, good, fair, poor), physical activity (0-499 kcal/week, 500-1,999 kcal/week, 2000+ kcal/week) and depressive symptoms. The Centers for Epidemiologic

Studies Depression (CES-D 10) short form scale (Andresen et al. 1994), which has a possible score range of 0-30 with higher scores indicative of more depressive symptoms, was used to measure depressive symptoms.

Statistical Analysis

We generated univariate statistics [mean±SD; frequencies (%)] on all variables to examine their distributions within the study population and used *t*-tests and chi-square tests to examine unadjusted relationships between each independent variable, including the covariables, with dementia. Multivariable linear regression modeled the associations between the different types of sedentary behavior (sitting time, TV time, and reading time) in 1999-2000 and 3MS, DSST, and CLOX 1 scores in 2006-2007, including covariables that were statistically significant in the unadjusted analyses. Parameter estimates, standard errors, and *p* values are reported for each type of sedentary behavior.

Multivariable linear regression also modeled associations between change from 1999-2000 to 2002-2003 in each sedentary behavior and 3MS, DSST, and CLOX 1 scores in 2006-2007. Parameter estimates, standard errors, and *p* values are reported for each sedentary behavior change category (maintained, increased, and decreased for sitting and reading time and 0-27 hours/week both years, 28+ hours/week both years, increased, and decreased for TV time). Multivariable logistic regression modeled the associations between change from 1999-2000 to 2002-2003 in each sedentary behavior and odds of dementia. Odds ratios (OR) and 95% confidence intervals (CI) are reported for each sedentary behavior change category to describe the odds of dementia relative to the referent group.

Results

Descriptive statistics and univariate analyses are reported in **Table 13**. The cumulative incidence of dementia was 17.7%. Participants at baseline had an average age of 75.2±2.8 years old, 52% were female, 69% were white, and 51% reported attaining at least postsecondary education. The sample was healthy: 89% reported their health as good or better, only 5% were current smokers, and 75% were in the high or medium

Table 13. Descriptive statistics (N=1,487).

	Dementia			
		Yes (n=264)	No (n=1,223)	*p*
Mean age (SD)	75.19 (2.77)	75.88 (2.93)	75.04 (2.71)	<0.0001
Female, n (%)	774 (52.05)	136 (51.52)	638 (52.17)	0.85
Race, n (%)				0.74
Black	455 (30.60)	83 (31.44)	372 (30.42)	
White	1,032 (69.40)	181 (68.56)	851 (69.58)	
Educational attainment, n (%)				0.21
Less than high school	234 (15.74)	51 (19.32)	183 (14.96)	
High school graduate	488 (32.82)	82 (31.06)	406 (33.20)	
Postsecondary	765 (51.45)	131 (49.62)	634 (51.84)	
Self-rated health, n (%)				0.12
Excellent	219 (14.73)	38 (14.39)	181 (14.80)	
Very good	556 (37.39)	88 (33.33)	468 (38.27)	
Good	548 (37.12)	98 (37.12)	450 (36.79)	
Fair	156 (14.02)	37 (14.02)	119 (9.73)	
Poor	8 (0.54)	3 (1.14)	5 (0.41)	
Smoking status, n (%)				0.36
Never smoker	718 (48.29)	134 (50.76)	584 (47.75)	
Current smoker	74 (4.98)	9 (3.41)	65 (5.31)	
Former smoker	695 (46.74)	121 (45.83)	574 (46.93)	
Physical activity, n (%)				0.48
2,000+ kcal/week	611 (41.09)	101 (38.26)	510 (41.70)	
500-1,999 kcal/week	503 (33.83)	90 (34.09)	413 (33.77)	
0-499 kcal/week	373 (25.08)	73 (27.65)	300 (24.53)	
Mean BMI (SD)	27.17 (4.51)	26.57 (4.59)	27.29 (4.48)	<0.05
Mean CES-D 10 score (SD)	3.94 (3.66)	4.20 (3.93)	3.88 (3.59)	0.21
Mean hours sitting per day (SD)	6.76 (3.35)	6.65 (3.35)	6.79 (3.36)	0.54
Hours watching TV, n (%)				0.71
0-27 hours/week	1,193 (80.23)	214 (81.06)	979 (80.05)	
28+ hours/week	294 (19.77)	50 (18.94)	244 (19.95)	
Mean hours reading per week	12.46 (8.74)	11.48 (9.48)	12.68 (8.56)	0.06

physical activity level categories. Participants on average were overweight, with a BMI of 27.2±4.5, and depressive symptomology was low with an average CES-D score of 3.9±3.7. In terms of sedentary behaviors at baseline, participants reported a low amount of sitting (6.8±3.4 hours/day) and TV watching (64% in the 0-20 hours/week group) and a high amount of reading (12.5±8.7 hours/week). **Table 13** also displays the unadjusted analyses, in which age (t=-4.48, p<0.0001) and BMI (t=2.36, p<0.05) were significantly associated with dementia status.

The results of the multivariable linear regressions modeling the associations between each sedentary behavior at baseline with 3MS, DSST, and CLOX 1 scores at follow-up are reported in **Tables 14-16**. There were no statistically significant associations between sitting time and cognitive function, as measured by the 3MS and CLOX 1 but there was a positive association between sitting and DSST score, wherein each 1-hour increase in baseline sitting time was associated with a 0.2-point (SE=0.10) increase in DSST score (p<.05) 7 years later (**Table 14**). TV watching at baseline was not associated with 3MS, DSST, or CLOX 1 scores at follow-up (**Table 15**). Reading time at baseline was positively associated with 3MS and DSST scores, where increasing the amount of time spent reading by 1 hour per week was associated with a 0.09-point (SE=0.03) increase in 3MS score (p<0.05) and 0.01-point (SE=0.01) increase in DSST score (p<0.01; **Table 16**). In each model, age, sex, race, and educational attainment were associated with cognitive function where older age, black race, and lower educational attainment were typically associated with worse cognitive function. Women had uniformly better cognitive function test scores than men. In the 3MS and DSST models, worse health was associated with worse cognitive function (except in the reading model)

and, in the 3MS models for sitting and TV time, depressive symptoms were negatively associated with cognitive function.

Table 14. Associations of baseline sitting time with 3MS, DSST, and CLOX 1 scores 7 years later.

	3MS Score			***DSST Score***			***CLOX 1 Score***		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Hours sitting per day	0.13	0.07		0.21	0.10	*	0.01	0.02	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.22	0.55		0.46	0.77		0.18	0.15	
0-499 kcal/week	-1.13	0.62		-0.33	0.88		0.29	0.18	
Age	-0.46	0.09	**	-0.83	0.12	**	-0.10	0.02	**
Female	1.70	0.49	**	4.38	0.68	**	0.52	0.14	**
Black race	-3.33	0.56	**	-6.15	0.79	**	-0.31	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.51	0.54	**	-3.11	0.76	**	-0.53	0.15	**
Less than high school	-6.91	0.74	**	-10.95	1.04	**	-1.01	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.20	0.78		-2.28	1.00	*	-0.15	0.20	
Good	-1.52	0.74	*	-4.62	1.04	**	-0.32	0.21	
Fair	-2.00	1.02	*	-6.00	1.44	**	-0.51	0.29	
Poor	-1.44	3.45		-9.18	4.82		-1.05	0.97	
CES-D 10 score	-0.14	0.07	*	-0.17	0.10		-0.03	0.02	
BMI	0.08	0.06		-0.10	0.08		0.01	0.02	
	N=1,250 R^2=0.18 F(14, 1235)=18.74 Model *p*<.0001			N=1,229 R^2=0.26 F(14, 1214)=30.33 Model *p*<.0001			N=1,245 R^2=0.07 F(14, 1230)=6.46 Model *p*<.0001		

**p<.01. *p<.05

Table 15. Associations of baseline TV watching with 3MS, DSST, and CLOX 1 scores 7 years later.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
TV Watching									
0-27 hours/week	REF			REF			REF		
28+ hours/week	-0.32	0.61		0.59	0.85		-0.27	0.17	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.21	0.55		0.39	0.77		0.19	0.15	
0-499 kcal/week	-1.08	0.63		-0.37	0.88		0.31	0.18	
Age	-0.46	0.09	**	-0.82	0.12	**	-0.10	0.02	**
Female	1.67	0.49	**	4.31	0.69	**	0.52	0.14	**
Black race	-3.30	0.57	**	-6.12	0.80	**	-0.31	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.39	0.52	**	-3.31	0.75	**	-0.52	0.15	**
Less than high school	-7.01	0.74	**	-11.21	1.04	**	-1.00	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.18	0.71		-2.26	1.00	*	-0.15	0.20	
Good	-1.50	0.74		-4.61	1.04	**	-0.31	0.21	
Fair	-1.98	1.02	*	-6.04	1.44	**	-0.50	0.29	
Poor	-1.65	3.46		-9.45	4.83	*	-1.08	0.97	
CES-D 10 score	-0.14	0.07	*	-0.17	0.10		-0.04	0.02	
BMI	0.09	0.06		-0.09	0.08		0.02	0.02	
	N=1,250 R^2=0.17 F(14, 1235)=18.48 Model *p*<.0001			N=1,229 R^2=0.26 F(14, 1214)=29.97 Model *p*<.0001			N=1,245 R^2=0.07 F(14, 1230)=6.64 Model *p*<.0001		

