Preventive Medicine Reports 22 (2021) 101302

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Building research in diet and cognition (BRIDGE): Baseline characteristics of older obese African American adults in a randomized controlled trial to examine the effect of the Mediterranean diet with and without weight loss on cognitive functioning

Jennifer C. Sanchez-Flack [a,f,*], Lisa Tussing-Humphreys [a,b,c], Melissa Lamar [d], Giamilla Fantuzzi [e], Linda Schiffer [a], Lara Blumstein [a], Andrew McLeod [a,b], Roxanne Dakers [a], Desmona Strahan [a], Leo Restrepo [a], Nefertiti Oji Njideka Hemphill [e], Leilah Siegel [a,c], Mirjana Antonic [a], Marian Fitzgibbon [a,b,c,f]

[a] Institute for Health Research and Policy, University of Illinois at Chicago, 1747 West Roosevelt Road, Chicago, IL 60608, United States
[b] Department of Medicine, University of Illinois at Chicago, 1853 West Polk Street, Chicago, IL 60612, United States
[c] University of Illinois Cancer Center, University of Illinois at Chicago, 818 South Wolcott Avenue, Chicago, IL 60612, United States
[d] Rush Alzheimer's Disease Center, Rush University, 1750 West Harrison Street, Chicago, IL 60612, United States
[e] Department of Kinesiology and Nutrition, University of Illinois at Chicago, 1919 W. Taylor Street, Chicago, IL 60612, United States
[f] Department of Pediatrics, University of Illinois at Chicago, 1200 West Harrison Street, Chicago, IL 60607, United States

ARTICLE INFO

Keywords:
African Americans
Cognitive functioning
Mediterranean diet
Weight loss
Dementia
Older adults

ABSTRACT

In the United States, >5.4 million people age 65 and older are affected by cognitive impairment and dementia, including Alzheimer's disease. African Americans are more likely than non-Hispanic whites to suffer from these disorders. Obesity is linked to accelerated age-related cognitive decline, and weight loss through caloric restriction is a potential strategy to prevent this cognitive impairment. Adherence to a healthful dietary pattern, such as the Mediterranean Diet (MedDiet), has also shown positive effects on reducing risk for dementia. African Americans are disproportionately affected by obesity and have less healthful diets than non-Hispanic whites. We present baseline characteristics from a three-arm randomized controlled trial that randomized 185 obese (BMI $\geq$ 30 kg/m^2 and $\leq$ 50 kg/m^2) healthy older adults (55–85 years of age) to: 1) Typical Diet Control (TDC); 2) MedDiet alone (MedDiet-A) intervention; or 3) MedDiet caloric restricted intervention to promote weight loss (MedDiet-WL). The majority of the sample was African American (91.4%) and female (85.9%). The two active interventions (MedDiet-A and MedDiet-WL) met once weekly for 8 months, and the TDC received weekly general health newsletters. Baseline data were collected between January 2017 and July 2019 in Chicago, IL. In our sample, closer adherence to a MedDiet pattern was associated with higher attention and information processing (AIP) and higher executive functioning (EF). Consistent with the literature, we saw that older participants performed more poorly on the cognitive assessments than younger participants, and women outperformed men across verbally mediated tasks, especially ones related to learning and memory.

1. Introduction

In the United States (US), >5.4 million people age 65 and older are affected by cognitive impairment and dementia, including Alzheimer's disease. (Alzheimer's Association, 2020, 2016). African Americans are more likely than non-Hispanic whites to suffer from these disorders (Chen and Zissimopoulos, 2018; Lines et al., 2014; Plassman et al., 2007; Zhang et al., 2016). Alzheimer's disease and related dementias (ADRD) are devastating and costly conditions, with a direct cost estimate to the US economy of $236 billion in 2016 (Alzheimer's Association, 2016). Reductions in cardiovascular diseases (CVD) over the last half of the 20th century are linked to some noted leveling off in the rates of ADRD in most developed and industrialized countries (Larson et al., 2013). However, obesity rates have increased dramatically during the last

* Corresponding author at: Institute for Health Research and Policy, University of Illinois at Chicago, 1747 West Roosevelt Road, Chicago, IL 60608, United States.
E-mail address: jsanch38@uic.edu (J.C. Sanchez-Flack).

https://doi.org/10.1016/j.pmedr.2020.101302
Received 3 August 2020; Received in revised form 24 November 2020; Accepted 1 December 2020
Available online 31 December 2020
2211-3355/Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

several decades, particularly among underrepresented minority populations, including African Americans (Ogden et al., 2020, 2015). Since obesity is associated with cognitive decline (Cournot et al., 2006; Elias et al., 2005; Wolf et al., 2007), this places these populations at increased risk of ADRD.

The exact mechanisms that link the increased risk of ADRD with obesity are not well understood (Singh-Manoux et al., 2018), and whether intentional weight loss in obese individuals can positively influence cognitive performance has not been determined (Siervo et al., 2011). However, obesity likely negatively influences cognition through its effect on CVD and metabolic risk factors, as well as associated adipocyte hormones, cytokines, and inflammatory markers (Lambert et al., 2013; Tosto and Reitz, 2013). Improving obesity-related lifestyle behaviors such as unhealthful diets and sedentary behaviors can decrease obesity, and may reduce the risk of cognitive decline through downstream physiological effects (Sherzai and Sherzai, 2019; Wright et al., 2017). Weight loss via caloric restriction is the primary treatment strategy to treat obesity, and modest weight loss (5–7%) is associated with a reduction in the risk of CVD and metabolic diseases (Fain, 2009; Logue et al., 2010; Mavri et al., 2011; Villareal et al., 2011). These changes are primarily due to the positive effects on metabolism, inflammatory markers, and oxidative stress (De Las Fuentes et al., 2009; Esposito et al., 2003).

Interventions focused on lifestyle factors such as a healthy diet and modest weight loss could provide a practical approach to prevent or offset the development of age-related cognitive decline (Kuczmarski et al., 2014). The Mediterranean Diet (MedDiet) pattern, defined as a plant-based diet, characterized by a high consumption of fruits, vegetables, and whole grains as well as fish, nuts, and legumes, unsaturated fatty acids, and low to moderate intake of alcohol (consumed with meal) is linked to slower cognitive decline, improved cognitive function, and decreased risk of dementia as evidenced in a number of observational studies (Aridi et al., 2017; Chen et al., 2019; Loughrey et al., 2017; Petersson and Philippou, 2016; Power et al., 2019; Solfrizzi et al., 2017). Adherence to the MedDiet is also associated with a reduced risk of multiple chronic diseases such as type 2 diabetes and cancer, among others, demonstrating its health benefits beyond cognition and contribution to overall well-being (Abenavoli et al., 2019).

Lourida et al. (2013) in a systematic review of 11 observational studies and one randomized controlled trial (RCT), reported a consistent pattern of associations between adherence to a MedDiet and lower risks of cognitive decline and better cognitive function. However, many of the observational studies had limitations that highlight the need for RCTs (Martínez-González et al., 2012). One RCT that tested the association in a sub-study of the "Primary Prevention of Cardiovascular Disease with a Mediterranean Diet" (*PREvencion con DIeta MEDiterranean)* (PREDIMED) (Valls-Pedret et al., 2015) reported cognitive improvement among participants randomized to the Med Diet group and cognitive decline in those randomized to the low-fat control group. The benefits of the MedDiet group were independent of sex, age, energy intake, cognitive associated variables such as education, APOE ε4 genotype and vascular risk factors. Results of this RCT provide stronger evidence of the effects of a MedDiet on cognition than those reported in observational studies (Lourida et al., 2013; Psaltopoulou et al., 2013; Singh et al., 2014).

To our knowledge, however, no RCTs have tested the combined effect on cognitive functioning of MedDiet with caloric restriction to promote weight loss (MedDiet-WL), compared to both a weight-stable condition with MedDiet alone (MedDiet-A) and a Typical Diet Control (TDC). Furthermore, secondary outcomes including weight status and cardiovascular, metabolic, and immune-related biomarkers are rarely investigated, despite their known associations with cognition and ADRD. This may be particularly important for African Americans, who not only have a higher prevalence of ADRD and obesity, but also poorer diet quality and higher levels of inactivity compared to non-Hispanic Whites (Hiza et al., 2013; Ogden et al., 2015; Saffer et al., 2013; Wang et al., 2014). Given that there are currently no effective pharmacological treatments to prevent, delay, or modify the course of cognitive decline and ADRD (Hebert et al., 2013), a focused study of lifestyle interventions that may delay the onset of cognitive decline or prevent the transition to ADRD in-at risk individuals, with a focus on obese African Americans, is needed (Lourida et al., 2013; Rolland et al., 2008; Valls-Pedret et al., 2015).

This paper describes the baseline characteristics of obese older African American adults enrolled in the Building Research in Diet and Cognition (BRIDGE) trial, a MedDiet and cognition RCT (Tussing-Humphreys et al., 2017). The BRIDGE study was approved by the University of Illinois at Chicago Institutional Review Board, and all participants provided written informed consent prior to enrollment.

2. Materials and methods

2.1. Design

The BRIDGE trial is an RCT testing whether participants randomized to MedDiet-WL will achieve greater improvements in cognition, CVD and metabolic risk factors, body weight, and body composition, compared to participants randomized to MedDiet-A (weight stable) and a TDC group without caloric restriction or weight loss. The trial design, including methodology, is described in detail elsewhere (Tussing-Humphreys et al., 2017).

Setting. Both active interventions were conducted in local community sites that routinely deliver programming to older adults.

Participants. The study was conducted in 3 cohorts of about 60 participants each. Participants were randomly assigned to MedDiet-WL (n = 75), MedDiet-A (n = 73), or TDC (n = 37). Eligible participants were 55–85 years old, with BMI 30.0–50.0 kg/m^2, Montreal Cognitive Assessment (MoCA) score $\geq$ 19, MedDiet adherence screener score $\leq$ 6, able to participate in intervention classes at the scheduled time and location, planning to reside in the Chicago area for the duration of the study, able to understand English, and willing to participate in data collection and be randomized. Exclusion criteria have been discussed in detail elsewhere (Tussing-Humphreys et al., 2017); they include inability to exercise, significant health conditions, hemoglobin A1c (HbA1c) > 9%, Coumadin use, neurological or psychiatric conditions, bariatric surgery, enrollment in a formal weight loss program, or other memory/concentration research in the past 12 months.

Recruitment. We used passive recruitment strategies that included advertising in local neighborhoods and older adult specific listservs and publications. We placed brochures in senior facilities and senior exercise classes sponsored by local community sites. Participants in a previous study who had agreed to be contacted in the future were also contacted with information about the current study.

Interventions. The MedDiet-WL (90 min) and MedDiet-A (60 min) interventions included 25 sessions and a final party. The group sessions occurred weekly, with dates skipped for holidays. For sessions 1–19, both groups received content on lifestyle changes to accommodate a MedDiet eating pattern. For the MedDiet-WL, there was additional content that focused on weight loss through caloric restriction and meeting physical activity guidelines consistent with current public health recommendations (CDC, 2018; USDA, 2015). For sessions 20–25, both intervention arms received instruction focused on maintaining lifestyle changes consistent with the MedDiet eating patterns, and the MedDiet-WL arm received content on weight loss maintenance.

For the MedDiet-WL group, at each group session, 30 min of supervised physical activity was offered, led by a physical activity instructor. Activities included stretching, flexibility, and moderate cardio exercises.

2.2. Measures

2.2.1. Socio-demographics

Participants were asked to report socio-demographic characteristics

such as age, educational attainment, health insurance status, and self-reported medical conditions, among others.

2.2.2. Anthropometrics

Participant body weight was measured in duplicate using a digital scale (Tanita, Arlington Heights, IL). Participant height was measured in duplicate using a stadiometer. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Body composition including fat mass, fat free mass and regional body fat distribution was assessed using the General Electric Lunar iDXA machine (GE Healthcare, US).

2.2.3. Cognition

The cognitive domains outlined below reflect previously published work by our group generally (Boots et al., 2019; Gonzales et al., 2017; Lamar et al., 2015) and as it relates to MedDiet adherence more specifically (Karstens et al., 2019).

Attention/Information Processing domain (AIP). AIP was assessed via raw scores from the Digit Span Forward subtest and the Digit Symbol subtest of the Wechsler Adult Intelligence Scale – IV (WAIS-IV; (Wechsler, 2008), time to completion on Part A of the Trail Making Test (TMT) (Reitan and Wolfson, 1985), and raw scores from the Stroop word and color subtests (Stroop, 1935).