**$p<.01$. *$p<.05$

Table 16. Associations of baseline reading with 3MS, DSST, and CLOX 1 scores 7 years later.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Hours reading per week	0.09	0.03	*	0.14	0.04	**	0.01	0.01	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.18	0.54		0.40	0.76		0.15	0.15	
0-499 kcal/week	-1.07	0.62		-0.24	0.88		0.27	0.17	
Age	-0.47	0.09	**	-0.84	0.12	**	-0.10	0.02	**
Female	1.63	0.48	**	4.29	0.68	**	0.52	0.14	**
Black race	-3.29	0.57	**	-6.14	0.79	**	-0.32	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.28	0.54	**	-2.72	0.76	**	-0.47	0.15	**
Less than high school	-6.55	0.74	**	-10.39	1.05	**	-0.96	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.22	0.71		-2.30	0.99	*	-0.16	0.20	
Good	-1.44	0.74		-4.53	1.03	**	-0.30	0.21	
Fair	-1.91	1.02		-5.83	1.43	**	-0.50	0.29	
Poor	-1.44	3.44		-9.15	4.80		-1.04	0.96	
CES-D 10 score	-0.13	0.07		-0.16	0.10		-0.03	0.02	
BMI	0.08	0.06		-0.10	0.08		0.01	0.02	
	N=1,252 R^2=0.18 F(14, 1234)=19.33 Model *p*<.0001			N=1,231 R^2=0.27 F(14, 1216)=31.37 Model *p*<.0001			N=1,247 R^2=0.07 F(14, 1232)=6.74 Model *p*<.0001		

***p*<.01. **p*<.05

The results of the linear regressions modeling the associations between change in each sedentary behavior from 1999-2000 to 2002-2003 with cognitive function in 2006-2007 are reported in **Tables 17-19**. Neither of the change in sitting time categories (increase or decrease) were associated with 3MS, DSST, or CLOX 1 scores, when compared to the referent group, who maintained the same level of sitting (**Table 17**).

Table 17. Associations of change in sitting time with 3MS, DSST, and CLOX 1 scores.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Change in sitting time									
Maintain	REF			REF			REF		
Increase	-0.60	0.73		-0.53	1.03		0.22	0.20	
Decrease	-0.36	0.73		-0.35	1.03		0.07	0.21	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.24	0.55		0.47	0.77		0.16	0.15	
0-499 kcal/week	-1.06	0.63		-0.24	0.88		0.28	0.18	
Age	-0.46	0.09	**	-0.83	0.12	**	-0.10	0.02	**
Female	1.65	0.49	**	4.32	0.68	**	0.52	0.14	**
Black race	-3.29	0.56	**	-6.15	0.79	**	-0.31	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.58	0.53	**	-3.22	0.75	**	-0.54	0.15	**
Less than high school	-6.96	0.73	**	-11.09	1.03	**	-1.05	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.17	0.71		-2.24	1.00	*	-0.16	0.20	
Good	-1.51	0.74	*	-4.64	1.04	**	-0.33	0.21	
Fair	-2.03	1.02	*	-6.02	1.44	**	-0.50	0.29	
Poor	-1.58	3.46		-9.44	4.83	*	-1.08	0.97	
CES-D 10 score	-0.14	0.07	*	-0.17	0.10		-0.04	0.02	
BMI	0.09	0.06		-0.09	0.08		0.01	0.02	
	N=1,253 R^2=0.17 F(15, 1237)=17.29 Model *p*<.0001			N=1,232 R^2=0.26 F(15, 1216)=28.14 Model *p*<.0001			N=1,248 R^2=0.07 F(15, 1232)=6.16 Model *p*<.0001		

**p<.01. *p<.05

However, moving from the low TV watching group (0-27 hours/week) at baseline to the high TV watching group (28+ hours) 3 years later was associated with a 1.5-point (SE=0.7) decrease in 3MS score (p <0.05) at follow-up, when compared to participants who maintained a low level of TV watching across both years (**Table 18).** There were no associations between change in TV watching and DSST or CLOX 1 scores. Lastly, there were no associations between change in reading time and scores on any of the three outcome cognitive measures (**Table 19**).

Table 18. Associations of change in TV watching time with 3MS, DSST, and CLOX 1 scores.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Change in TV watching									
0-27 hours/week both years	REF			REF			REF		
28+ hours/week both years	-0.12	0.79		1.60	1.11		-0.34	0.17	
Increase Y3 to Y6	-1.53	0.72	*	-0.70	1.01		0.07	0.20	
Decrease Y3 to Y6	-1.18	0.85		-0.92	1.20		-0.16	0.24	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.22	0.55		0.37	0.77		0.19	0.15	
0-499 kcal/week	-1.04	0.63		-0.38	0.89		0.31	0.18	
Age	-0.46	0.09	**	-0.82	0.12	**	-0.10	0.02	**
Female	1.67	0.49	**	4.37	0.69	**	0.52	0.14	**
Black race	-3.29	0.57	**	-6.16	0.80	**	-0.31	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.54	0.54	**	-3.30	0.76	**	-0.52	0.15	**
Less than high school	-6.87	0.74	**	-11.10	1.04	**	-1.01	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.22	0.71		-2.29	1.00	*	-0.14	0.20	
Good	-1.51	0.74	*	-4.63	1.04	**	-0.31	0.21	
Fair	-2.01	1.02	*	-6.02	1.44	**	-0.50	0.29	
Poor	-1.78	3.5		-9.67	4.83	*	-1.06	0.97	
CES-D 10 score	-0.12	0.07		-0.16	0.10		-0.03	0.02	
BMI	0.10	0.06		-0.09	0.08		0.02	0.02	
	N=1,250 R^2=0.18 F(16, 1233)=16.56 Model *p*<.0001			N=1,229 R^2=0.26 F(14, 1212)=26.45 Model *p*<.0001			N=1,245 R^2=0.07 F(16, 1228)=5.83 Model *p*<.0001		

**$p<.01$. *$p<.05$

Table 19. Associations of change in reading time with 3MS, DSST, and CLOX 1 scores.

	3MS Score			*DSST Score*			*CLOX 1 Score*		
	Coefficient	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***	**Coefficient**	**Std. Err**	***p***
Change in reading time									
Maintain	REF			REF			REF		
Increase	-.59	0.68		-1.09	0.96		-0.08	0.19	
Decrease	-0.80	0.68		-0.35	0.96		0.15	0.19	
Physical activity									
2,000+ kcal/week	REF			REF			REF		
500-1,999 kcal/week	0.22	0.55		0.42	0.77		0.16	0.15	
0-499 kcal/week	-1.12	0.63	*	-0.36	0.88		0.28	0.18	
Age	-0.45	0.09	**	-0.82	0.12	**	-0.10	0.02	**
Female	1.66	0.49	**	4.34	0.69	**	0.52	0.14	**
Black race	-3.27	0.57	**	-6.12	0.80	**	-0.32	0.16	*
Educational attainment									
Postsecondary	REF			REF			REF		
High school graduate	-2.62	0.53	**	-3.26	0.75	**	-0.53	0.15	**
Less than high school	-7.08	0.73	**	-11.15	1.04	**	-1.01	0.21	**
Self-rated health									
Excellent	REF			REF			REF		
Very good	-0.24	0.71		-2.29	1.00	*	-0.13	0.20	
Good	-1.54	0.74	*	-4.54	1.04	**	-0.30	0.21	
Fair	-2.01	1.02	*	-6.00	1.44	**	-0.51	0.29	*
Poor	-1.75	3.46		-9.57	4.83	*	-1.05	0.97	
CES-D 10 score	-0.14	0.07	*	-0.17	0.10		-0.03	0.02	
BMI	0.09	0.06		-0.09	0.08		0.01	0.02	
	N=1,253 R^2=0.17 F(15, 1234)=17.32 Model *p*<.0001			N=1,232 R^2=0.26 F(15, 1213)=28.06 Model *p*<.0001			N=1,248 R^2=0.07 F(15, 1229)=6.20 Model *p*<.0001		

**p<.01. *p<.05

Table 20 displays the results of the logistic regressions modeling the associations between change in the three sedentary behaviors with odds of dementia. Neither change in sitting time, TV time, nor reading time was associated with odds of dementia. Older age was associated with increased odds of dementia in each of the models (OR=1.10, 95% CI=1.05, 1.16). Higher BMI was associated with lower odds of dementia in each the models (OR=0.97, 95% CI = 0.93, 0.99). The lack of associations in these models can likely be attributed to insufficient statistical power leading to imprecise estimates.