The Executive Function domain (EF). EF was assessed using the raw scores from the Digit Span Backward and Sequencing subtests of the WAIS-IV, TMT Part B time to completion, total correct words produced on letter fluency (Lezak et al., 2004; Stroop, 1935), and the Stroop Color-Word Interference score.

Learning/Memory/Recognition domain (LMR). LMR was assessed using three measures from the California Verbal Learning Test – II (CVLT-II): total recall across the 5 learning trials, total delay free recall, and recognition discriminability scores (Delis et al., 2000).

Other Cognitive Measures. To screen for cognitive impairment during initial eligibility determinations, the MoCA screener (Nasreddine et al., 2005) was used as recommended by the National Institute of Neurological Diseases and Stroke and Canadian Stroke Network's Neuropsychology working group (Hachinski et al., 2006). The MoCA screener assesses different cognitive domains including attention and concentration, executive functions, memory, language, visual construction skills, conceptual thinking, calculations, and orientation.

We calculated predicted verbal IQ from the raw word reading score from the Wechsler Test of Adult Reading (Wechsler, 2001); these metrics are considered more accurate means of assessing and adjusting for educational quality than years of education in racially/ethnically diverse samples of older adults (Manly et al., 2002). To monitor test-taking effort across the intervention, the CVLT-II forced choice recognition trial was administered, with > 14 correct considered adequate effort (Schwartz et al., 2016).

Cognitive Composite Scores. A composite score was created for each of the three domains outlined above (AIP, EF, and LMR) by converting the relevant raw scores to z-scores, then taking the mean of the z-scores. The z-scores for the TMT Parts A and B were multiplied by -1 so that a higher z-score indicated better performance to be consistent with all other individual z-scores.

2.2.4. Dietary intake

Habitual dietary intake was estimated using the Harvard Food Frequency Questionnaire (HFFQ) (Willett et al., 1985). The HFFQ is a semi-quantitative questionnaire querying consumption of 131 foods and beverages during the previous 12 months. Completed HFFQ surveys were processed by the Channing Lab at Harvard University.

Adherence to a MedDiet-like pattern. Data from the HFFQ were used to calculate a MedDiet adherence score. The MedDiet score, first developed by Panagiotakos et al. (Panagiotakos et al., 2007) and later modified for a Chicago-based population by Tangney and colleagues (Tangney et al., 2011), was adapted further for applicability to the HFFQ variables and data. Briefly, food and beverage items from the HFFQ were used to create adherence scores (0–5) for 11 components: non-refined grains (summary variable included in the HFFQ output file), potatoes (1 item), fruit (19 items), vegetables (24 items), legumes and nuts (8 items), fish (4 items), red meat and processed meat (12 items), poultry (3 items), full-fat dairy products (8 items), olive oil (3 items), alcohol (milliliters per week based on 5 items). The score ranges from 0 to 55 points, with 5 points maximum for each component awarded for full compliance and scores scaled proportionately based on intake (Table 2). For example, for non-refined grains, those consuming 33 or more servings weekly received 5 points, 19–32 servings 4 points, 13–18 servings 3 points, 7–12 servings 2 points, 1–6 servings 1 point and consuming 0 servings 0 points. *MedDiet Adherence Screener.* To assess eligibility, participants completed a 13-item screener (Martinez-Gonzalez et al., 2012) adapted for a U.S. population. One item was removed (sofrito) given that it is not a commonly known or consumed condiment/food in the US among our target population of African Americans. Scores can range from 0 to 13, and only those with scores ≤ 6 were eligible to participate.

2.2.5. Physical activity

To objectively measure physical activity, the ActiGraph wGT3x triaxial wrist accelerometer was used (Santos-Lozano et al., 2012), as compliance with accelerometers is higher when worn on the wrist (Freedson and John, 2013; Troiano et al., 2014). Participants were asked to wear the accelerometer on their non-dominant wrist for 7 days. Data were included if the participant wore the accelerometer for ≥ 4 days and ≥ 10 h/day. Data were processed via two methods. With the first method, ActiLife v6.13.4 software (ActiGraph, Pensacola, FL) was used to extract data, validate wear time, and compute physical activity levels with data converted to 60-s epochs. Average counts per minute (CPM) are reported. Additionally, moderate-to-vigorous physical activity (MVPA) was quantified using a cut-point of ≥ 7500 counts per minute (Kamada et al., 2016), which was derived by examining the physical activity of older women assessed by hip- and wrist-worn accelerometers.

In the second method, accelerometer data were downloaded using ActiLife, saved in raw format as GT3X files, and converted to CSV format. Raw data files were processed in R (http://cran.r-project.org) using the GGIR package (Migueles et al., 2019; Sabia et al., 2014; van Hees et al., 2013). GGIR consists of two major processing components. In Part 1, raw triaxial acceleration values are converted into one omnidirectional measures of body acceleration by taking the vector magnitude from the three axes and subtracting by the value of gravity, after which negative values are rounded to zero. The resulting metric is referred to as the Euclidean norm minus one (ENMO) (van Hees et al., 2013). Data are further reduced by calculating the average values per 1-s epoch. In Part 2 of the data processing component, daily-level summary files are produced based on the acceleration summary data generated from Part 1. The daily summaries are generated using the intensity-specific milli-g cut-points from Hildebrand et al. regression equations (Hildebrand et al., 2014), which estimates minutes of MVPA.

Self-Reported Physical Activity. The Godin-Shepard Leisure Time Physical Activity Questionnaire was used to measure self-reported leisure time physical activity (Godin, 2011). A total score and an MVPA score were calculated using the standard scoring instructions, and participants were categorized as insufficiently active, moderately active, or active.

Mobility. Mobility and functional exercise capacity were measured using the six-minute walk test, in which participants were asked to walk as far as possible in 6 min (Guyatt et al., 1985; Naylor et al., 2014). An 18-meter walking course was marked with cones in a level, tiled hallway, and total distance walked was recorded. Participants were instructed to walk as quickly as possible for 6 min. Assistive devices could be used.

2.2.6. Clinical measures

Blood Lipids. Fasting total cholesterol, low density lipoprotein cholesterol (calculated), high density lipoprotein cholesterol and

triglycerides were measured by spectrophotometry at Quest Diagnostics (Wood Dale, IL).

Blood Pressure. Systolic and diastolic blood pressure and pulse rate were assessed in duplicate using the Omron HEM-907 (Lake Forest, IL) electronic blood pressure monitor with the participants seated (Pickering et al., 2005).

Markers of Metabolic Risk. Fasting insulin and glucose were assessed from serum via immunoassay (insulin) or spectrophotometry (glucose) at Quest Diagnostics (Wood Dale, IL). HbA1c was measured in whole blood via enzymatic assay by the same commercial lab.

Systemic Inflammation. Serum levels of high sensitivity C-reactive protein (hs-CRP) from fasting venipunctures were assessed via an immunoturbidimetric assay by Quest Diagnostics (Wood Dale, IL). The upper and lower limit of detection for this assay are 0.3–10.0 mg/L. Values coded as > 10 mg/L were excluded from analyses. Values below the lower limit of detection (usually 0.3, 0.2 for some early assays) were imputed as the limit of detection divided by the square root of 2 (Ong et al., 2013).

2.2.7. Psychosocial measures

Quality of life. Perceived quality of life was assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) Global Health Scale version 1.2 (Reeve et al., 2007). Global scores for physical health and mental health were calculated and converted to T-scores. A score of 50 represents the mean for the U.S. general population; the SD for the U.S. is 10.

Mood. Depressive symptomatology was measured using the Center for Epidemiologic Studies of Depression Scale (CES-D) (Radloff, 1977), a

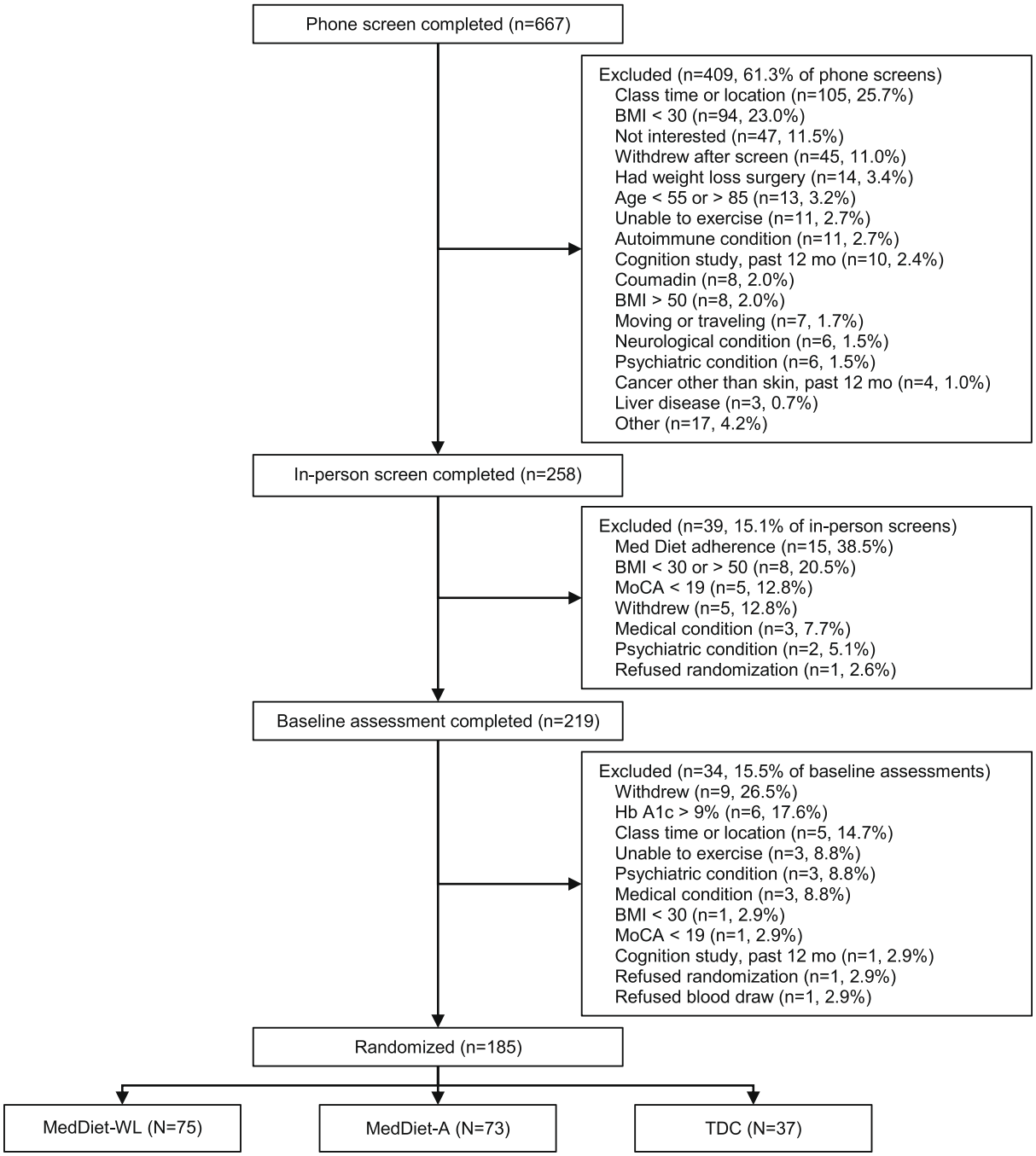

Fig. 1. CONSORT Diagram (data collected January 2017 and July 2019 in Chicago, IL).

20-item scale with scores ranging from 0 to 60.

Social Support. This was evaluated by the Modified Medical Outcomes Study Social Support Survey (mMOS-SS) (Moser et al., 2012). The mMOS-SS includes 8 items covering two domains, emotional and instrumental (tangible) social support. Scores can range from 0 to 100.

2.2.8. Randomization

A stratified block randomization sequence with a 2:2:1 allocation to MedDiet-WL, MedDiet-A, and TDC, respectively, was created in SAS and imported into the Research Electronic Data Capture (REDCap) randomization module. Randomization was stratified by program cohort (1–3), age (55–69 and 70–85 years), and MoCA score (19–25 and 26–30). The data manager, who had no contact with participants, was responsible for randomization.

2.2.9. Statistical analyses

We calculated Cronbach's coefficient alpha for each of the cognitive composites to estimate internal consistency. We used Pearson correlations to explore the relationship between social support and global mental health or depressive symptoms. We used t-tests with pooled variance to test for associations between the cognitive composite scores (AIP, EF, and LMR, separately) and participant characteristics: age (55–69 or ≥ 70 years), BMI (<40 or ≥ 40 kg/m2) and gender (female, male). We also tested for associations between MedDiet score and age, BMI, and gender using linear regression models adjusted for energy. We used Pearson partial correlations to test for associations between the cognitive composites and MedDiet score, adjusted for energy. Finally, we tested for independent predictors of cognition using three multivariable linear regression models with cognitive composite score (AIP, EF, or LMR) as the continuous dependent variable and age, BMI, gender, MedDiet score, energy and WTAR raw score as independent predictor variables in the same model.

3. Results

The study exceeded its target recruitment of 180 participants, as shown in Fig. 1. We randomized 185 participants: 75 to MedDiet-WL, 73 to MedDiet-A, and 37 to TDC. Table 1 reports the baseline demographic characteristics of study participants. Most of the participants were < 70 years of age and primarily identified as non-Hispanic Black or African American (91.4%). Most of the sample was female (85.9%), and 30.4% reported a graduate or professional degree. Reported income was < $20,000 for 22.2% of the sample, between $20,000 and $39,999 for 23.3%, and ≥ $40,000 for 54.4%.

Table 1 also shows self-reported past or current medical conditions: 67.0% reported high blood pressure, 38.9% reported high cholesterol, 16.2% reported type 2 diabetes, and 24.9% reported sleep apnea. Mean BMI was 37.1 kg/m^2, with 35.7% of the sample in obesity class I (30 to < 35 kg/m^2), 41.6% in obesity class II (35 to < 40 kg/m^2), and 22.7% in obesity class III (≥40 kg/m^2). The mean percent body fat for the sample was 47.7% (SD = 6.0%), and the mean estimated visceral mass was 1,621 g (SD = 774 g).

Table 2 shows MedDiet adherence at baseline, including the number of servings needed to score a full 5 points for a given component of the MedDiet adherence score (column 2), mean servings per week of each component (column 3) and corresponding mean score (column 4) estimated from HFFQ responses. The unadjusted mean total MedDiet score was 32.8 (SD = 5.5). Participants were most adherent with the full-fat dairy (4.6), poultry (3.9) and legumes and nuts (3.8) components and least adherent to the potatoes (0.9), olive oil (1.8) and fish (2.2) components.

Table 3 shows baseline cognitive characteristics of our sample, including composite domain scores and individual raw scores for each domain. It should be noted that standardized Cronbach's alpha coefficients for our cognitive domains were deemed adequate: 0.68 for AIP, 0.65 for EF, and 0.85 for LMR. The mean MoCA score of 25.1 (SD = 2.5) fell between reported means for normal aging (~27) and mild cognitive impairment (~22) found in the literature and was well within limits set by our study eligibility threshold, i.e., ≥ 19. Additionally, the mean predicted verbal IQ (pVIQ) score from the WTAR, 94.5 (8.5), fell within the average range. Lastly, based on the CVLT-II Forced Choice Recognition Trial, over 98% of participants met the threshold for test taking effort during their baseline visit. Within this context, mean scores across AIP, EF, and LMR were commensurate with MoCA and pVIQ scores. For example, participants recalled, on average, 9.5 digits forward and 7.4 digits backward on the Digit Span Test (see Table 3). Additionally, Digit Sequencing raw scores were also, on average, 7.4 items recalled correctly. Participants, on average, produced 37 words during Letter Fluency and recalled approximately 9 words during the CVLT-II Delay Free Recall, with Recognition Discriminability Scores averaging

Table 1
Participant characteristics at baseline.

	N	Mean or %	SD or N	Median	IQR
Age at randomization, yr	185	66.3	(6.1)	66.0	(8.2)
55–69		75.7%	(140)		
≥ 70		24.3%	(45)		
Gender	185				
Female		85.9%	(159)		
Male		14.1%	(26)		
Race	185				
Black or African-American, not Hispanic		91.4%	(169)		
Hispanic		1.1%	(2)		
White, not Hispanic		1.1%	(2)		
Native American		0.5%	(1)		
Multiracial		5.9%	(11)		
Education, yr	184	15.1	(2.4)	16.0	(5.0)
Not HS graduate		2.2%	(4)		
HS graduate		37.5%	(69)		
Associate's degree		9.8%	(18)		
College graduate		20.1%	(37)		
Graduate or professional degree		30.4%	(56)		
Employed full or part-time	185	28.1%	(52)		
Marital status	185				
Single		25.4%	(47)		
Married		27.6%	(51)		
Widowed		15.7%	(29)		
Divorced		31.4%	(58)		
Income (median)	180			50,000	(40,000)
<$20,000		22.2%	(40)		
$20,000-$40,000		23.3%	(42)		
≥$40,000		54.4%	(98)		
Has health insurance[a]	185	98.9%	(183)		
Medical conditions[b]					
High blood pressure	185	67.0%	(124)		
High cholesterol	185	38.9%	(72)		
Type 2 diabetes	185	16.2%	(30)		
Sleep apnea	185	24.9%	(46)		
Total prescription medications	184	2.5	(2.1)	2.0	(3.0)
MedDiet screener score (0–6)[c]	185	4.2	(1.4)	4.0	(2.0)
Weight, kg	185	100.5	(14.5)	98.8	(19.9)
Height, cm	185	164.6	(7.4)	164.2	(9.0)
BMI, kg/m^2	185	37.1	(4.8)	36.0	(5.9)
BMI category	185				
Obesity class I (30-<35 kg/m^2)		35.7%	(66)		
Obesity class II (35-<40 kg/m^2)		41.6%	(77)		
Obesity class III (≥40 kg/m^2)		22.7%	(42)		
Percent body fat	184	47.7	(6.0)	48.4	(7.7)
VAT mass, g	174	1621	(774)	1492	(736)

[a] Medicare, Medicaid, or private insurance.
[b] Self-reported, current or past conditions.
[c] Screener scores can range from 0 to 13, with higher scores indicating greater adherence. Only those with scores < 7 were eligible for the study.

Table 2
Mediterranean Diet Adherence from MedDiet Score, N = 185.

	Servings/wk for max score of 5	Self-reported Servings/wk from FFQ		MedDiet score[a]			
		Mean	SD	Mean	SD	Median	IQR
MedDiet score components (0–5)							
Non-refined grains	≥ 33	15.9	(9.8)	2.8	(1.2)	3.0	(2.0)
Potatoes	≥ 14	0.9	(1.2)	0.9	(0.7)	1.0	(1.0)
Fruit	≥ 23	17.0	(11.6)	3.4	(1.2)	3.0	(3.0)
Vegetables	≥ 34	21.0	(14.5)	3.1	(1.2)	3.0	(2.0)
Legumes and nuts	≥ 7	7.5	(6.9)	3.8	(1.2)	4.0	(2.0)
Fish	≥ 7	2.3	(2.3)	2.2	(1.2)	2.0	(2.0)
Red meat and processed meat	≤ 1	5.1	(5.4)	3.0	(1.7)	3.0	(2.0)
Poultry	≤ 3	4.3	(4.0)	3.9	(1.4)	4.0	(2.0)
Full-fat dairy products	≤ 10	7.1	(6.5)	4.6	(0.8)	5.0	(1.0)
Olive oil	≥ 7	1.8	(3.2)	1.8	(1.6)	2.0	(3.0)
Alcohol (mL)[b]	1–299	28.1	(64.9)	3.3	(2.4)	5.0	(5.0)
MedDiet score (0–55)	–	–	–	32.8	(5.5)	33.0	(7.0)

[a] A higher score indicates greater adherence to the Mediterranean diet.
[b] A score of 0 was assigned for either 0 or ≥ 700 mL/wk of alcohol.

Table 3
Cognitive Composite Scores and Raw Scores for the Underlying Variables.

Composites[a] and Raw Scores[b]	N	Mean or %	SD or N	Min	Max	Median	IQR
Attention/Information Processing (AIP) Composite	184	0.0	(0.7)	−1.8	2.2	0.0	(0.9)
Digit Span Forward	185	9.5	(2.0)	5	15	9.0	(2.0)
Digit Symbol	185	56.3	(11.5)	26	87	56.0	(18.0)
Trail Making Test Part A[c]	184	35.1	(12.1)	16	107	34.0	(14.0)
Stroop Word Score	185	86.1	(14.0)	52	131	87.0	(19.0)
Stroop Color Score	185	63.1	(9.7)	28	95	63.0	(13.0)
Executive Function (EF) Composite	179	0.0	(0.6)	−1.5	1.7	0.1	(0.9)
Digit Span Backward	185	7.4	(2.1)	2	15	7.0	(3.0)
Digit Span Sequencing	185	7.4	(2.1)	1	12	8.0	(3.0)
Trail Making Test Part B[c]	179	105.8	(51.1)	40	300	88.0	(53.0)
Letter Fluency	185	36.9	(10.0)	14	69	36.0	(12.0)
Stroop Color-Word Interference Score	185	31.8	(7.9)	10	51	33.0	(11.0)
Learning/Memory/Recognition (LMR) Composite	185	0.0	(0.9)	−3.0	1.8	0.0	(1.2)
CVLT-II Trials 1 thru 5 Total Learning	185	45.2	(9.3)	5	67	46.0	(12.0)
CVLT-II Delay Free Recall	185	9.2	(3.2)	0	16	9.0	(4.0)
CVLT-II Recognition Discriminability	185	88.7	(9.1)	54.2	100	89.6	(10.4)
Other Variables							
MoCA	185	25.1	(2.5)	19	30	25.0	(4.0)
Predicted verbal IQ from WTAR	182	94.5	(8.5)	76	126	94.0	(13.0)
CVLT-II Forced Choice Recognition Trial ≥ 14, % (N)	185	98.4%	(182)	–	–	–	–

[a] Composite scores are created by standardizing the variables that make up the composite and taking the mean of the resulting z-scores. Z-scores for trail-making are multiplied by −1 so that a higher score always indicates better performance. If any of the underlying variables are missing, the composite is not calculated.
[b] Except where otherwise noted, a higher score indicates better performance.
[c] Higher trail-making raw scores indicate lower performance.

nearly 90% (see Table 3 for details).

Table 4 shows clinical and circulating cardiometabolic and inflammatory biomarkers. Mean systolic blood pressure was slightly above American Heart Association cut-points for normal at 133.6 mmHg (SD = 17.7), as was diastolic blood pressure, 79.8 (11.5) mmHg. Pulse per minute showed a mean of 73.1 (10.2). As per American Diabetes Association categorizations, mean HbA1c was within the prediabetes range at 6.1 (0.9)%, as was mean fasting glucose at 102.6 (24.1) mg/dL; average fasting insulin was 11.6 (8.7) ulU/mL. Mean total cholesterol was188.9 (36.9) mg/dL, HDL was 59.2 (15.3) mg/dL, and LDL was 109.8 (32.6) mg/dL. Mean hs-CRP was 3.9 (2.5) mg/L.

Table 4
Clinical Measures: Blood Pressure, Glucose Metabolism, Cholesterol, and Inflammation.

	N	Mean	SD	Median	IQR
Systolic BP, mmHg	185	133.6	(17.7)	133.0	(21.0)
Diastolic BP, mmHg	185	79.8	(11.5)	80.0	(15.0)
Pulse, per minute	185	73.1	(10.2)	73.0	(13.0)
HbA1c, %	185	6.1	(0.9)	5.8	(0.7)
Glucose, mg/dL	185	102.6	(24.1)	96.0	(16.0)
Insulin, uIU/mL	185	11.6	(8.7)	9.2	(6.7)
Total chol, mg/dL	185	188.9	(36.9)	187.0	(46.0)
HDL, mg/dL	185	59.2	(15.3)	58.0	(17.0)
LDL, mg/dL	185	109.8	(32.6)	108.0	(43.0)
Non-HDL chol, mg/dL	185	129.7	(35.9)	129.0	(47.0)
Cholesterol/HDLC	185	3.4	(1.0)	3.3	(1.2)
Triglycerides, mg/dL	185	99.4	(42.0)	91.0	(53.0)
hs-CRP[a] mg/L	156	3.9	(2.5)	3.6	(4.1)

[a] hs-CRP values > 10 mg/L excluded.