Table 20. Associations of change in sitting time, TV watching, and reading with dementia (N=1,487).

	Change in sitting			Change in TV			Change in reading		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Change in sitting time									
Maintain	1.00								
Increase	0.96	0.63, 1.47	0.86						
Decrease	1.01	0.67, 1.54	0.95						
Change in TV watching									
0-27 hours/week both years				1.00					
28+ hours/week both years				0.80	0.03, 1.28	0.36			
Increase Y3 to Y6				1.09	0.73, 1.63	0.68			
Decrease Y3 to Y6				1.13	0.70, 1.83	0.62			
Change in reading time									
Maintain							1.00		
Increase							1.05	0.70, 1.58	0.81
Decrease							1.18	0.79, 1.76	0.42
Physical activity									
2,000+ kcal/week	1.00			1.00			1.00		
500-1,999 kcal/week	1.07	0.78 1.47	0.69	1.07	0.78 1.48	0.66	1.06	0.77, 1.46	0.71
0-499 kcal/week	1.09	0.77, 1.55	0.63	1.10	0.78, 1.56	0.59	1.09	0.77, 1.54	0.63
Age	1.10	1.05, 1.16	<0.001	1.10	1.05, 1.16	<0.001	1.10	1.05, 1.16	<0.001
Female	0.99	0.75, 1.31	0.94	0.98	0.74, 1.30	0.90	0.99	0.75, 1.31	0.94
Black race	1.07	0.78, 1.48	0.66	1.10	0.82, 1.47	0.65	1.07	0.77, 1.47	0.70
Educational attainment									
Postsecondary	1.00			1.00			1.00		
High school graduate	1.08	0.81, 1.43	0.94	0.99	0.72, 1.35	0.94	0.98	0.72, 1.35	0.92
Less than high school	1.50	1.05, 2.15	0.20	1.29	0.87, 1.91	0.21	1.29	0.87, 1.92	0.20
Self-rated health									
Excellent	1.00			1.00			1.00		
Very good	0.88	0.58, 1.34	0.55	0.88	0.58, 1.35	0.57	0.89	0.58, 1.36	0.58
Good	0.99	0.64, 1.52	0.95	0.99	0.64, 1.53	0.97	0.99	0.65, 1.53	0.98
Fair	1.32	0.75, 2.31	0.34	1.32	0.75, 2.32	0.33	1.33	0.76, 2.33	0.32
Poor	2.63	0.57, 12.10	0.22	2.73	0.59, 12.54	0.20	2.64	0.57, 12.22	0.21
CES-D 10 score	1.01	0.97, 1.05	0.55	1.01	0.97, 1.05	0.59	1.01	0.97, 1.05	0.56
BMI	0.97	0.94, 0.99	<0.05	0.97	0.93, 0.99	<0.05	0.97	0.93, 0.99	<0.05

Post hoc statistical power analyses for all models were conducted used G*Power 3.1.9.7. The linear regression modeling sitting time with 3MS score had 14 predictors and R^2=0.18. The sample size needed to achieve 95% power in this model was N=137, which was surpassed by the actual analytical sample size (N=1,250). The linear regression modeling sitting time with DSST score had 14 predictors and R^2=0.26. The sample size needed to achieve 95% power in this model was N=91, which was surpassed by the actual analytical sample size (N=1,229). The linear regression modeling sitting time with CLOX 1 score had 14 predictors and R^2=0.07. The sample size needed to achieve 95% power in this model was N=374, which was surpassed by the actual analytical sample size (N=1,245). Similar R^2 and analytic sample size values were observed for the TV and reading time linear regression models, indicating sufficient statistical power for those as well.

The linear regression modeling change in sitting time with 3MS score had 15 predictors and R^2=0.17. The sample size needed to achieve 95% power in this model was N=149, which was surpassed by the actual analytical sample size (N=1,253). The linear regression modeling sitting time with DSST score had 15 predictors and R^2=0.26. The sample size needed to achieve 95% power in this model was N=93, which was surpassed by the actual analytical sample size (N=1,232). The linear regression modeling sitting time with CLOX 1 score had 15 predictors and R^2=0.07. The sample size needed to achieve 95% power in this model was N=383, which was surpassed by the actual analytical sample size (N=1,248). Similar R^2 and analytic sample size values were observed for the change in reading time linear regression models, which had the same number of predictors, indicating sufficient statistical power. The change in TV time linear

regression models contained 16 predictors. The 3MS score model needed a sample size of N=144 to achieve 95% power, given R^2=0.18, which was surpassed by the analytical sample size of N=1,250. The DSST score model needed a sample size of N=95 to achieve 95% power, given R^2=0.26, which was surpassed by the analytical sample size of N=1,229. The CLOX 1 score model needed a sample size of N=392 to achieve 95% power, given R^2=0.07, which was surpassed by the analytical sample size of N=1,245.

The analytic sample for the three logistic regressions modeling change in sitting time, TV time, and reading time with odds of dementia was 1,487. A power analysis of the sitting time change model revealed insufficient power (15%) to detect an odds ratio of 0.96, which represented the odds of dementia associated with increased sitting compared to maintaining sitting time over the 3-year period. A power analysis of the TV change model revealed insufficient power (35%) to detect an odds ratio of 1.09, which represented the odds of dementia associated with increased TV time compared to maintaining a low level of TV watching over the 3-year period. A power analysis of the reading time change model revealed insufficient power (19%) to detect an odds ratio of 1.05, which represented the odds of dementia associated with increased reading time compared to maintaining reading time over the 3-year period.

Discussion

This study is among the first to examine how different types of sedentary behavior as well as trajectories of those behaviors over time are associated with cognitive function in generally well-functioning older adults. Our hypotheses were partially supported. While reading was protective against cognitive decline seven years later as we expected, lower sitting time was also protective and there was no deleterious association

with excessive TV watching. In terms of change in sedentary behavior, we found that increased TV watching was associated with poorer cognitive function as anticipated but change in sitting or reading time was not associated with cognitive function. This suggests that sedentary behavior may have important contributions to cognitive function in older age, but that these relationships are complex. Lastly, change in any of the sedentary behaviors was not associated with dementia risk, which was likely due to insufficient statistical power.

We expected that participants who sat more at baseline or who increased their amount of sitting time would exhibit worse cognitive function due to lack of movement because physical activity has been demonstrated to improve brain health (PAGAC, 2018). Additionally, excess sedentary behavior has been associated with other negative health outcomes (Copeland et al., 2017; Madden, Feldman, & Chase, 2021; Ekelund et al., 2019). Our findings together with other work suggest that the relationship between sitting and cognitive function is necessarily more complex. Previous research on this topic has yielded mixed results (Falck et al., 2017; Olanrewaju, et al., 2020) and one potential explanation is that while lack of movement may be generally worse for cognitive function, many cognitively stimulating activities are typically performed while seated. The question about sitting time in Health ABC asked participants about all time spent sitting, including both cognitively stimulating and other activities, which makes it difficult to interpret our finding that participants who sat more at baseline had better cognitive function at follow-up.

In light of this complexity, we also investigated reading and TV time to examine the relationships between one typically sedentary activity considered to be cognitively

stimulating and the other not. We found TV watching (an activity that we did not expect to be cognitively stimulating) at baseline was not associated with cognitive function. These findings do not necessarily contradict existing literature because while some studies found a link between TV watching and cognitive function, there were key differences between those studies and the present study. Kesee-Guyot and colleagues (2012) examined these associations in a younger cohort (mean age of 55); Da Ronch and colleagues (2015) employed a cross-sectional analysis; and Fancourt & Steptoe (2019), Hamer and Stamatakis (2014), and Bakrania and colleagues (2017) analyzed different subdomains of cognitive function than those included here. In addition, Fajersztajn and colleagues (2021) did not find an association with global cognitive function, which was included in this study through use of the 3MS. The variability in study population characteristics, cognitive assessment approach, and length of follow-up suggests the need for more research in this area.

We found that increased reading time was associated with small improvements on the 3MS and DSST seven years later. This finding aligns with results from previous research, which have demonstrated positive associations between reading and cognitive function, although, similar to the literature on TV watching and cognitive function, there is variability in the samples and measurement of constructs (Kurita et al., 2018; Nemoto et al., 2018). While more work is needed to improve rigor and reproducibility in this line of research, it would appear that encouraging and facilitating reading may be a promising area for intervention development to promote brain health in old age.