Table 5
Physical Activity, Measured by Accelerometer, N = 183.[a]

	Mean	SD	Median	IQR
Counts per minute[b]	1528	(504)	1454	(639.2)
MVPA/day, fixed cutpoints[b]	9.4	(8.3)	7.0	(10.0)
MVPA/day, intensity-specific cutpoints[c]	8.9	(10.9)	5.5	(9.6)

[a] Two participants are excluded: one did not have a valid record (worn ≥ 10 hr on ≥ 4 days); one record was lost due to accelerometer malfunction.
[b] Calculated using the ActiLife program; MVPA was defined as ≥ 7500 counts per minute (Kamada et al., 2016).
[c] Calculated in R using the GGIR package; MVPA was calculated using intensity-specific cutpoints (Hildebrand et al., 2014).

Table 5 shows baseline accelerometer-assessed physical activity. Wear time ranged from 10.0 to 24.0 h per day with a mean wear time of 21.1 (SD = 4.5) hours per day. With the ActiLife data processing method, mean number of minutes of MVPA per day was 9.4 (8.3), and the mean counts per minute was 1528 (504). With the GGIR data processing method, the mean number of minutes of MVPA was 8.9 (10.9). On the Godin Leisure Time Exercise Scale, the mean overall score was 21.9 (20.0) (Table 6). Among our sample, 54.6% were categorized as insufficiently active (<14), 22.2% were moderately active (14–23), and 23.2% (≥24) were considered active, based on their self-reported activity. Mean 6-minute walk distance was 352.9 (76.0) m.

On the PROMIS measure (Table 6), the mean for physical health was 49.8 (SD = 7.5) and for mental health, 52.7 (7.8). The mean score on the CES-D, measuring depressive symptoms, was 7.3 (6.1). The mean score for social support (mMOS-SS) was 74.8 (22.4), and social support was associated with both better reported overall mental health ($r = 0.41$, $p < 0.001$) and fewer depressive symptoms ($r = -0.28$, $p < 0.001$).

Table 7 explores associations between age, BMI, and gender and both the cognitive composite scores and the energy-adjusted MedDiet adherence score. Attention/Information Processing performance was lower for older (≥70 y) compared to younger (55–69 y) participants (mean = -0.3 vs 0.1, $p = 0.002$) and higher in participants with higher (≥40 kg/m^2) BMI (0.2 vs −0.1, $p = 0.006$). Compared to women, men showed lower AIP scores (0.1 vs −0.4, $p = 0.001$). Higher Executive Functioning was associated with higher BMI (0.3 vs −0.1, $p < 0.001$). Compared to women, men showed lower Learning/Memory/Recognition Processing performance (0.1 vs −0.4, $p = 0.02$). The energy-adjusted MedDiet adherence score did not differ significantly by age, BMI, or gender (Table 7). Additional Pearson partial correlation analyses between MedDiet adherence score and individual cognitive domains, adjusted for energy, had the following results: $r = 0.19$ ($p = 0.01$) for Attention/Information Processing $r = 0.21$ ($p = 0.006$) for Executive Functioning, and $r = 0.13$ ($p = 0.08$) for Learning/Memory/Recognition Processing, indicating that higher MedDiet scores were associated with higher cognitive performance.

When considering age, BMI, gender, and MedDiet score together as predictors of individual cognitive composite scores in three multivariable linear regression models (Table 8), results were somewhat different from the unadjusted results reported above and shown in Table 7. After adjusting for energy and the WTAR raw score, age ($b = -0.04$, $p < 0.001$) and gender ($b = -0.41$, $p = 0.002$) were still significantly associated with AIP, but BMI and MedDiet were not. For EF, age was a significant independent predictor of performance ($b = -0.02$, $p = 0.002$), and MedDiet score was also a significant predictor ($b = 0.02$, $p = 0.047$). For LMR, gender continued to significantly associate with performance ($b = -0.42$, $p = 0.02$), and there was a suggestion that age was also a predictor ($b = -0.02$, $p = 0.050$).

Table 6
Self-Reported Physical Activity, Mobility, and Psychosocial Measures N = 185.[a]

	Mean or %	SD or N	Median	IQR
Godin Leisure-Time Exercise[b]				
Godin score	21.9	(20.0)	18.0	(26.0)
Godin moderate/strenuous score	13.7	(17.4)	10.0	(20.0)
Godin categories, % (n)				
Active (≥24)	23.2%	(43)		
Moderately active (14–23)	22.2%	(41)		
Insufficiently active (<14)	54.6%	(101)		
6-minute walk distance, m	352.9	(76.0)	356.8	(92.7)
PROMIS Global Health[c]				
Global physical health	49.8	(7.5)	50.8	(9.2)
Global mental health	52.7	(7.8)	53.3	(10.2)
Depressive symptoms (CES-D, 0–60)[d]	7.3	(6.1)	6.0	(7.0)
Social support (mMOS-SS, 0–100)[e]	74.8	(22.4)	81.3	(31.3)

[a] N = 184 for global mental health.
[b] Higher scores indicate more physical activity.
[c] Higher scores indicate better health. US mean = 50, SD = 10.
[d] Higher scores indicate worse depressive symptoms.
[e] Higher scores indicate more social support.

4. Discussion

Epidemiologic data show that approximately one third of US older adults are obese, with the highest rates of obesity among African American older adults, aged 65–74 years (Fakhouri et al., 2012). African Americans are also at increased risk for adverse subclinical brain changes and associated cognitive impairment and ADRD (Gottesman et al., 2015; Ho et al., 2010). Weight loss, through caloric restriction, that can positively influence vascular (e.g., hypertension) and metabolic (e.g., insulin resistance, inflammation, dyslipidemia) risk factors in obese individuals, may provide secondary benefits for cognitive functioning (Passini and Wolfe, 2001). Different dietary strategies have also been found to affect cognitive functioning depending on the energy content and macronutrient composition. (D-Anci et al., 2020; Gillette-Guyonnet et al., 2003) Current research does not provide complete conclusions on the effect of dietary patterns on ADRD (Vinciguerra et al., 2020). However, of the available evidence, the MedDiet, a particularly antioxidant-rich dietary pattern, has been shown to confer cognitive benefits and a reduced risk of dementia (Valls-Pedret et al., 2015). More specifically, in observational studies, close adherence to a MedDiet pattern is associated with reduced cognitive decline and decreased risk of ADRD (Anastasiou et al., 2017; Dinu et al., 2018; Loughrey et al., 2017; Pelletier et al., 2015; Samieri et al., 2013; Tangney et al., 2014). However, we know of no RCTs that have tested whether the combined effects of a caloric restricted MedDiet designed to achieve modest weight loss (MedDiet-WL) will achieve greater improvements in cognition compared to an isocaloric MedDiet (MedDiet-A) designed to be weight stable and a typical diet control (TDC). Additionally, whether MedDiet-WL will achieve greater improvements in cognition compared to MedDiet-A will be assessed.

To our knowledge, the baseline results for our sample of obese, predominantly African American older adults are the first to document that closer self-reported adherence to a MedDiet like pattern is associated not only with higher AIP, but also with higher EF. There are several differences between our study and previous reports. Specifically, in studies outlined in the Van Den Brink 2019 review (Van Den Brink et al., 2019) only one found higher MedDiet adherence was associated with higher EF (i.e., (Anastasiou et al., 2017)). This may be due, in part, to across study variations in ethnicity, age, baseline overall physical and mental health status, as well as variations in the approaches to assessing adherence to a MedDiet like pattern. Notably, in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a longitudinal cohort of >2000 individuals recruited as young adults, 45% black and 57% female, a higher adherence to a MedDiet was associated with statistically superior cognitive performance, including EF, at 30-year follow-up (Mcevoy et al., 2019). Other studies have reported that higher MedDiet adherence is significantly associated with higher LMR (e.g., (Karstens et al., 2019)); while our results did not reach significance, they did suggest a similar association was present in our sample regardless of adjustments.

Additional results of our baseline evaluation revealed similarities to other cohort studies of dietary patterns, which supports generalizability of the results of our intervention when completed. For example, the Chicago Health and Aging Project (CHAP) (Tangney et al., 2011), a longitudinal cohort study of Midwest, urban, older adults (≥65 years), included 2280 African Americans and 1510 non-Hispanic whites, and the sample had a mean BMI of 27.1 kg/m^2 (SD = 5.5), and mean MedDiet adherence scores of 27.6 (CI 95%: 27.4, 27.7) and 29.2 (CI 95%: 29.0, 29.4), for African American and non-Hispanic whites, respectively. In our sample of Midwest urban obese predominantly African American older adults, adherence to a MedDiet like pattern, evaluated using a similar dietary survey and dietary index score as CHAP, had a slightly

Table 7
Cognitive Composite Scores[a] and Energy-Adjusted MedDiet Score[b] by Age, BMI, and Gender.

	Age, y					BMI, kg/m^2					Gender				
	55–69 (N = 140)		≥ 70 (N = 45)			<40 (N = 143)		≥40 (N = 42)			Female (N = 159)		Male (N = 26)		
	Mean	SE	Mean	SE	p[c]	Mean	SE	Mean	SE	p[c]	Mean	SE	Mean	SE	p[c]
AIP	0.1	(0.1)	−0.3	(0.1)	0.002	−0.1	(0.1)	0.2	(0.1)	0.006	0.1	(0.0)	−0.4	(0.1)	0.001
EF	0.1	(0.1)	−0.1	(0.1)	0.06	−0.1	(0.1)	0.3	(0.1)	<0.001	0.0	(0.1)	−0.1	(0.1)	0.34
LMR	0.1	(0.1)	−0.2	(0.1)	0.06	0.0	(0.1)	0.1	(0.1)	0.21	0.1	(0.1)	−0.4	(0.2)	0.02
MedDiet	32.6	(0.5)	33.3	(0.8)	0.48	32.7	(0.5)	33.2	(0.8)	0.61	32.9	(0.4)	31.9	(1.1)	0.35

[a] AIP: Attention/Information Processing; EF: Executive Function; LMR: Learning/Memory/Recognition. Higher scores indicate higher performance. Due to missing data, N = 184 for AIP and 179 for EF.
[b] Higher scores indicate greater adherence to Mediterranean diet. Means are least-squares means from linear regression models with energy as a covariate.
[c] From t-tests with pooled variance for cognitive composites and linear regression models adjusted for energy for MedDiet score.

Table 8
Age, BMI, Gender, and MedDiet Score as Predictors[a] of Cognitive Composite Scores, Adjusted for Energy and Word Reading Score.

	AIP[b] (N = 181)			EF[b] (N = 177)			LMR[b] (N = 182)		
	b	SE (b)	p	b	SE (b)	p	b	SE (b)	p
Intercept	0.84	(0.67)	0.21	−0.43	(0.68)	0.53	−0.07	(0.96)	0.94
Age, yr	−0.04	(0.01)	<0.001	−0.02	(0.01)	0.002	−0.02	(0.01)	0.050
BMI, kg/m^2	0.01	(0.01)	0.14	0.02	(0.01)	0.08	0.01	(0.01)	0.56
Male (ref = Female)	−0.41	(0.13)	0.002	−0.11	(0.13)	0.40	−0.42	(0.18)	0.02
MedDiet score[c]	0.02	(0.01)	0.06	0.02	(0.01)	0.047	0.01	(0.01)	0.21
Energy (kcal)	0.00	(0.00)	0.80	0.00	(0.00)	0.81	0.00	(0.00)	0.92
Word Reading Score[d]	0.02	(0.00)	<0.001	0.03	(0.00)	<0.001	0.02	(0.01)	<0.001

Note: Data collected between January 2017 and July 2019 in Chicago, IL.
[a] From multivariable linear regression models with cognitive component score (AIP, EF, or LMR) as the dependent variable and age, BMI, gender, MedDiet score, energy and WTAR raw score as independent variables.
[b] AIP: Attention/Information Processing; EF: Executive Function; LMR: Learning/Memory/Recognition. Higher scores indicate higher performance.
[c] Higher scores indicate greater adherence to the Mediterranean diet.
[d] WTAR raw score.

higher mean 32.8 (5.5). This may reflect our participants' interest in diet and chronic disease prevention given their desire to participate in a dietary lifestyle intervention trial.

Likewise, a review of our cognitive data and the associations with basic demographic characteristics suggests that our participants reflect the larger current literature on cognitive aging. For example, it is well documented that older adults perform more poorly on cognitive assessments than mid-to young-old adults (Park et al., 1999), particularly within the areas of attention and information processing (Rabbitt and Goward, 1994). Likewise, women traditionally outperform men across verbally mediated tasks (Aartsen et al., 2004; Barrett-connor and Kritz-silverstein, 1999; Kramer et al., 1988), especially ones related to learning and memory (Sundermann et al., 2017, 2016), and results related to our composite scores with and without adjustment are consistent. In our sample, in unadjusted analyses, a higher BMI was associated with improved cognitive functioning, which is not consistent with other literature reporting that individuals with elevated BMI have reduced executive function (Gunstad et al., 2007) and additional literature that links obesity to poor cognitive outcomes (Gustafson et al., 2004, 2003). However, when adjusting for age and gender, this relationship was no longer significant, suggesting the mediating effect of other participant attributes to this result. Counterintuitive associations between obesity and cognitive functioning are documented in the literature among older adult populations, with some studies reporting that obesity among older adults may provide cognitive benefits and decreased risk for cognitive decline (Hsu et al., 2015; Kuo et al., 2006). However, other studies do not support what is referred to as the "obesity paradox" (Nilsson and Nilsson, 2009; Strandberg et al., 2013; Tobias et al., 2014). The outcomes from our MedDiet-WL group will help to shed light on these initial conflicting results. Our study fills a gap for the need to help clarify the directionality of the relationship between BMI and cognitive performance, particularly as our study is assessing cognitive performance prior to, and following, intentional weight loss. It Is also important to highlight that our participants reflect a relatively healthy older adult population, with clinical measures such as blood pressure, heart rate, HbA1c, insulin, total cholesterol, and triglycerides all within normal ranges. Excluding potential participants with significant medical conditions provides us with the opportunity to more clearly assess the association between elevated BMI and AIP, EF, and LMR.

More than half of our sample were classified as insufficiently active based on self-reported leisure activity which is consistent with other studies conducted with diverse samples of overweight/obese older adults (Diaz et al., 2016; Emerson and Gay, 2017; Gothe, 2018; Zhu et al., 2017). Our accelerometer results do demonstrate that that our sample is sedentary, with an average of 9.4 min (SD = 8.3) of MVPA per day. Cross-sectional and some prospective studies in predominantly non-Hispanic white samples suggest that aerobic fitness can enhance cognitive function (Barnes et al., 2013; Kramer et al., 2006, 2003). The mechanisms by which physical activity affects cognitive function remain to be fully elucidated, but this study will allow us to assess the associations between objectively measured physical activity and specific domains of cognition. It was evident that the wrist-worn accelerometers are acceptable to this population, and adherence to wear-time protocol was high. At baseline, 99% of our participants had a valid record. This is in contrast to a prior study we conducted with obese African American women, where only 74% (70/94) of the participants had valid records (Fitzgibbon et al., 2008), which is similar to the 71% adherence reported by the National Health and Nutritional Examination Survey (NHANES) for hip-worn accelerometers (Troiano et al., 2008). This suggests that the wrist placement may be an ideal location for objective activity measurement in older African American adults (Diaz et al., 2018; Doherty et al., 2017; Wolpern et al., 2019). On the measure of mobility, the mean 6-minute walk distance was 352.9 m (SD = 76.0), which is similar to another study we conducted with overweight and obese older African Americans with osteoarthritis (356.3 m) (Fitzgibbon et al., 2018), but lower than another RCT (N = 401) of younger (mean age, 56.3 years)

obese individuals with arthritis that included approximately 44% African Americans (M = 493.0 m) (Hughes et al., 2020).

Regarding psychosocial variables, the results for our sample are consistent with other studies. On average, participants reported few depressive symptoms, with a mean CES-D score of 7.3. Scores ranged from 0 to 27, with 20 participants (10.8%) at or above the 16-point cut-off identifying those at high risk for depression (Radloff, 1977; Zich et al., 1990). There is a growing literature reporting that older African Americans have a lower prevalence of mood disorders than their younger counterparts and that African Americans populations, in general, have lower prevalence rates than non-Latino whites of mood disorders (Mezuk et al., 2013). We will administer this measure at each study visit to continue to investigate these profiles.

On measures of global health, our participants scored similarly to a sample of participants who were recruited via an internet survey company (www.op4g.com) that maintains a panel of respondents from the general population. In this sample of 2025 participants, 49% were male, and the mean age was 46 years (SD = 18). Scores were 48.3 (9.0) and 48.5 (10.0), for global physical health and global mental health, respectively (Schalet et al., 2015). Self-reported social support (mMOS-SS) for our participants was relatively high, with a score of 74.8 out of a possible 100. In a study of early stage breast cancer patients (N = 541) and matched controls (N = 542), mean age = 57.7 y, that included 23% African American women, the mean mMOS-SS score was slightly higher, 84.6 (SD = 17.9) (Thompson et al., 2013). In another study of African American women participating in a two-year RCT, the reported baseline social support score was 81.9 (SD = 19.8) (Thompson et al., 2017). Not surprisingly, in our sample, social support was associated with both better reported overall mental health and fewer self-reported depressive symptoms

5. Conclusions

Strengths of the present study include the RCT design, a sample of relatively healthy older obese African American adults, a well-validated dietary questionnaire, well-validated psychosocial measures, objectively measured physical activity, and the inclusion of a number of tests to measure cognitive functioning. The cognitive domain scores were drawn from previously published literature in aging and cognition (Boots et al., 2019; Gonzales et al., 2017; Lamar et al., 2015) as well as MedDiet adherence studies (Blumenthal et al., 2017; Karstens et al., 2019). While certain cognitive domains are not represented, e.g., visuospatial abilities, our represented cognitive domain scores were extracted from a larger neuropsychological protocol. Thus, we will be able to assess other cognitive abilities, albeit not at the composite level. The opportunity to assess other cognitive abilities including visuospatial skills may also counter the female advantage seen for several of our composite scores.

Our ability to generalize our baseline findings to other populations may be limited in several ways. Our sample was predominantly African American, so we cannot necessarily extend our findings to other racial/ethnic groups. Our participants also resided in a large urban city, so we cannot necessarily generalize our findings to rural settings. We also do not have information on the duration of obesity for our participants. We know of no studies that have examined the duration of obesity and cognitive performance in relatively healthy older adults, but it is possible that individuals with a longer history of obesity perform differently on tests of cognition (Wagner et al., 2020). We also do not have information about physical activity earlier in life. Some findings suggest that midlife physical activity may play a role in preserving cognitive health as people age (Najar et al., 2019). In addition, people with high MedDiet adherence at baseline (screener scores $\geq$ 7) were ineligible for the study, so the associations seen in our baseline analyses may not apply at higher levels of adherence. Lastly, our study did not account for genetic predisposition to ADRD, which has been shown to be associated with cognitive decline later in life (Deary et al., 2004).

Despite these potential limitations, to our knowledge ours is the first RCT to directly compare the independent effect of the MedDiet and combined effects of the MedDiet and weight loss on cognition in obese African American older adults. Our study will help to clarify the relationship between BMI and cognitive performance, particularly as it relates to cognitive assessment before and after intentional weight loss.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to acknowledge study participants for giving generously of their time and effort on this study. We would also like to thank John Healy, General Manager at Columbus Vegetable Oils, and Judy Scott-Mckay of the Almond Board of California, for their contribution of olive oil and almonds, respectively, to the study.

This work was supported by the National Heart Lung and Blood Institute of the National Institutes of Health [R01HL129153], the NCI Training Program: Cancer Education & Career Development Program [T32CA057699] and U54MD12523-03 Sub-project ID:7086.

References

Aartsen, M.J., Martin, M., Zimprich, D., 2004. Gender differences in level and change in cognitive functioning: Results from the longitudinal aging study Amsterdam. Gerontology 50, 35–38. https://doi.org/10.1159/000074387.

Abenavoli, L., Boccuto, L., Federico, A., Dallio, M., Loguercio, C., Di Renzo, L., De Lorenzo, A., 2019. Diet and non-alcoholic fatty liver disease: The mediterraneanway. Int. J. Environ. Res. Public Health 16. https://doi.org/10.3390/ijerph16173011.

Anastasiou, C.A., Yannakoulia, M., Kosmidis, M.H., Dardiotis, E., Hadjigeorgiou, G.M., Sakka, P., Arampatzi, X., Bougea, A., Labropoulos, I., Scarmeas, N., 2017. Mediterranean diet and cognitive health: Initial results from the Hellenic Longitudinal Investigation of Ageing and Diet. PLoS ONE 12. https://doi.org/10.1371/journal.pone.0182048.

Aridi, Y., Walker, J., Wright, O., 2017. The Association between the Mediterranean Dietary Pattern and Cognitive Health: A Systematic Review. Nutrients 9, 674. https://doi.org/10.3390/nu9070674.

Association, A., 2020. 2020 Alzheimer's Disease Facts and Figures Special Report On the Front Lines: Primary Care Physicians and Alzheimer's Care in America..

Association, A., 2016. 2016 Alzheimer's disease facts and figures. Alzheimer's Dement. 12, 459–509. https://doi.org/10.1016/j.jalz.2016.03.001.

Barnes, D.E., Santos-Modesitt, W., Poelke, G., Kramer, A.F., Castro, C., Middleton, L.E., Yaffe, K., 2013. The mental activity and eXercise (MAX) trial: A randomized controlled trial to enhance cognitive function in older adults. JAMA Intern Med 173 (9), 797. https://doi.org/10.1001/jamainternmed.2013.189.

Barrett-connor, E., Kritz-silverstein, D., 1999. Gender differences in cognitive function with age: the rancho bernardo study. J. Am. Geriatr. Soc. 47, 159–164.

Blumenthal, J.A., Smith, P.J., Mabe, S., Hinderliter, A., Welsh-Bohmer, K., Browndyke, J. N., Lin, P.-H., Kraus, W., Doraiswamy, P.M., Burke, J., Sherwood, A., 2017. Lifestyle and neurocognition in older adults with cardiovascular risk factors and cognitive impairment. Psychosom. Med. 79 (6), 719–727. https://doi.org/10.1097/PSY.0000000000000474.

Boots, E.A., Zhan, L., Dion, C., Karstens, A.J., Peven, J.C., Ajilore, O., Lamar, M., 2019. Cardiovascular disease risk factors, tract-based structural connectomics, and cognition in older adults. NeuroImage 196, 152–160. https://doi.org/10.1016/j.neuroimage.2019.04.024.

Chen, C., Zissimopoulos, J.M., 2018. Racial and ethnic differences in trends in dementia prevalence and risk factors in the United States. Alzheimer's Dement. Transl. Res. Clin. Interv. 4 (1), 510–520. https://doi.org/10.1016/j.trci.2018.08.009.

Chen, X.i., Maguire, B., Brodaty, H., O'Leary, F., 2019. Dietary patterns and cognitive health in older adults: a systematic review. J. Alzheimer's Dis. 67 (2), 583–619. https://doi.org/10.3233/JAD-180468.

Cournot, M., Marquie, J.C., Ansiau, D., Martinaud, C., Fonds, H., Ferrieres, J., Ruidavets, J.B., 2006. Relation between body mass index and cognitive function in healthy middle-aged men and women. Neurology 67 (7), 1208–1214. https://doi.org/10.1212/01.wnl.0000238082.13860.50.

De Las Fuentes, L., Waggoner, A.D., Mohammed, B.S., Stein, R.I., Miller Iii, B.V., Foster, G.D., Wyatt, H.R., Klein, S., Davila-Roman, V.G., Louis, S., Philadelphia, M., Denver, P., 2009. QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES cardiovascular risk and diet and smoking effect of moderate diet-induced weight loss and weight regain on cardiovascular structure and function. J. Am. Coll. Cardiol. 54, 2376–2381. https://doi.org/10.1016/j.jacc.2009.07.054.

Deary, I.J., Whiteman, M.C., Starr, J.M., Whalley, L.J., Fox, H.C., 2004. The impact of childhood intelligence on later life: following up the scottish mental surveys of 1932 and 1947. J. Pers. Soc. Psychol. https://doi.org/10.1037/0022-3514.86.1.130.

Delis, D., Kramer, J., Kaplan, E., Antonio, B.O.-S., Psychological, T.T., 2000, undefined, n.d. Manual for the California Verbal Learning Test (CVLT-II).

Diaz, K.M., Howard, V.J., Hutto, B., Colabianchi, N., Vena, J.E., Blair, S.N., Hooker, S.P., 2016. Patterns of sedentary behavior in US middle-age and older adults: The REGARDS study. Med. Sci. Sports Exercise 48 (3), 430–438. https://doi.org/10.1249/MSS.0000000000000792.

Diaz, K.M., Krupka, D.J., Chang, M.J., Kronish, I.M., Moise, N., Goldsmith, J., Schwartz, J.E., 2018. Wrist-based cut-points for moderate- and vigorous-intensity physical activity for the Actical accelerometer in adults. J. Sports Sci. 36 (2), 206–212. https://doi.org/10.1080/02640414.2017.1293279.