Our analyses did not uncover associations between trajectories of the different sedentary behavior measures and cognitive function, excepting TV watching, in which

moving from the low category (0-27 hours/week) at baseline to the high category (28+ hours/week) three years later was associated with a 1.5-point decrease in 3MS score compared to remaining in the low category across the 3-year period. To our knowledge, Kesse-Guyot and colleagues' (2012) study is the only other attempt to examine whether change in different types of sedentary behavior is associated with cognitive function. Although they did not find a relationship between increased TV viewing and cognitive decline, the average age of participants in their study was 55 years. It is possible that we observed an effect because our study sample was substantially older (75 years old on average), suggesting that increased time spent watching TV could be an indicator of declining cognitive function, rather than a cause of it. As cognitive function declines, older adults may begin to spend more time in passive activities such as TV watching rather than engaging in more cognitively demanding activities. Future research should consider examining how the habits of older adults change over time, including the amount of time allotted to different leisure activities, to determine whether this could help loved ones of older adults and clinicians better monitor age-related cognitive decline. In addition, studies seeking to analyze associations of these factors with odds of dementia will likely need larger samples than we had available in this study to have adequate statistical power.

The strengths of this analysis include the prospective design, relatively large sample size that was balanced by sex, and inclusion of physical activity as a control variable, which is often not typical in research on sedentary behavior (Olanrewaju et al., 2020). We also tried to reduce the possibility of reverse causality by removing all participants who screened positive for dementia at baseline based on a cutoff score of

77/78 on the 3MS. However, 69% of the study population were white and 51% had some post-secondary level of educational attainment, which may diminish the generalizability of the findings. Also, information on physical activity and sitting time was self-reported, which could lead to bias as physical activity tends to be over-reported and sedentary behavior tends to be under-reported compared to objective measurements (Sallis & Saelens, 2000; Banda et al., 2010). This dynamic may have occurred in this study, where 40% of participants reported high amounts of physical activity and the average time spent sitting was 6.8 hours per day. Another limitation of this work is that the sedentary behavior assessments were single item measures.

Our findings and those of others indicate that the relationship between sedentary behavior and cognitive function is likely to be complex. Researchers should continue to investigate the pathways through which sedentary behaviors may affect brain health and whether interventions aimed at promoting cognitively stimulating activities and/or reducing the time spent on non-stimulating seated activities may improve cognitive function or slow cognitive decline among older adults. In addition, future research should consider examining whether changes in time spent on different leisure activities in old age are indicative of cognitive decline, with the goal of enabling loved ones and care providers to intervene early. Given aging demographics and the fact that older adults may spend up to 60% of their waking hours sitting or reclining (Matthews et al., 2008), there is a substantial public health benefit to understanding how sedentary behavior affects brain health in older age.

Chapter 5: Conclusion

Overview

This dissertation aimed to explore the different ways that movement is longitudinally related to cognitive function and dementia among older adults making use of the data available in the Health ABC study. Manuscript 1 examined the independent and joint associations between physical activity and sitting time with dementia and cognitive function. The findings from this study revealed that neither excessive sitting nor low physical activity were independently associated with increased odds of dementia. In addition, the joint associations models indicated that the odds of dementia was no greater among participants who moved the least, that is, those who sat more than nine hours per day and expended fewer than 500 kcal/week in physical activity. The hypothesis that the odds of dementia would increase in a dose-response manner along with decreasing levels of movement was also not supported. Low physical activity was independently associated with poorer global cognitive function, as measured by the 3MS, but the independent association of sitting time and the joint associations of physical activity and sitting time with cognitive function were not statistically significant.

Manuscript 2 investigated the hypothesis that some types of sedentary behavior may be less harmful and potentially even beneficial to cognitive function by analyzing whether and how different sedentary behaviors as well as change in those behaviors over time are longitudinally related to cognitive outcomes after controlling for physical activity. Specifically, the study modeled the relationships between time spent sitting, watching TV (a non-cognitively stimulating activity), and reading (a cognitively stimulating activity) at one time point and then again across two time points with cognitive function and dementia. Results indicated that TV watching was not associated

with cognitive function, but that increased time spent sitting was associated with better performance on the DSST. In addition, reading time had a slight protective effect, leading to improved scores on two of the cognitive function measures, the 3MS and the DSST. In terms of trajectories of these behaviors, change in either direction of sitting or reading time was not associated with cognitive function or dementia. However, increased TV time over a period of three years was associated with a 1.5-point decrease on the 3MS, compared those who maintained a low level of TV watching over the same period. There was no association between change in TV watching with odds of dementia, which can likely be attributed to a low number of dementia cases in the study.

Limitations

While Health ABC is one of a few studies to include items measuring all the constructs studied here, the sample constituted a healthy subset of the population; that is, individuals with no reported mobility limitations at study enrollment. The sample was further restricted to those who reported little or no difficulty walking and those who were free of any evidence of dementia three years after Health ABC began, which was baseline for the present research. The better than average health of the sample is further evidenced by the atypically high rates of activity among participants, with most reporting low levels of sitting and medium or high levels of physical activity. Relatedly, some research indicates that poor cognitive function is associated with greater risk of death and conversely, engaging in healthy behaviors is associated with a longer life expectancy free of dementia, meaning that the participants with worse health and/or cognitive function who otherwise may have developed dementia would be lost to follow-up and thus excluded from the study (Perls, Morris, Ooi, & Lipsitz, 1993; Stewart, Zelinski, &

Wallace, 2000; Dhana et al., 2022). This selective survival, along with the overall health and high activity levels of the participants, may have diminished the ability to detect associations between physical activity, sedentary behavior, and dementia.

A key limitation of the second manuscript was that the study likely had insufficient statistical power to detect associations of the independent variables with odds of dementia. We used continuous measures of cognitive function as outcome variables in both manuscripts to address this limitation as well as to examine whether physical activity and sedentary behavior were associated with cognitive decline that did not reach the threshold of dementia. The findings for Manuscript 1, that physical activity and sedentary behavior are not jointly associated with dementia, did not change when using the cognitive function measures. However, for Manuscript 2, increasing TV time over a period of three years was associated with a lower score on the 3MS, an effect that was not observed in the dementia model, indicating that the association between change in TV watching and dementia should be investigated further in studies with more cases of dementia.

Another limitation of this body of work was the measurement of the movement constructs. For example, the physical activity questionnaire assessed only the past seven days of physical activity. While this may improve recall of activities among older people, it may not be representative of typical activity patterns occurring over several years that may affect cognitive function. Additionally, the sedentary behavior questions were single item measures. The sitting time question specifically asked about sitting upright and did not include time spent reclining or lying down, which may have led to underestimates of actual sedentary time. The TV watching and reading questions did not specifically

reference sitting and so may have included standing or active time, for example, individuals watching TV while walking on a treadmill.

Lastly, the majority of the study population was white and had some post-secondary level of educational attainment, which may diminish the generalizability of the findings. Also, information on physical activity and sitting time was self-reported, which could lead to bias as physical activity tends to be over-reported and sedentary behavior tends to be under-reported compared to objective measurements (Sallis & Saelens, 2000; Banda et al., 2010). This dynamic may have occurred in this study, where a large proportion of participants reported high amounts of physical activity and low amounts of sitting time.

Strengths

The strengths of these studies include that they are among the first to provide a nuanced examination into how different components of movement are associated with cognitive function and dementia in older age. While much research has explored the relationship between physical activity and/or dementia, the potential of joint association models of physical activity and sitting time has not been fully realized. In addition, some research has examined how different types of sedentary behavior, including those are cognitively stimulating and those that are not, are prospectively associated with cognitive function and dementia, but none have investigated how change in the amount of time spent performing these activities is associated with cognitive function in older adults.

Additional strengths include the longitudinal cohort design of Health ABC, which provided the ability to use exposure variables that occurred up to fourteen years earlier than the outcome variables. In both studies, to strengthen causal inference, the possibility

of reverse causality was reduced by removing all participants who screened positive for dementia or who reported difficult walking at baseline to limit the confounding effects of some unmeasured health or social factor related to physical activity, sitting, cognitive function, and/or dementia. Lastly, Health ABC also had a relatively large sample size that was balanced by sex and assessed the constructs of interest to these two manuscripts, which is not common among studies today, let alone one that was initiated over two decades ago.

Implications for Future Research

Future research should build upon the work described here by improving measurement to better elucidate the pathways through which movement may be related to cognitive function among older adults. For example, objective measures of physical activity and sedentary time are likely to be more accurate than self-report measures and may allow for more precise estimates. This is especially important because some participants may have been misclassified (e.g., in the low sitting time category as opposed to high sitting category) due to the bias inherent in self-report assessments. In addition, longitudinal studies should develop and employ valid and reliable measures of different types of sedentary behavior to help explicate whether performing cognitively stimulating activities, even while in a seated or reclined position, can offset the potentially deleterious effects of lack of movement. Studies should also examine the associations of movement with cognitive function over longer follow-up periods to better disentangle whether decreased movement in older age is a cause or an indicator of cognitive impairment and/or dementia. Lastly, it will be important for future research to try to estimate the cumulative lifelong benefits of engaging in physical activity or

reducing sedentary time. It may be the case that these behaviors do affect cognitive function, but that they need to be performed early and often to have a benefit.