Dinu, M., Pagliai, G., Casini, A., Sofi, F., 2018. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. Eur. J. Clin. Nutr. 72 (1), 30–43. https://doi.org/10.1038/ejcn.2017.58.

Doherty, A., Jackson, D., Hammerla, N., Plötz, T., Olivier, P., Granat, M.H., White, T., Van Hees, V.T., Trenell, M.I., Owen, C.G., Preece, S.J., Gillions, R., Sheard, S., Peakman, T., Brage, S., Wareham, N.J., 2017. Large scale population assessment of physical activity using wrist worn accelerometers: The UK biobank study. PLoS ONE 12. https://doi.org/10.1371/journal.pone.0169649.

Elias, M.F., Elias, P.K., Sullivan, L.M., Wolf, P.A., D'Agostino, R.B., 2005. Obesity, diabetes and cognitive deficit: The Framingham Heart Study. Neurobiol. Aging 26 (1), 11–16. https://doi.org/10.1016/j.neurobiolaging.2005.08.019.

Emerson, K.G., Gay, J., 2017. Physical activity and cardiovascular disease among older adults: The case of race and ethnicity. J. Aging Phys. Act. 25, 505–509. https://doi.org/10.1123/japa.2016-0012.

Esposito, K., Pontillo, A., Di Palo, C., Giugliano, G., Masella, M., Marfella, R., Giugliano, D., 2003. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. JAMA 289 (14), 1799. https://doi.org/10.1001/jama.289.14.1799.

Fain, J.A., 2009. The Diabetes Prevention Program: Replicating/Translating the Results, 179 179 Diabetes Educ 35 (2). https://doi.org/10.1177/0145721709350020301.

Fakhouri, T.H.I., Ogden, C.L., Carroll, M.D., Kit, B.K., Flegal, K.M., 2012. Key findings Prevalence of Obesity Among Older Adults in the.

Fitzgibbon, M.L., Stolley, M., Schiffer, L., Sharp, L., Singh, V., Van Horn, L., Dyer, A., 2008. Obesity Reduction Black Intervention Trial (ORBIT): Design and Baseline Characteristics. Journal of Women's Health 17 (7), 1099–1110. https://doi.org/10.1089/jwh.2007.0614.

Fitzgibbon, M.L., Tussing-Humphreys, L., Schiffer, L., Smith-Ray, R., Demott, A.D., Martinez, M., Berbaum, M.L., Huber, G.M., Hughes, S.L., 2018. Fit & strong! Plus: descriptive demographic and risk characteristics in a comparative effectiveness trial for older african-american adults with osteoarthritis HHS public access. J. Aging Res. Clin. Pr. 7, 9–16. https://doi.org/10.14283/jarcp.2018.3.

Freedson, P.S., John, D., 2013. Comment on "Estimating Activity and Sedentary Behavior from an Accelerometer on the Hip and Wrist". Med. Sci. Sports Exercise 45 (5), 962–963. https://doi.org/10.1249/MSS.0b013e31827f024d.

Gillette-Guyonnet, S., Nourhashemi, F., Andrieu, S., Cantet, C., Micas, M., Ousset, P.J., Vellas, B., 2003. The REAL. FR research program on Alzheimer's disease and its management: methods and preliminary results. J. Nutrition Health Aging 7 (2), 91–96.

Godin, G., 2011. The godin-shephard leisure-time physical activity questionnaire. Heal. Fit. J. Canada 4, 18–22.

Gonzales, M.M., Ajilore, O., Charlton, R.C., Cohen, J., Yang, S., Sieg, E., Bhaumik, D.K., Kumar, A., Lamar, M., 2017. Divergent Influences of cardiovascular disease risk factor domains on cognition and gray and white matter morphology. Psychosom. Med. 79 (5), 541–548. https://doi.org/10.1097/PSY.0000000000000448.

Gothe, N.P., 2018. Correlates of physical activity in urban African American adults and older adults: testing the social cognitive theory. Ann. Behav. Med. 52, 743–751. https://doi.org/10.1093/abm/kax038.

Gottesman, R., Fornage, M., Knopman, D., Mosley, T., 2015. Brain aging in African-Americans: the atherosclerosis risk in communities (ARIC) experience. Curr. Alzheimer Res. 12, 607–613. https://doi.org/10.2174/1567205012666150701102445.

Gunstad, J., Paul, R.H., Cohen, R.A., Tate, D.F., Spitznagel, M.B., Gordon, E., 2007. Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. Comprehens. Psychiatry 48 (1), 57–61. https://doi.org/10.1016/j.comppsych.2006.05.001.

Gustafson, D., Lissner, L., Bengtsson, C., Bjorkelund, C., Skoog, I., 2004. A 24-year follow-up of body mass index and cerebral atrophy. Neurology 63 (10), 1876–1881. https://doi.org/10.1212/01.WNL.0000141850.47773.5F.

Gustafson, D., Rothenberg, E., Blennow, K., Steen, B., Skoog, I., 2003. An 18-year follow-up of overweight and risk of Alzheimer disease. Arch Intern Med 163 (13), 1524. https://doi.org/10.1001/archinte.163.13.1524.

Guyatt, G.H., Sullivan, M.J., Thompson, P.J., Fallen, E.L., Pugsley, S.O., Taylor, D.W., Berman, L.B., 1985. The 6-minute walk: A new measure of exercise capacity in patients with chronic heart failure. Can. Med. Assoc. J. 132, 919–921.

Hachinski, V., Iadecola, C., Petersen, R.C., Breteler, M.M., Nyenhuis, D.L., Black, S.E., Powers, W.J., DeCarli, C., Merino, J.G., Kalaria, R.N., Vinters, H.V., Holtzman, D.M., Rosenberg, G.A., Wallin, A., Dichgans, M., Marler, J.R., Leblanc, G.G., 2006. National Institute of neurological disorders and stroke–Canadian Stroke network vascular cognitive impairment harmonization standards. Stroke 37 (9), 2220–2241. https://doi.org/10.1161/01.STR.0000237236.88823.47.

Hebert, L.E., Weuve, J., Scherr, P.A., Evans, D.A., 2013. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology 80 (19), 1778–1783. https://doi.org/10.1212/WNL.0b013e31828726f5.

Hildebrand, M., Van Hees, V.T., Hansen, B.H., Ekelund, U., 2014. Age group comparability of raw accelerometer output from wrist- and hip-worn monitors. Med. Sci. Sports Exercise 46 (9), 1816–1824. https://doi.org/10.1249/MSS.0000000000000289.

Hiza, H.A.B., Casavale, K.O., Guenther, P.M., Davis, C.A., 2013. Diet quality of americans differs by age, sex, race/ethnicity, income, and education level. J. Acad. Nutrit. Diet. 113 (2), 297–306. https://doi.org/10.1016/j.jand.2012.08.011.

Ho, A.J., Raji, C.A., Becker, J.T., Lopez, O.L., Kuller, L.H., Hua, X., Lee, S., Hibar, D., Dinov, I.D., Stein, J.L., Jack Jr., C.R., Weiner, M.W., Toga, A.W., Thompson, P.M., 2010. Obesity is linked with lower brain volume in 700 AD and MCI patients. Neurobiol. Aging 31 (8), 1326–1339. https://doi.org/10.1016/j.neurobiolaging.2010.04.006.

Hsu, C.L., Voss, M.W., Best, J., Handy, T.C., Madden, K., Bolandzadeh, N., Liu-Ambrose, T., 2015. Elevated body mass index and maintenance of cognitive function in late life: Exploring underlying neural mechanisms. Front. Aging Neurosci. 7, 155. https://doi.org/10.3389/fnagi.2015.00155.

Hughes, S.L., Tussing-Humphreys, L., Schiffer, L., Smith-Ray, R., Marquez, D.X., DeMott, A.D., Berbaum, M.L., Fitzgibbon, M.L., 2020. Fit & strong! plus trial outcomes for obese older adults with osteoarthritis. Gerontologist 60, 558–570. https://doi.org/10.1093/geront/gny146.

Kamada, M., Shiroma, E.J., Harris, T.B., Lee, I.-M., 2016. Comparison of physical activity assessed using hip- and wrist-worn accelerometers. Gait Posture 44, 23–28. https://doi.org/10.1016/j.gaitpost.2015.11.005.

Karstens, A.J., Tussing-Humphreys, L., Zhan, L., Rajendran, N., Cohen, J., Dion, C., Zhou, X.J., Lamar, M., 2019. Associations of the Mediterranean diet with cognitive and neuroimaging phenotypes of dementia in healthy older adults. Am. J. Clin. Nutr. 109, 361–368. https://doi.org/10.1093/ajcn/nqy275.

Kramer, A.F., Boot, W.R., McCarley, J.S., Peterson, M.S., Colcombe, A., Scialfa, C.T., 2006. Aging, memory and visual search. Acta Psychol. 122 (3), 288–304. https://doi.org/10.1016/j.actpsy.2005.12.007.

Kramer, A.F., Colcombe, S.J., McAuley, E., Eriksen, K.I., Scalf, P., Jerome, G.J., Marquez, D.X., Elavsky, S., Webb, A.G., 2003. Enhancing Brain and cognitive function of older adults through fitness training. J. Mol. Neurosci. https://doi.org/10.1385/JMN:20:3:213.

Kramer, J.H., Delis, D.C., Daniel, M., 1988. Sex differences in verbal learning. J. Clin. Psychol. 44, 907–915. https://doi.org/10.1002/1097-4679(198811)44:6<907::AID-JCLP2270440610>3.0.CO;2-8.

Kuczmarski, M.F., Allegro, D., Stave, E., 2014. The association of healthful diets and cognitive function: a review. J. Nutrit. Gerontol. Geriatr. 33 (2), 69–90. https://doi.org/10.1080/21551197.2014.907101.

Kuo, H.-K., Jones, R.N., Milberg, W.P., Tennstedt, S., Talbot, L., Morris, J.N., Lipsitz, L.A., 2006. Cognitive function in normal-weight, overweight, and obese older adults: an analysis of the advanced cognitive training for independent and vital elderly cohort. J. Am. Geriatr. Soc. 54, 97–103. https://doi.org/10.1111/j.1532-5415.2005.00522.x.

Lamar, M., Rubin, L.H., Ajilore, O., Charlton, R., Zhang, A., Yang, S., Cohen, J., Kumar, A., 2015. What metabolic syndrome contributes to brain outcomes in African American & Caucasian Cohorts. Curr. Alzheimer Res. 12, 640–647. https://doi.org/10.2174/1567205012666150701102325.

Lambert, J.-C., Ibrahim-Verbaas, C.A., Harold, D., Naj, A.C., Sims, R., Bellenguez, C., Jun, G., DeStefano, A.L., Bis, J.C., Beecham, G.W., Grenier-Boley, B., Russo, G., Thornton-Wells, T.A., Jones, N., Smith, A.V., Chouraki, V., Thomas, C., Ikram, M.A., Zelenika, D., Vardarajan, B.N., Kamatani, Y., Lin, C.-F., Gerrish, A., Schmidt, H., Kunkle, B., Dunstan, M.L., Ruiz, A., Bihoreau, M.-T., Choi, S.-H., Reitz, C., Pasquier, F., Hollingworth, P., Ramirez, A., Hanon, O., Fitzpatrick, A.L., Buxbaum, J. D., Campion, D., Crane, P.K., Baldwin, C., Becker, T., Gudnason, V., Cruchaga, C., Craig, D., Amin, N., Berr, C., Lopez, O.L., De Jager, P.L., Deramecourt, V., Johnston, J.A., Evans, D., Lovestone, S., Letenneur, L., Morón, F.J., Rubinsztein, D. C., Eiriksdottir, G., Sleegers, K., Goate, A.M., Fiévet, N., Huentelman, M.J., Gill, M., Brown, K., Kamboh, M.I., Keller, L., Barberger-Gateau, P., McGuinness, B., Larson, E. B., Green, R., Myers, A.J., Dufouil, C., Todd, S., Wallon, D., Love, S., Rogaeva, E., Gallacher, J., St George-Hyslop, P., Clarimon, J., Lleo, A., Bayer, A., Tsuang, D.W., Yu, L., Tsolaki, M., Bossù, P., Spalletta, G., Proitsi, P., Collinge, J., Sorbi, S., Sanchez-Garcia, F., Fox, N.C., Hardy, J., Naranjo, M.C.D., Bosco, P., Clarke, R., Brayne, C., Galimberti, D., Mancuso, M., Matthews, F., Moebus, S., Mecocci, P., Del Zompo, M., Maier, W., Hampel, H., Pilotto, A., Bullido, M., Panza, F., Caffarra, P., Nacmias, B., Gilbert, J.R., Mayhaus, M., Lannfelt, L., Hakonarson, H., Pichler, S., Carrasquillo, M. M., Ingelsson, M., Beekly, D., Alvarez, V., Zou, F., Valladares, O., Younkin, S.G., Coto, E., Hamilton-Nelson, K.L., Gu, W., Razquin, C., Pastor, P., Mateo, I., Owen, M. J., Faber, K.M., Jonsson, P.V., Combarros, O., O'Donovan, M.C., Cantwell, L.B., Soininen, H., Blacker, D., Mead, S., Mosley Jr, T.H., Bennett, D.A., Harris, T.B., Fratiglioni, L., Holmes, C., de Bruijn, R.F.A.G., Passmore, P., Montine, T.J., Bettens, K., Rotter, J.I., Brice, A., Morgan, K., Foroud, T.M., Kukull, W.A., Hannequin, D., Powell, J.F., Nalls, M.A., Ritchie, K., Lunetta, K.L., Kauwe, J.S.K., Boerwinkle, E., Riemenschneider, M., Boada, M., Hiltunen, M., Martin, E.R., Schmidt, R., Rujescu, D., Wang, L.-S., Dartigues, J.-F., Mayeux, R., Tzourio, C., Hofman, A., Nöthen, M.M., Graff, C., Psaty, B.M., Jones, L., Haines, J.L., Holmans, P. A., Lathrop, M., Pericak-Vance, M.A., Launer, L.J., Farrer, L.A., van Duijn, C.M., Van Broeckhoven, C., Moskvina, V., Seshadri, S., Williams, J., Schellenberg, G.D., Amouyel, P., 2013. Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. Nat Genet 45 (12), 1452–1458. https://doi.org/10.1038/ng.2802.

Larson, E.B., Yaffe, K., Langa, K.M., 2013. New Insights into the Dementia Epidemic. N. Engl. J. Med. 369, 2275–2277. https://doi.org/10.1056/NEJMp1314529.
Lezak, M., Howieson, D., Loring, D., Fischer, J., 2004. Neuropsychological assessment.
Lines, L.M., Sherif, N.A., Wiener, J.M., 2014. Racial and Ethnic Disparities Among Individuals with Alzheimer' s Disease in the United States: A Literature Review ReseaRch RepoRt. https://doi.org/10.3768/rtipress.2014.RR.0024.1412.
Logue, J., Thompson, L., Romanes, F., Wilson, D.C., Thompson, J., Sattar, N., 2010. Management of obesity: summary of SIGN guideline. c154 c154 BMJ 340 (feb24 2). https://doi.org/10.1136/bmj.c154.
Loughrey, D.G., Lavecchia, S., Brennan, S., Lawlor, B.A., Kelly, M.E., 2017. The impact of the mediterranean diet on the cognitive functioning of healthy older adults: a systematic review and meta-analysis. Adv. Nutr. 8, 571–586. https://doi.org/10.3945/an.117.015495.
Lourida, I., Soni, M., Thompson-Coon, J., Purandare, N., Lang, I.A., Ukoumunne, O.C., Llewellyn, D.J., 2013. Mediterranean diet, cognitive function, and dementia: A systematic review. Epidemiology 24 (4), 479–489. https://doi.org/10.1097/EDE.0b013e3182944410.
Manly, J.J., Jacobs, D.M., Touradji, P., Small, S.A., Stern, Y., 2002. Reading level attenuates differences in neuropsychological test performance between African American and White elders. J. Int. Neuropsychol. Soc. 8 (3), 341–348. https://doi.org/10.1017/S1355617702813157.
Martinez-Gonzalez, M.A., Corella, D., Salas-Salvado, J., Ros, E., Covas, M.I., Fiol, M., Warnberg, J., Aros, F., Ruiz-Gutierrez, V., Lamuela-Raventos, R.M., Lapetra, J., Munoz, M.A., Martinez, J.A., Saez, G., Serra-Majem, L., Pinto, X., Mitjavila, M.T., Tur, J.A., Portillo, M.d.P., Estruch, R., 2012. Cohort Profile: Design and methods of the PREDIMED study. Int. J. Epidemiol. 41 (2), 377–385. https://doi.org/10.1093/ije/dyq250.
Mavri, A., Poredoš, P., Šuran, D., Gaborit, B., Juhan-Vague, I., Poredoš, P., 2011. Effect of diet-induced weight loss on endothelial dysfunction: early improvement after the first week of dieting. Heart Vessels 26 (1), 31–38. https://doi.org/10.1007/s00380-010-0016-1.
McEvoy, C.T., Hoang, T., Sidney, S., Steffen, L.M., Jacobs Jr, D.R., Shikany, J.M., Wilkins, J.T., Yaffe, K., 2019. Dietary patterns during adulthood and cognitive performance in midlife: The CARDIA study. Neurology 92 (14), e1589–e1599. https://doi.org/10.1212/WNL.0000000000007243.
Mezuk, B., Abdou, C.M., Hudson, D., Kershaw, K.N., Rafferty, J.A., Lee, H., Jackson, J.S., 2013. "White Box" epidemiology and the social neuroscience of health behaviors: the environmental affordances model. Soc. Mental Health 3 (2), 79–95. https://doi.org/10.1177/2156869313480892.
Migueles, J., Rowlands, A.V., Huber, F., Sabia, S., van Hees, V.T., 2019. GGIR: a research community–driven open source R package for generating physical activity and sleep outcomes from multi-day raw accelerometer data. J. Meas. Phys. Behav. 2, 188–196.
Moser, A., Stuck, A.E., Silliman, R.A., Ganz, P.A., Clough-Gorr, K.M., 2012. The eight-item modified Medical Outcomes Study Social Support Survey: psychometric evaluation showed excellent performance. J. Clin. Epidemiol. 65 (10), 1107–1116. https://doi.org/10.1016/j.jclinepi.2012.04.007.
Najar, J., Östling, S., Gudmundsson, P., Sundh, V., Johansson, L., Kern, S., Guo, X., Hällström, T., Skoog, I., 2019. Cognitive and physical activity and dementia: A 44-year longitudinal population study of women. Neurology 92 (12), e1322–e1330. https://doi.org/10.1212/WNL.0000000000007021.
Nasreddine, Z.S., Phillips, N.A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J.L., Chertkow, H., 2005. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J. Am. Geriatr. Soc. 53, 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x.
Naylor, J.M., Hayen, A., Davidson, E., Hackett, D., Harris, I.A., Kamalasena, G., Mittal, R., 2014. Minimal detectable change for mobility and patient-reported tools in people with osteoarthritis awaiting arthroplasty. BMC Musculoskelet Disord 15 (1). https://doi.org/10.1186/1471-2474-15-235.
NILSSON, L.-G., NILSSON, E., 2009. Overweight and cognition. Scand. J. Psychol. 50, 660–667. https://doi.org/10.1111/j.1467-9450.2009.00777.x.
Ogden, C.L., Carroll, M.D., Fryar, C.D., Flegal, K.M., 2015. Prevalence of obesity among adults and youth: United States, 2011–2014. NCHS Data Brief. https://doi.org/10.1017/S1368980017000088.
Ogden, C.L., Fryar, C.D., Martin, C.B., Freedman, D.S., Carroll, M.D., Gu, Q., Hales, C.M., 2020. Trends in obesity prevalence by race and hispanic origin—1999-2000 to 2017-2018. JAMA 324 (12), 1208. https://doi.org/10.1001/jama.2020.14590.
Ong, K.L., Allison, M.A., Cheung, B.M.Y., Wu, B.J., Barter, P.J., Rye, K.-A., 2013. Trends in C-reactive protein levels in US adults from 1999 to 2010. Am. J. Epidemiol. 177 (12), 1430–1442. https://doi.org/10.1093/aje/kws443.
Panagiotakos, D.B., Pitsavos, C., Arvaniti, F., Stefanadis, C., 2007. Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore. Prevent. Med. 44 (4), 335–340. https://doi.org/10.1016/j.ypmed.2006.12.009.
Park, D.C., Nisbett, R., Hedden, T., 1999. Aging, culture, and cognition. J. Gerontol. Series B: Psychol. Sci. Soc. Sci. 54B (2), P75–P84. https://doi.org/10.1093/geronb/54B.2.P75.
Passini, M.A., Wolfe, J.H., 2001. Widespread gene delivery and structure-specific patterns of expression in the brain after intraventricular injections of neonatal mice with an adeno-associated virus vector. J. Virol. 75 (24), 12382–12392.
Pelletier, A., Barul, C., Féart, C., Helmer, C., Bernard, C., Periot, O., Dilharreguy, B., Dartigues, J.F., Allard, M., Barberger-Gateau, P., Catheline, G., Samieri, C., 2015. Mediterranean diet and preserved brain structural connectivity in older subjects. Alzheimer's Dement. 11, 1023–1031. https://doi.org/10.1016/j.jalz.2015.06.1888.
Petersson, S.D., Philippou, E., 2016. Mediterranean Diet, Cognitive Function, and Dementia: A Systematic Review of the Evidence. Adv. Nutr. 7, 889–904. https://doi.org/10.3945/an.116.012138.
Pickering, T.G., Hall, J.E., Appel, L.J., Falkner, B.E., Graves, J., Hill, M.N., Jones, D.W., Kurtz, T., Sheps, S.G., Roccella, E.J., 2005. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: A statement for professionals from the subcommittee of professional and public education of the american heart association council on high blood pressure research. Circulation 111 (5), 697–716. https://doi.org/10.1161/01.CIR.0000154900.76284.F6.
Plassman, B.L., Langa, K.M., Fisher, G.G., Heeringa, S.G., Weir, D.R., Ofstedal, M.B., Burke, J.R., Hurd, M.D., Potter, G.G., Rodgers, W.L., Steffens, D.C., Willis, R.J., Wallace, R.B., 2007. Prevalence of Dementia in the United States: The Aging, Demographics, and Memory Study. Neuro-epidemiology 29, 125–132. https://doi.org/10.1159/000109998.
Power, R., Prado-Cabrero, A., Mulcahy, R., Howard, A., Nolan, J.M., 2019. The role of nutrition for the aging population: implications for cognition and Alzheimer's disease. Annu. Rev. Food Sci. Technol. 10 (1), 619–639. https://doi.org/10.1146/annurev-food-030216-030125.
Psaltopoulou, T., Sergentanis, T.N., Panagiotakos, D.B., Sergentanis, I.N., Kosti, R., Scarmeas, N., 2013. Mediterranean diet, stroke, cognitive impairment, and depression: A meta-analysis. Ann Neurol. 74 (4), 580–591. https://doi.org/10.1002/ana.23944.
Rabbitt, P., Goward, L., 1994. Age, information processing speed, and intelligence. Quart. J. Experiment. Psychol. Sect. A 47 (3), 741–760. https://doi.org/10.1080/14640749408401135.
Radloff, L.S., 1977. The CES-D Scale: A self-report depression scale for research in the general population. Appl. Psychol. Measur. 1 (3), 385–401. https://doi.org/10.1177/014662167700100306.
Reeve, B.B., Hays, R.D., Bjorner, J.B., Cook, K.F., Crane, P.K., Teresi, J.A., Thissen, D., Revicki, D.A., Weiss, D.J., Hambleton, R.K., Liu, H., Gershon, R., Reise, S.P., Lai, J.-S., Cella, D., 2007. Psychometric evaluation and calibration of health-related quality of life item banks: plans for the patient-reported outcomes measurement information system (PROMIS). Med. Care 45 (Suppl 1), S22–S31. https://doi.org/10.1097/01.mlr.0000250483.85507.04.
Reitan, R., Wolfson, D., 1985. The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation.
Rolland, Y., Abellan van Kan, G., Vellas, B., 2008. Physical activity and Alzheimer's disease: from prevention to therapeutic perspectives. J. Am. Med. Direct. Assoc. 9 (6), 390–405. https://doi.org/10.1016/j.jamda.2008.02.007.
Sabia, S., van Hees, V.T., Shipley, M.J., Trenell, M.I., Hagger-Johnson, G., Elbaz, A., Kivimaki, M., Singh-Manoux, A., 2014. Association between questionnaire- and accelerometer-assessed physical activity: the role of sociodemographic factors. Am. J. Epidemiol. 179 (6), 781–790. https://doi.org/10.1093/aje/kwt330.
Saffer, H., Dave, D., Grossman, M., Ann Leung, L., 2013. Racial, ethnic, and gender differences in physical activity. J. Human Capital 7 (4), 378–410. https://doi.org/10.1086/671200.
Samieri, C., Okereke, O.I., Devore, E., Grodstein, F., 2013. Long-term adherence to the mediterranean diet is associated with overall cognitive status, but not cognitive decline. Women. J. Nutr. 143, 493–499. https://doi.org/10.3945/jn.112.169896.
Santos-Lozano, A., Marín, P.J., Torres-Luque, G., Ruiz, J.R., Lucía, A., Garatachea, N., 2012. Technical variability of the GT3X accelerometer. Med. Eng. Phys. 34 (6), 787–790. https://doi.org/10.1016/j.medengphy.2012.02.005.
Schalet, B.D., Rothrock, N.E., Hays, R.D., Kazis, L.E., Cook, K.F., Rutsohn, J.P., Cella, D., 2015. Linking physical and mental health summary scores from the veterans RAND 12-item health survey (VR-12) to the PROMIS® global health scale. J. Gen. Intern. Med. 30 (10), 1524–1530. https://doi.org/10.1007/s11606-015-3453-9.
Schwartz, E.S., Erdodi, L., Rodriguez, N., Ghosh, J.J., Curtain, J.R., Flashman, L.A., Roth, R.M., 2016. CVLT-II forced choice recognition trial as an embedded validity indicator: a systematic review of the evidence. J. Int. Neuropsychol. Soc. 22 (8), 851–858. https://doi.org/10.1017/S1355617716000746.
Services, U.S.D. of H. and H., 2018. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC.
Services, U.S.D. of H. and H., Agriculture, U.S.D. of, 2015. 2015-2020 Dietary Guidelines for Americans. 8th Edition.
Sherzai, D., Sherzai, A., 2019. Preventing Alzheimer's: Our Most Urgent Health Care Priority. Am. J. Lifestyle Med. 13 (5), 451–461. https://doi.org/10.1177/1559827619843465.
Siervo, M., Arnold, R., Wells, J.C.K., Tagliabue, A., Colantuoni, A., Albanese, E., Brayne, C., Stephan, B.C.M., 2011. Intentional weight loss in overweight and obese individuals and cognitive function: A systematic review and meta-analysis. Obes. Rev. 12, 968–983. https://doi.org/10.1111/j.1467-789X.2011.00903.x.
Singh-Manoux, A., Dugravot, A., Shipley, M., Brunner, E.J., Elbaz, A., Sabia, S., Kivimaki, M., 2018. Obesity trajectories and risk of dementia: 28 years of follow-up in the Whitehall II Study. Alzheimer's Dementia 14 (2), 178–186. https://doi.org/10.1016/j.jalz.2017.06.2637.
Singh, B., Parsaik, A.K., Mielke, M.M., Erwin, P.J., Knopman, D.S., Petersen, R.C., Roberts, R.O., 2014. Association of mediterranean diet with mild cognitive impairment and Alzheimer's disease: A systematic review and meta-analysis. JAD 39 (2), 271–282. https://doi.org/10.3233/JAD-130830.
Solfrizzi, V., Custodero, C., Lozupone, M., Imbimbo, B.P., Valiani, V., Agosti, P., Schilardi, A., D'Introno, A., La Montagna, M., Calvani, M., Guerra, V., Sardone, R., Abbrescia, D.I., Bellomo, A., Greco, A., Daniele, A., Seripa, D., Logroscino, G., Sabbá, C., Panza, F., 2017. Relationships of dietary patterns, foods, and micro- and macronutrients with Alzheimer's disease and late-life cognitive disorders: a systematic review. JAD 59 (3), 815–849. https://doi.org/10.3233/JAD-170248.