Moving forward, studies should also consider how cognitive function and dementia are assessed. In the present research, the associations between independent variables that are typically powerful predictors of dementia, like education, were not statistically significant in the logistic regression models, which used a binary indicator variable for dementia. The associations were stronger in models that used continuous outcome measures of cognitive function. This may be because of the increased variability and statistical power afforded by the continuous variables, but on the other hand, it may be because the cognitive function measures are able to detect cognitive decline that does not meet or surpass the threshold for dementia. These continuous measures can potentially serve as early warning indicators of dementia. Additionally, the extant literature utilizes measures of various subdomains of cognitive function, which increases the difficulty in making cross-study comparisons. This dissertation research employed a global cognitive function measure; a polyfactorial measure of motor skills, attention, and executive function; and an executive function measure, where other researchers have used assessments of other subdomains, such as verbal fluency and recall. This is important because movement may affect some of these subdomains differently than others and without that nuance, understanding these relationships is challenging. If investigators were able to agree on a common set of assessments that includes as broad a representation of the different subdomains (and combination thereof) as possible, it would also enhance rigor and reproducibility.

Implications for Public Health Practice

While the findings from Manuscript 1 were null and those from Manuscript 2 were mixed, they still carry several public health practice implications. For example, the fact that there were no associations, independently or jointly, between physical activity and sitting time and dementia within a healthy sample of older adults could inform movement guidelines for this population. If healthy older adults do not experience an additional benefit from movement on cognitive function, then perhaps recommendations could focus on other activities to improve cognitive function. Of course, increasing physical activity and reducing time spent sedentary is important for other health outcomes, but in terms of improving cognitive function or preventing or delaying cognitive decline, efforts may be better directed in other directions. This may not be the case for older adults who are less healthy or younger than those included in the present research, but more complexity in recommendations may be necessary as opposed to blanket statements, particularly as some older adults view needing to sit more for reasons of their age and/or ability as a moral failing due to stigma around being sedentary (Palmer et al., 2021).

The findings from Manuscript 2 offer insight into potential interventions to promote brain health among older adults. While older adults tend to be more sedentary than other segments of the population, it appears that some forms of sedentary behavior are worse than others for cognitive function. For example, the fact that reading was associated with better cognitive function may indicate that potential interventions should focus on replacing seated non-cognitively stimulating activities with those that are stimulating. This may be particularly relevant for those who are not sedentary by choice

and who are interested in ways to improve their cognitive function. In addition, the association between increased TV watching over time and worse cognitive function may not be an indication that watching more TV over time is bad for the brain, but rather that change in the time that older adults spend doing non-cognitively stimulating leisure activities could be a prodromal signal of cognitive decline or dementia, which could help early intervention efforts.

Conclusion

The relationship between movement and cognitive function in older adults is complex and difficult to study, highlighting the need for further investigation in this line of research. However, given aging demographics and the global economic burden associated with dementia-related disability, there is a substantial public health benefit to understanding how movement affects cognitive function, including dementia, in older age. This is particularly important as older adults tend to be less physically active and more sedentary than other age groups, although some types of sedentary behavior may have benefits for cognitive function in older adults, outweighing the potential harms associated with lack of movement. This work takes preliminary steps to uncover the different ways in which movement and lack thereof are associated with the cognitive health of older adults.

References

Ainsworth, B. E., Haskell, W. L., Herrmann, S. D., Meckes, N., Bassett Jr, D. R., Tudor-Locke, C., ... & Leon, A. S. (2011). 2011 Compendium of Physical Activities: a second update of codes and MET values. *Medicine & Science in Sports & Exercise*, *43*(8), 1575-1581.

Andresen, E. M., Malmgren, J. A., Carter, W. B., Patrick, D. L. (1994). Screening for depression in well older adults: Evaluation of a short form of the CES-D. *Am J Prev Med*, *10(2),* 77–84.

Bakrania, K., Edwardson, C. L., Khunti, K., Bandelow, S., Davies, M. J., & Yates, T. (2018). Associations between sedentary behaviors and cognitive function: cross-sectional and prospective findings from the UK biobank. *American Journal of Epidemiology*, *187*(3), 441-454.

Banda, J. A., Hutto, B., Feeney, A., Pfeiffer, K. A., McIver, K., Lamonte, M. J., ... & Hooker, S. P. (2010). Comparing physical activity measures in a diverse group of midlife and older adults. *Medicine & Science in Sports & Exercise*, *42*(12), 2251-2257.

Baumgart, M., Snyder, H. M., Carrillo, M. C., Fazio, S., Kim, H., & Johns, H. (2015). Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a population-based perspective. *Alzheimer's & Dementia, 11*(6), 718-726.

Beavers, K. M., Hsu, F. C., Houston, D. K., Beavers, D. P., Harris, T. B., Hue, T. F., ... & Nicklas, B. J. (2013). The role of metabolic syndrome, adiposity, and inflammation in physical performance in the Health ABC Study. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *68*(5), 617-

623.

Bherer, L., Erickson, K. I., & Liu-Ambrose, T. (2013). A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. *Journal of Aging Research, 2013*, 57508.

Bland, R. C., & Newman, S. C. (2001). Mild dementia or cognitive impairment: the Modified Mini-Mental State examination (3MS) as a screen for dementia. *The Canadian Journal of Psychiatry*, *46*(6), 506-510.

Blondell, S. J., Hammersley-Mather, R., & Veerman, J. L. (2014). Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis of longitudinal studies. *BMC Public Health, 14*(1), 510.

Blough, J., & Loprinzi, P. D. (2019). Experimental Evaluation of the Joint Effects of Exercise and Sedentary Behavior on Cognitive Function. *Journal of Lifestyle Medicine, 9*(1), 52.

Brach, J. S., Simonsick, E. M., Kritchevsky, S., Yaffe, K., Newman, A. B., & Health, Aging and Body Composition Study Research Group. (2004). The association between physical function and lifestyle activity and exercise in the health, aging and body composition study. *Journal of the American Geriatrics Society, 52*(4), 502-509.

Chastin, S. F., McGregor, D. E., Biddle, S. J., Cardon, G., Chaput, J. P., Dall, P. M., ... & Van der Ploeg, H. P. (2021). Striking the Right Balance: Evidence to Inform Combined Physical Activity and Sedentary Behavior Recommendations. *Journal of Physical Activity and Health*, *18*(6), 631-637.

Choi, H., Schoeni, R. F., Martin, L. G., & Langa, K. M. (2018). Trends in the prevalence

and disparity in cognitive limitations of Americans 55–69 years old. *The Journals of Gerontology: Series B, 73*(suppl_1), S29-S37.

Clark, L. R., Schiehser, D. M., Weissberger, G. H., Salmon, D. P., Delis, D. C., & Bondi, M. W. (2012). Specific measures of executive function predict cognitive decline in older adults. *Journal of the International Neuropsychological Society*, *18*(1), 118.

Colbert, L. H., Visser, M., Simonsick, E. M., Tracy, R. P., Newman, A. B., Kritchevsky, S. B., ... & Harris, T. B. (2004). Physical activity, exercise, and inflammatory markers in older adults: findings from the Health, Aging and Body Composition Study. *Journal of the American Geriatrics Society, 52*(7), 1098-1104.

Copeland, J. L., Ashe, M. C., Biddle, S. J., Brown, W. J., Buman, M. P., Chastin, S., ... & Dogra, S. (2017). Sedentary time in older adults: a critical review of measurement, associations with health, and interventions. *British Journal of Sports Medicine*, *51*(21), 1539-1539.

Da Ronch, C., Canuto, A., Volkert, J., Massarenti, S., Weber, K., Dehoust, M. C., ... & Grassi, L. (2015). Association of television viewing with mental health and mild cognitive impairment in the elderly in three European countries, data from the MentDis_ICF65+ project. *Mental Health and Physical Activity*, *8*, 8-14.

Davis, T. C., Long, S. W., Jackson, R. H., Mayeaux, E. J., George, R. B., Murphy, P. W., & Crouch, M. A. (1993). Rapid estimate of adult literacy in medicine: a shortened screening instrument. *Family Medicine*, *25*(6), 391-395.

Demurtas, J., Schoene, D., Torbahn, G., Marengoni, A., Grande, G., Zou, L., ... & Veronese, N. (2020). Physical activity and exercise in mild cognitive impairment

and dementia: an umbrella review of intervention and observational studies. *Journal of the American Medical Directors Association*, *21*(10), 1415-1422.

Dhana, K., Franco, O. H., Ritz, E. M., Ford, C. N., Desai, P., Krueger, K. R., ... & Rajan, K. B. (2022). Healthy lifestyle and life expectancy with and without Alzheimer's dementia: population based cohort study. *BMJ*, *377*.

Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, *64*, 135-168.

Diaz, K. M., Howard, V. J., Hutto, B., Colabianchi, N., Vena, J. E., Safford, M. M., ... & Hooker, S. P. (2017). Patterns of sedentary behavior and mortality in US middle-aged and older adults: a national cohort study. *Annals of Internal Medicine*, *167*(7), 465-475.

Dillon, K., & Gardiner, P. A. (2021). Association between sedentary behaviour and risk of dementia: an evidence gap. *Translational Psychiatry*, *11*(1), 1-3.

DiPietro, L., Jin, Y., Talegawkar, S., & Matthews, C. E. (2018). The joint associations of sedentary time and physical activity with mobility disability in older people: the NIH-AARP diet and health study. *The Journals of Gerontology: Series A, 73*(4), 532-538.

DiPietro, L., Al-Ansari, S. S., Biddle, S. J., Borodulin, K., Bull, F. C., Buman, M. P., ... & Willumsen, J. F. (2020). Advancing the global physical activity agenda: recommendations for future research by the 2020 WHO physical activity and sedentary behavior guidelines development group. *International Journal of Behavioral Nutrition and Physical Activity*, *17*(1), 1-11.

Edwards, M. K., & Loprinzi, P. D. (2017a). The association between sedentary behavior

and cognitive function among older adults may be attenuated with adequate physical activity. *Journal of Physical Activity and Health, 14*(1), 52-58.

Edwards, M. K., & Loprinzi, P. D. (2017b). Combined associations of sedentary behavior and cardiorespiratory fitness on cognitive function among older adults. *International Journal of Cardiology, 229*, 71-74.

Ekelund, U., Steene-Johannessen, J., Brown, W. J., Fagerland, M. W., Owen, N., Powell, K. E., ... & Lancet Sedentary Behaviour Working Group. (2016). Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *The Lancet, 388*(10051), 1302-1310.

Ekelund, U., Tarp, J., Steene-Johannessen, J., Hansen, B. H., Jefferis, B., Fagerland, M. W., ... & Lee, I. M. (2019). Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ*, *366*.

Engel, G. L. (1977). The need for a new medical model: a challenge for biomedicine. *Science*, *196*(4286), 129-136.

Etnier, J. L., Nowell, P. M., Landers, D. M., & Sibley, B. A. (2006). A meta-regression to examine the relationship between aerobic fitness and cognitive performance. *Brain Research Reviews, 52*(1), 119-130.

Evenson, K. R., Buchner, D. M., & Morland, K. B. (2012). Objective measurement of physical activity and sedentary behavior among US adults aged 60 years or older. *Preventing Chronic Disease, 9*.

Farina, M. P., Zhang, Y. S., Kim, J. K., Hayward, M. D., & Crimmins, E. M. (2022).

Trends in Dementia Prevalence, Incidence, and Mortality in the United States (2000–2016). *Journal of Aging and Health*, *34*(1), 100-108.

Fajersztajn, L., Di Rienzo, V., Nakamura, C. A., & Scazufca, M. (2021). Watching TV and Cognition: The SPAH 2-Year Cohort Study of Older Adults Living in Low-Income Communities. *Frontiers in Neurology*, *12*.

Falck, R. S., Landry, G. J., Best, J. R., Davis, J. C., Chiu, B. K., & Liu-Ambrose, T. (2017). Cross-sectional relationships of physical activity and sedentary behavior with cognitive function in older adults with probable mild cognitive impairment. *Physical Therapy, 97*(10), 975-984.

Fancourt, D., & Steptoe, A. (2019). Television viewing and cognitive decline in older age: findings from the English Longitudinal Study of Ageing. *Scientific Reports*, *9*(1), 1-8.

Feter, N., Leite, J. S., Smith, E., Coombes, J., & Rombaldi, A. (2020). Trajectory of physical activity and risk of dementia: A national-based cohort study: Epidemiology: Lifestyle risk factors. *Alzheimer's & Dementia*, *16*, e041333.

Friedman, E., Shih, R. E., Langa, K. M., et al. (2013). US prevalence and predictors of informal caregiving for dementia. *Health Aff (Millwood), 34*, 1637-1641.

Gennuso, K. P., Gangnon, R. E., Matthews, C. E., Thraen-Borowski, K. M., & Colbert, L. H. (2013). Sedentary behavior, physical activity, and markers of health in older adults. *Medicine and Science in Sports and Exercise, 45*(8), 1493.

Gilbert, S. J., & Burgess, P. W. (2008). Executive function. *Current Biology*, *18*(3), R110-R114.

Guallar-Castillón, P., Bayán-Bravo, A., León-Muñoz, L. M., Balboa-Castillo, T., López-

García, E., Gutierrez-Fisac, J. L., & Rodríguez-Artalejo, F. (2014). The association of major patterns of physical activity, sedentary behavior and sleep with health-related quality of life: a cohort study. *Preventive Medicine, 67*, 248-254.

Guitar, N. A., Connelly, D. M., Nagamatsu, L. S., Orange, J. B., & Muir-Hunter, S. W. (2018). The effects of physical exercise on executive function in community-dwelling older adults living with Alzheimer's-type dementia: a systematic review. *Ageing Research Reviews*, *47*, 159-167.

Guure, C. B., Ibrahim, N. A., Adam, M. B., & Said, S. M. (2017). Impact of physical activity on cognitive decline, dementia, and its subtypes: meta-analysis of prospective studies. *BioMed Research International, 2017*, Article ID 9016924.

Groot, C., Hooghiemstra, A. M., Raijmakers, P. G., van Berckel, B. N., Scheltens, P., Scherder, E. J., ... & Ossenkoppele, R. (2016). The effect of physical activity on cognitive function in patients with dementia: a meta-analysis of randomized control trials. *Ageing Research Reviews*, *25*, 13-23.

Hamer, M., & Stamatakis, E. (2014). Prospective study of sedentary behavior, risk of depression, and cognitive impairment. *Medicine and Science in Sports and Exercise*, *46*(4), 718.

Hamer, M., Terrera, G. M., & Demakakos, P. (2018). Physical activity and trajectories in cognitive function: English longitudinal study of ageing. *Journal of Epidemiology & Community Health*, *72*(6), 477-483.

Harvey, J., Chastin, S., & Skelton, D. (2013). Prevalence of sedentary behavior in older adults: a systematic review. *International Journal of Environmental Research and*

Public health, 10(12), 6645-6661.

Harvey, J. A., Chastin, S. F., & Skelton, D. A. (2015). How sedentary are older people? A systematic review of the amount of sedentary behavior. *Journal of Aging & Physical Activity*, *23*(3).

Harvey, P. D. (2019). Domains of cognition and their assessment. *Dialogues in Clinical Neuroscience*, *21*(3), 227.

Havlik, R. J., Simonsick, E. M., Sutton-Tyrrell, K., Newman, A., Danielson, M. E., Brock, D. B., ... & Vaitkevicius, P. (2003). Association of physical activity and vascular stiffness in 70-to 79-year-olds: The Health ABC Study. *Journal of Aging and Physical Activity, 11*(2), 156-166.

Health ABC. (n.d.). Operations Manual: Teng Mini-Mental State Examination (3MS). https://healthabc.nia.nih.gov/sites/default/files/mmse_0.pdf.

Hebert, L. E., Weurve, J., Scherr, P.A., et al. (2013). Alzheimer's Disease in the United States (2010-2050) estimated using the 2010 census. *Neurology, 80*, 1778-1783.

Heron, M. (2019). Deaths: Leading Causes for 2017. *National Vital Statistics Reports, 68*(6). Hyattsville, MD: National Center for Health Statistics.

Hoang, T. D., Reis, J., Zhu, N., Jacobs, D. R., Launer, L. J., Whitmer, R. A., ... & Yaffe, K. (2016). Effect of early adult patterns of physical activity and television viewing on midlife cognitive function. *JAMA Psychiatry*, *73*(1), 73-79.

Hurd, M. D., Martorell, P., Delavande, A., Mullen, K. J., & Langa, K. M. (2013). Monetary costs of dementia in the United States. *New England Journal of Medicine*, *368*(14), 1326-1334.

Jaeger, J. (2018). Digit symbol substitution test: the case for sensitivity over specificity in

neuropsychological testing. *Journal of Clinical Psychopharmacology*, *38*(5), 513.

Jette, M., Sidney, K., & Blümchen, G. (1990). Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clinical Cardiology*, *13*(8), 555-565.

Kane, R.L., Butler, M., Fink, H.A., Brasure, M., Davila, H., Desai, P., Jutkowitz, E., … & Barclay, T. (2017). Interventions To Prevent Age-Related Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer's-Type Dementia. *Comparative Effectiveness Review No. 188*. Rockville, MD: Agency for Healthcare Research and Quality.

Katzmarzyk, P. T. (2010). Physical activity, sedentary behavior, and health: paradigm paralysis or paradigm shift?. *Diabetes, 59*(11), 2717-2725.