Strandberg, T.E., Stenholm, S., Strandberg, A.Y., Salomaa, V.V., Pitkala, K.H., Tilvis, R.S., 2013. The "Obesity Paradox", Frailty, Disability, and Mortality in Older Men: A Prospective, Longitudinal Cohort Study. Am. J. Epidemiol. 178, 1452–1460. https://doi.org/10.1093/aje.

Stroop, J.R., 1935. Studies of interference in serial verbal reactions. J. Exp. Psychol. 18 (6), 643–662. https://doi.org/10.1037/h0054651.

Sundermann, E.E., Biegon, A., Rubin, L.H., Lipton, R.B., Landau, S., Maki, P.M., Pike, K., 2017. Does the female advantage in verbal memory contribute to underestimating Alzheimer's disease pathology in women versus men? JAD 56 (3), 947–957. https://doi.org/10.3233/JAD-160716.

Sundermann, E.E., Maki, P.M., Rubin, L.H., Lipton, R.B., Landau, S., Biegon, A., 2016. Female advantage in verbal memory: Evidence of sex-specific cognitive reserve. Neurology 87 (18), 1916–1924. https://doi.org/10.1212/WNL.0000000000003288.

Tangney, C.C., Kwasny, M.J., Li, H., Wilson, R.S., Evans, D.A., Morris, M.C., 2011. Adherence to a Mediterranean-type dietary pattern and cognitive decline in a community population. Am. J. Clin. Nutrit. 93 (3), 601–607. https://doi.org/10.3945/ajcn.110.007369.

Tangney, C.C., Li, H., Wang, Y., Barnes, L., Schneider, J.A., Bennett, D.A., Morris, M.C., 2014. Relation of DASH- and Mediterranean-like dietary patterns to cognitive decline in older persons. Neurology 83 (16), 1410–1416. https://doi.org/10.1212/WNL.0000000000000884.

Thompson, T., Pérez, M., Kreuter, M., Margenthaler, J., Colditz, G., Jeffe, D.B., 2017. Perceived social support in African American breast cancer patients: Predictors and effects. Soc. Sci. Med. 192, 134–142. https://doi.org/10.1016/j.socscimed.2017.09.035.

Thompson, T., Rodebaugh, T.L., Pérez, M., Schootman, M., Jeffe, D.B., 2013. Perceived social support change in patients with early stage breast cancer and controls. Heal. Psychol. 32, 886–895. https://doi.org/10.1037/a0031894.

Tobias, D.K., Pan, A.n., Jackson, C.L., O'Reilly, E.J., Ding, E.L., Willett, W.C., Manson, J. E., Hu, F.B., 2014. Body-mass index and mortality among adults with incident Type 2 diabetes. N. Engl. J. Med. 370 (3), 233–244. https://doi.org/10.1056/NEJMoa1304501.

Tosto, G., Reitz, C., 2013. Genome-wide association studies in Alzheimer's disease: A review. Curr. Neurol. Neurosci. Rep. 13 (10) https://doi.org/10.1007/s11910-013-0381-0.

Troiano, R.P., Berrigan, D., Dodd, K.W., Mâsse, L.C., Tilert, T., Mcdowell, M., 2008. Physical Activity in the United States Measured by Accelerometer. Med. Sci. Sports Exercise 40 (1), 181–188. https://doi.org/10.1249/mss.0b013e31815a51b3.

Troiano, R.P., McClain, J.J., Brychta, R.J., Chen, K.Y., 2014. Evolution of accelerometer methods for physical activity research. Br. J. Sports Med. 48 (13), 1019–1023. https://doi.org/10.1136/bjsports-2014-093546.

Tussing-Humphreys, L., Lamar, M., Blumenthal, J.A., Babyak, M., Fantuzzi, G., Blumstein, L., Schiffer, L., Fitzgibbon, M.L., 2017. Building research in diet and cognition: The BRIDGE randomized controlled trial. Contemp. Clin. Trials 59, 87–97. https://doi.org/10.1016/j.cct.2017.06.003.

Valls-Pedret, C., Sala-Vila, A., Serra-Mir, M., Corella, D., de la Torre, R., Martínez-González, M.Á., Martínez-Lapiscina, E.H., Fitó, M., Pérez-Heras, A., Salas-Salvadó, J., Estruch, R., Ros, E., 2015. Mediterranean diet and age-related cognitive decline: a randomized clinical trial. JAMA Intern Med 175 (7), 1094. https://doi.org/10.1001/jamainternmed.2015.1668.

Van Den Brink, A.C., Brouwer-Brolsma, M., Berendsen, A.A., Van De Rest, O., 2019. The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease-A Review. Adv. Nutr. 10, 1040–1065. https://doi.org/10.1093/advances/nmz054.

van Hees, V.T., Gorzelniak, L., Dean León, E.C., Eder, M., Pias, M., Taherian, S., Ekelund, U., Renström, F., Franks, P.W., Horsch, A., Brage, S., 2013. Separating Movement and Gravity Components in an Acceleration Signal and Implications for the Assessment of Human Daily Physical Activity. PLoS One 8, e61691. https://doi.org/10.1371/journal.pone.0061691.

Villareal, D.T., Chode, S., Parimi, N., Sinacore, D.R., Hilton, T., Armamento-Villareal, R., Napoli, N., Qualls, C., Shah, K., 2011. Weight loss, exercise, or both and physical function in obese older adults. N. Engl. J. Med. 364 (13), 1218–1229. https://doi.org/10.1056/NEJMoa1008234.

Vinciguerra, F., Graziano, M., Hagnäs, M., Frittitta, L., Tumminia, A., 2020. Influence of the mediterranean and ketogenic diets on cognitive status and decline: A narrative review. Nutrients 12, 1–22. https://doi.org/10.3390/nu12041019.

Wagner, M., Grodstein, F., Proust-Lima, C., Samieri, C., 2020. Long-Term Trajectories of Body Weight, Diet, and Physical Activity From Midlife Through Late Life and Subsequent Cognitive Decline in Women. Am. J. Epidemiol. 189, 305–313. https://doi.org/10.1093/aje/kwz262.

Wang, D.D., Leung, C.W., Li, Y., Ding, E.L., Chiuve, S.E., Hu, F.B., Willett, W.C., 2014. Trends in Dietary Quality Among Adults in the United States, 1999 Through 2010. JAMA Intern Med 174 (10), 1587. https://doi.org/10.1001/jamainternmed.2014.3422.

Wechsler, D., 2008. Wechsler Adult Intelligence Scale: Technical and interpretative manual-Fourth Edition (WAIC-IV): Administration and scoring manual. Pearson, San Antonio, TX.

Wechsler, D., 2001. Wechsler Test of Adult Reading: WTAR. Psychological Corporation, San Antonio, TX.

Willett, W.C., Sampson, L., Stampfer, M.J., Rosner, B., Bain, C., Witschi, J., Hennekens, C.H., Speizer, F.E., 1985. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am. J. Epidemiol. 122, 51–65. https://doi.org/10.1093/oxfordjournals.aje.a114086.

Wolf, P., Beiser, A., Elias, M., Au, R., Vasan, R., Seshadri, S., 2007. Relation of Obesity to Cognitive Function: Importance of Central Obesity and Synergistic Influence of Concomitant Hypertension. The Framingham Heart Study. Curr. Alzheimer Res. 4, 111–116. https://doi.org/10.2174/156720507780362263.

Wolpern, A.E., Sherwin, K.J., Moss, W.D., Nygaard, I.E., Egger, M.J., Brusseau, T.A., Shaw, J.M., 2019. Compliance with wrist-worn accelerometers in primiparous early postpartum women. Heliyon 5 (1), e01193. https://doi.org/10.1016/j.heliyon.2019.e01193.

Wright, R.S., Waldstein, S.R., Kuczmarski, M.F., Pohlig, R.T., Gerassimakis, C.S., Gaynor, B., Evans, M.K., Zonderman, A.B., 2017. Diet quality and cognitive function in an urban sample: findings from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study. Public Health Nutr. 20 (1), 92–101. https://doi.org/10.1017/S1368980016001361.

Zhang, Z., Hayward, M.D., Yu, Y.-L., 2016. Life course pathways to racial disparities in cognitive impairment among older Americans. J Health Soc Behav 57 (2), 184–199. https://doi.org/10.1177/0022146516645925.

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. Med. Sci. Sports Exerc. 49, 47–53. https://doi.org/10.1249/MSS.0000000000001079.

Zich, J.M., Attkisson, C.C., Greenfield, T.K., 1990. Screening for depression in primary care clinics: The CES-D and the BDI. Int J Psychiatry Med 20 (3), 259–277. https://doi.org/10.2190/LYKR-7VHP-YJEM-MKM2.