Katzmarzyk, P. T., Powell, K. E., Jakicic, J. M., Troiano, R. P., Piercy, K., Tennant, B., & 2018 Physical Activity Guidelines Advisory Committee. (2019). Sedentary behavior and health: update from the 2018 Physical Activity Guidelines Advisory Committee. *Medicine and Science in Sports and Exercise, 51*(6), 1227.

Kaup, A. R., Simonsick, E. M., Harris, T. B., Satterfield, S., Metti, A. L., Ayonayon, H. N., ... & Yaffe, K. (2014). Older adults with limited literacy are at increased risk for likely dementia. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *69*(7), 900-906.

Kelley, A. S., McGarry, K., Gorges, R., & Skinner, J. S. (2015). The burden of health care costs for patients with dementia in the last 5 years of life. *Annals of Internal Medicine, 163*(10), 729-736.

Kesse-Guyot, E., Charreire, H., Andreeva, V. A., Touvier, M., Hercberg, S., Galan, P., &

Oppert, J. M. (2012). Cross-sectional and longitudinal associations of different sedentary behaviors with cognitive performance in older adults. *PLoS One, 7*(10), e4783.1

Koster, A., Patel, K. V., Visser, M., Van Eijk, J. T. M., Kanaya, A. M., De Rekeneire, N., ... & Health, Aging and Body Composition Study. (2008). Joint effects of adiposity and physical activity on incident mobility limitation in older adults. *Journal of the American Geriatrics Society, 56*(4), 636-643.

Ku, P. W., Liu, Y. T., Lo, M. K., Chen, L. J., & Stubbs, B. (2017). Higher levels of objectively measured sedentary behavior is associated with worse cognitive ability: two-year follow-up study in community-dwelling older adults. *Experimental Gerontology, 99*, 110-114.

Kurita, S., Doi, T., Tsutsumimoto, K., Hotta, R., Nakakubo, S., Kim, M., & Shimada, H. (2019). Cognitive activity in a sitting position is protectively associated with cognitive impairment among older adults. *Geriatrics & Gerontology International*, *19*(2), 98-102.

Lambiase, M. J., Gabriel, K. P., Kuller, L. H., & Matthews, K. A. (2014). Sleep and executive function in older women: the moderating effect of physical activity. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *69*(9), 1170-1176.

Langa, K. M., Larson, E. B., Crimmins, E. M., Faul, J. D., Levine, D. A., Kabeto, M. U., & Weir, D. R. (2017). A comparison of the prevalence of dementia in the United States in 2000 and 2012. *JAMA Internal Medicine, 177*(1), 51-58.

Lange-Maia, B. S., Strotmeyer, E. S., Harris, T. B., Glynn, N. W., Simonsick, E. M.,

Brach, J. S., ... & Health, Aging, and Body Composition Study. (2015). Physical activity and change in long distance corridor walk performance in the health, aging, and body composition study. *Journal of the American Geriatrics Society, 63*(7), 1348-1354.

Lee, A. T. C., Richards, M., Chan, W. C., Chiu, H. F. K., Lee, R. S. Y., & Lam, L. C. W. (2018). Association of Daily Intellectual Activities With Lower Risk of Incident Dementia Among Older Chinese Adults. *JAMA Psychiatry*, 75(7), 697–703.

Lee, J. (2018). The relationship between physical activity and dementia: a systematic review and meta-analysis of prospective cohort studies. *Journal of Gerontological Nursing*, *44*(10), 22-29.

Lin, F. R., Yaffe, K., Xia, J., Xue, Q. L., Harris, T. B., Purchase-Helzner, E., ... & Health ABC Study Group, F. (2013). Hearing loss and cognitive decline in older adults. *JAMA Internal Medicine*, *173*(4), 293-299.

Maasakkers, C. M., Claassen, J. A., Gardiner, P. A., Rikkert, M. G. O., Lipnicki, D. M., Scarmeas, N., ... & Haan, M. N. (2020). The association of sedentary behaviour and cognitive function in people without dementia: a coordinated analysis across five cohort studies from COSMIC. *Sports Medicine*, *50*(2), 403-413.

Madden, K. M., Feldman, B., & Chase, J. (2021). Sedentary time and metabolic risk in extremely active older adults. *Diabetes Care*, *44*(1), 194-200.

Matthews, C. E., Chen, K. Y., Freedson, P. S., Buchowski, M. S., Beech, B. M., Pate, R. R., & Troiano, R. P. (2008). Amount of time spent in sedentary behaviors in the United States, 2003–2004. *American Journal of Epidemiology*, *167*(7), 875-881.

Nagamatsu, L. S., Chan, A., Davis, J. C., Beattie, B. L., Graf, P., Voss, M. W., ... & Liu-

Ambrose, T. (2013). Physical activity improves verbal and spatial memory in older adults with probable mild cognitive impairment: a 6-month randomized controlled trial. *Journal of Aging Research, 2013*, 861893.

National Institute on Aging (n.d.). *Introducing the Health ABC Study: The Dynamics of Health, Aging, and Body Composition*. https://healthabc.nia.nih.gov/.

National Institute on Aging. (2017a). *Memory, Forgetfulness, and Aging: What's Normal and What's Not?* https://www.nia.nih.gov/health/memory-forgetfulness-and-aging-whats-normal-and-whats-not.

Nemoto, Y., Sato, S., Takahashi, M., Takeda, N., Matsushita, M., Kitabatake, Y., ... & Arao, T. (2018). The association of single and combined factors of sedentary behavior and physical activity with subjective cognitive complaints among community-dwelling older adults: Cross-sectional study. *PLoS One*, *13*(4), e0195384.

Öhman, H., Savikko, N., Strandberg, T. E., & Pitkälä, K. H. (2014). Effect of physical exercise on cognitive performance in older adults with mild cognitive impairment or dementia: a systematic review. *Dementia and Geriatric Cognitive Disorders*, *38*(5-6), 347-365.

Olanrewaju, O., Stockwell, S., Stubbs, B., & Smith, L. (2020). Sedentary behaviours, cognitive function, and possible mechanisms in older adults: a systematic review. *Aging Clinical and Experimental Research*, *32*(6), 969-984.

Palmer, V. J., Gray, C. M., Fitzsimons, C., Mutrie, N., Wyke, S., Der, G., ... & Stewart, S. (2021). Sitting as a moral practice: Older adults' accounts from qualitative interviews on sedentary behaviours. *Sociology of Health & Illness*, *43*(9), 2102-

2120.

Penninx, B. W., Kritchevsky, S. B., Yaffe, K., Newman, A. B., Simonsick, E. M., Rubin, S., ... & Pahor, M. (2003). Inflammatory markers and depressed mood in older persons: results from the Health, Aging and Body Composition study. *Biological Psychiatry, 54*(5), 566-572.

Perls, T. T., Morris, J. N., Ooi, W. L., & Lipsitz, L. A. (1993). The relationship between age, gender and cognitive performance in the very old: the effect of selective survival. *Journal of the American Geriatrics Society*, *41*(11), 1193-1201.

Peterson, M. J., Giuliani, C., Morey, M. C., Pieper, C. F., Evenson, K. R., Mercer, V., ... & Simonsick, E. M. (2009). Physical activity as a preventative factor for frailty: the health, aging, and body composition study. *The Journals of Gerontology: Series A*, *64*(1), 61-68.

Physical Activity Guidelines Advisory Committee. (2018). Physical Activity Guidelines Advisory Committee Report, 2018. Washington, DC:US Department of Health and Human Services; 2008. https://health.gov/paguidelines/guidelines/report.aspx.

Plassman, B. L., Langa, K. M., Fisher, G. G., Heeringa, S. G., Weir, D. R., Ofstedal, M. B., ... & Steffens, D. C. (2008). Prevalence of cognitive impairment without dementia in the United States. *Annals of Internal Medicine, 148*(6), 427-434.

Prince, M., Ali, G. C., Guerchet, M., Prina, A. M., Albanese, E., & Wu, Y. T. (2016). Recent global trends in the prevalence and incidence of dementia, and survival with dementia. *Alzheimer's Research & Therapy, 8*(1), 23.

Rajan, K. B., Weuve, J., Barnes, L. L., McAninch, E. A., Wilson, R. S., & Evans, D. A. (2021). Population estimate of people with clinical Alzheimer's disease and mild

cognitive impairment in the United States (2020–2060). *Alzheimer's & Dementia*, *17*(12), 1966-1975.

Rollo, S., Antsygina, O., & Tremblay, M. S. (2020). The whole day matters: Understanding 24-hour movement guideline adherence and relationships with health indicators across the lifespan. *Journal of Sport and Health Science*. https://doi.org/10.1016/j.jshs.2020.07.004.

Rosano, C., Newman, A. B., Katz, R., Hirsch, C. H., & Kuller, L. H. (2008). Association between lower digit symbol substitution test score and slower gait and greater risk of mortality and of developing incident disability in well-functioning older adults. *Journal of the American Geriatrics Society*, *56*(9), 1618-1625.

Ross, R., Chaput, J. P., Giangregorio, L. M., Janssen, I., Saunders, T. J., Kho, M. E., ... & Tremblay, M. S. (2020). Canadian 24-Hour Movement Guidelines for Adults aged 18–64 years and Adults aged 65 years or older: an integration of physical activity, sedentary behaviour, and sleep. *Applied Physiology, Nutrition, and Metabolism*, *45*(10), S57-S102.

Royall, D. R., Cordes, J. A., & Polk, M. (1998). CLOX: an executive clock drawing task. *Journal of Neurology, Neurosurgery & Psychiatry*, *64*(5), 588-594.

Royall, D. R., Mahurin, R. K., & Gray, K. F. (1992). Bedside assessment of executive cognitive impairment: the executive interview. *Journal of the American Geriatrics Society*, *40*(12), 1221-1226.

Sabia, S., Dugravot, A., Dartigues, J. F., Abell, J., Elbaz, A., Kivimäki, M., & Singh-Manoux, A. (2017). Physical activity, cognitive decline, and risk of dementia: 28 year follow-up of Whitehall II cohort study. *BMJ*, *357*.

Sallis, J. F., & Saelens, B. E. (2000). Assessment of physical activity by self-report: status, limitations, and future directions. *Research Quarterly for Exercise and Sport*, *71*(sup2), 1-14.

Sanders, L. M., Hortobágyi, T., la Bastide-van Gemert, S., van der Zee, E. A., & van Heuvelen, M. J. (2019). Dose-response relationship between exercise and cognitive function in older adults with and without cognitive impairment: a systematic review and meta-analysis. *PloS One*, *14*(1), e0210036.

Simonsick, E. M., Newman, A. B., Ferrucci, L., Satterfield, S., Harris, T. B., Rodondi, N., & Bauer, D. C. (2009). Subclinical hypothyroidism and functional mobility in older adults. *Archives of internal medicine*, *169*(21), 2011-2017.

Sink, K. M., Espeland, M. A., Castro, C. M., Church, T., Cohen, R., Dodson, J. A., ... & Williamson, J. D. (2015). Effect of a 24-month physical activity intervention vs health education on cognitive outcomes in sedentary older adults: the LIFE randomized trial. *JAMA*, *314*(8), 781-790.

Sofi, F., Valecchi, D., Bacci, D., Abbate, R., Gensini, G. F., Casini, A., & Macchi, C. (2011). Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *Journal of Internal Medicine, 269*(1), 107-117.

Spector, A., & Orrell, M. (2010). Using a biopsychosocial model of dementia as a tool to guide clinical practice. *International Psychogeriatrics*, *22*(6), 957.

Stewart, S. T., Zelinski, E. M., & Wallace, R. B. (2000). Age, medical conditions, and gender as interactive predictors of cognitive performance: The effects of selective survival. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *55*(6), P381-P383.

Stokes, A. C., Weiss, J., Lundberg, D. J., Xie, W., Kim, J. K., Preston, S. H., & Crimmins, E. M. (2020). Estimates of the Association of Dementia With US Mortality Levels Using Linked Survey and Mortality Records. *JAMA Neurology*. doi:10.1001/jamaneurol.2020.2831.

Svanberg, E., Spector, A., & Stott, J. (2011). The impact of young onset dementia on the family: a literature review. *International Psychogeriatrics, 23*(3), 356.

Taylor, H. L., Jacobs Jr, D. R., Schucker, B., Knudsen, J., Leon, A. S., & Debacker, G. (1978). A questionnaire for the assessment of leisure time physical activities. *Journal of chronic diseases*, *31*(12), 741-755.

The Sedentary Behaviour Research Network. (2012). Letter to the Editor: Standardized use of the terms" sedentary" and" sedentary behaviours". *Applied Physiology Nutrition and Metabolism-Physiologie Appliquee Nutrition Et Metabolisme, 37*, 540-542.

Tremblay, M. S., Aubert, S., Barnes, J. D., Saunders, T. J., Carson, V., Latimer-Cheung, A. E., ... & Chinapaw, M. J. (2017). Sedentary behavior research network (SBRN)–terminology consensus project process and outcome. *International Journal of Behavioral Nutrition and Physical Activity, 14*(1), 75.

U.S. Department of Health and Human Services (2018). 2018 Physical Activity Guidelines for Americans, 2nd Edition. (Office of Disease Prevention and Health Promotion, Washington, DC).

Visser, M., Simonsick, E. M., Colbert, L. H., Brach, J., Rubin, S. M., Kritchevsky, S. B., ... & Health ABC Study. (2005). Type and intensity of activity and risk of mobility limitation: the mediating role of muscle parameters. *Journal of the*

American Geriatrics Society, 53(5), 762-770.

Wade, D. T., & Halligan, P. W. (2017). The biopsychosocial model of illness: a model whose time has come. *Clinical Rehabilitation, 31*(8), 995-1004.

Wahl, D., Solon-Biet, S. M., Cogger, V. C., Fontana, L., Simpson, S. J., Le Couteur, D. G., & Ribeiro, R. V. (2019). Aging, lifestyle and dementia. *Neurobiology of Disease*, *130*, 104481.

Waring, S. C., Doody, R. S., Pavlik, V. N., Massman, P. J., & Chan, W. (2005). Survival among patients with dementia from a large multi-ethnic population. *Alzheimer Disease & Associated Disorders, 19*(4), 178-183.

Weuve, J., Proust-Lima, C., Power, M. C., Gross, A. L., Hofer, S. M., Thiébaut, R., ... & MELODEM Initiative. (2015). Guidelines for reporting methodological challenges and evaluating potential bias in dementia research. *Alzheimer's & Dementia*, *11*(9), 1098-1109.

Wheeler, M. J., Dempsey, P. C., Grace, M. S., Ellis, K. A., Gardiner, P. A., Green, D. J., & Dunstan, D. W. (2017). Sedentary behavior as a risk factor for cognitive decline? A focus on the influence of glycemic control in brain health. *Alzheimer's & Dementia: Translational Research & Clinical Interventions, 3*(3), 291-300.

Williams, J. A., Sink, K. M., Tooze, J. A., Atkinson, H. H., Cauley, J. A., Yaffe, K., ... & Houston, D. K. (2015). Low 25-hydroxyvitamin D concentrations predict incident depression in well-functioning older adults: the health, aging, and body composition study. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *70*(6), 757-763.

Wimo, A., Jönsson, L., Bond, J., Prince, M., Winblad, B., & Alzheimer Disease

International. (2013). The worldwide economic impact of dementia 2010. *Alzheimer's & Dementia, 9*(1), 1-11.

Xu, W., Wang, H. F., Wan, Y., Tan, C. C., Yu, J. T., & Tan, L. (2017). Leisure time physical activity and dementia risk: a dose-response meta-analysis of prospective studies. *BMJ Open*, *7*(10), e014706.

Yaffe, K., Fiocco, A. J., Lindquist, K., Vittinghoff, E., Simonsick, E. M., Newman, A. B., ... & Harris, T. B. (2009). Predictors of maintaining cognitive function in older adults: the Health ABC study. *Neurology, 72*(23), 2029-2035.

Yaffe, K., Lindquist, K., Shlipak, M. G., Simonsick, E., Fried, L., Rosano, C., ... & Kurella-Tamura, M. (2008). Cystatin C as a marker of cognitive function in elders: findings from the health ABC study. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, *63*(6), 798-802.

Yan, S., Fu, W., Wang, C., Mao, J., Liu, B., Zou, L., & Lv, C. (2020). Association between sedentary behavior and the risk of dementia: a systematic review and meta-analysis. *Translational Psychiatry*, *10*(1), 1-8.

Yerramalla, M. S., McGregor, D. E., van Hees, V. T., Fayosse, A., Dugravot, A., Tabak, A. G., ... & Sabia, S. (2021). Association of daily composition of physical activity and sedentary behaviour with incidence of cardiovascular disease in older adults. *International Journal of Behavioral Nutrition and Physical Activity*, *18*(1), 1-13.

Young, J., Angevaren, M., Rusted, J., & Tabet, N. (2015). Aerobic exercise to improve cognitive function in older people without known cognitive impairment.

Cochrane Database of Systematic Reviews, (4), CD005381.

Zheng, P., Pleuss, J. D., Turner, D. S., Ducharme, S. W., & Aguiar, E. J. (2022). Dose–Response Association Between Physical Activity (Daily MIMS, Peak 30-Minute MIMS) and Cognitive Function Among Older Adults: NHANES 2011–2014. *The Journals of Gerontology: Series A*.

Zhu, W., Wadley, V. G., Howard, V. J., Hutto, B., Blair, S. N., & Hooker, S. P. (2017). Objectively measured physical activity and cognitive function in older adults. *Medicine and Science in Sports and Exercise, 49*(1), 47.