WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE
Claude D. Pepper Older Americans Independence Center

Stephen Kritchevsky, Ph.D. **Principal Investigator**	336-713-8548	skritche@wakehealth.edu
Dalane Kitzman, MD **Co-Principal Investigator**		dkitzman@wakehealth.edu
Kimberly Kennedy, MS, CCRC **Program Administrator**	336-713-8567	kkennedy@wakehealth.edu

CENTER DESCRIPTION

The WF OAIC Leadership and Administrative Core (LAC) sets the scientific direction, optimizes administrative and fiscal operations, and ensures the scientific integrity and coherence of the WF OAIC. LAC co-leaders Drs. Kritchevsky and Kitzman will use a proven collaborative leadership model that fosters operational efficiency, high productivity, and innovative translational and multidisciplinary research focused on our theme, “Integrating pathways affecting physical function for new approaches to disability treatment and prevention”.

The **Specific Aims** of the Leadership and Administrative Core are to:

1. Provide overall scientific leadership and direction for the WF OAIC. The LAC co-leaders will synthesize information regarding the local and national research environment with input from the OAIC Executive Committee, the OAIC External Advisory Board, the REC Advisory Committee and WF’s senior administrative leadership to guide the direction of the OAIC through: the mix of Core services; the focus of research development projects; the tailoring of pilot award RFAs; interactions with the OAIC Coordinating Center, other OAICs and other aging-focused research centers; and the selection of early- career faculty for Research Education Component (REC) support. The LAC will integrate WF OAIC Core activities to advance the OAIC’s scientific agenda, improve efficiency, and foster translation between basic and clinical research.

2. Efficiently manage the resources of the WF OAIC in compliance with applicable institutional and NIA/NIH policies. The LAC will: 1) provide administrative and budgetary support to the WF OAIC according to OAIC priorities; 2) seek additional institutional resources to extend the scope of its activities; 3) arrange for the scientific review of pilot and research development projects and candidates seeking REC support; 4) monitor all OAIC activities for timely completion and achievement of targeted goals and milestones, and intervene to remove roadblocks or (if necessary) redirect resources; and 5) assure all OAIC-supported activities follow federal and institutional rules, regulations, and guidelines and promote the responsible conduct of research and participant safety.

3. Increase WF OAIC’s impact by attracting new investigators, capturing new resources, and translating findings beyond traditional research settings. The LAC will attract new researchers and research capabilities to OAIC-supported research by engaging the local and regional academic communities, in coordination with resources from WF’s Sticht Center for Healthy Aging and Alzheimer’s Prevention, the Section of Gerontology and Geriatric Medicine, and other academic and service units. The LAC will also promote the NIA’s goals for the OAIC program by translating its research to affect the clinical care of older adults and the health and well-being of older adults in the community.

During the current cycle, the WF OAIC achieved high productivity and innovation, and enhanced its strategic positioning and prominence within Wake Forest and enhanced its local and national impact. **Compared to the previous cycle, publication productivity was increased 5% and OAIC-related extramural funding increased 91%.** The outstanding productivity of OAIC investigators occurred despite the challenging funding environment and is attributable (in part) to our innovative strategies to promote efficiency (e.g., thematic alignment, the OAIC Integrated Aging Studies Databank and Repository), and the LAC's success in leveraging $4.3 million in institutional funds in support of the OAIC mission.

WF OAIC involvement was critical in securing high-impact awards that enhance the breadth and depth of research resources available to the OAIC, including a new CTSA and a new Alzheimer's Disease Core Center. As an Associate Director of the Wake Forest Clinical and Translational Science Institute and director of its KL-2 program, Dr. Kritchevsky aligned CTSI resources with the OAICs for their mutual benefit. His role as Associate Dean for Research Development provides him with influence over WF's research priorities. Locally, the OAIC has successfully expanded our research partnerships to deliver interventions in innovative settings (Meals-on-Wheels, Agricultural Extension Service, YMCA's and Continuing-Care communities). WF OAIC leaders have been national advocates for the OAIC's mission and have helped develop multi-centered trials testing hypotheses generated from OAIC work (e.g. LIFE, ENRGISE, PCORI/STRIDE) and pivot large multi-center trials towards OAIC relevant outcomes (e.g., SPRINT, Look AHEAD). The WF OAIC, under the leadership of Drs. Kritchevsky and Kitzman, will use OAIC support to sustain the LAC's continual innovation through the 2018-2023 cycle.

To address these objectives our OAIC is composed of seven cores, which currently supports 4 REC Scholars, 17 clinical studies (all which are funded by the NIH), 2 research development projects, and 8 pilot studies.

CORES

Leadership and Administrative Core (LAC)

Leader 1: Stephen Kritchevsky, PhD skritche@wakehealth.edu
Leader 2: Dalane Kitzman, MD dkitzman@wakehealth.edu

The Leadership and Administrative Core is responsible for scientific leadership and direction of the center. It coordinates the functions of the OAIC cores and projects in order to facilitate communication and foster translation between basic and clinical research and ensure access of investigators to core resources. It assures the coordination of OAIC resources and functions with other research and training grants and institutional resources. It is supported by the OAIC Executive Committee, the Joint Scientific Review Panel, and the External Advisory Committee. The core communicates with other OAICs and the NIA and fosters collaborations with other OAICs including UTMB, University of Maryland and Duke. Maintains the OAIC web-based tracking and monitoring system and promotes the use of uniform assessment batteries in all OAIC supported studies. The LAC works with Core leaders to identify, review, and support projects and activities which serve to advance the scientific goals of the OAIC. The LAC and Executive Committee actively identify promising projects and REC candidates through informal networks, review of all new faculty hires at WF, and all new grant awards to WF faculty. WF OAIC overarching resource allocation priorities are based on: 1) scientific merit; 2) theme relevance; 3) REC scholar/junior faculty involvement; 4) Pilot/Exploratory study support; 5) research development projects; and 6) externally supported projects. This priority maintains our thematic coherence and enhances support for projects that may need it.

Research Education Component (REC)

Leader 1: Stephen Kritchevsky, PhD skritche@wakehealth.edu
Leader 2: Denise Houston, PhD dhouston@wakehealth.edu
Leader 3: Heidi Klepin, MD

The Research Education Component (REC) continues to promote the development of future research leaders in the area of focus of this OAIC application, integrating pathways affecting physical function for new approaches to disability treatment and prevention. The core emphasizes development of skills for translating basic findings into clinical research, and clinical findings into basic research. Resources of this core are integrated with other external sources for career support, such as NIH career development and research awards, fellowships, and non-NIH career and research awards. Resources of the REC are also leveraged with assets of the Wake Forest Clinical and Translational Science Institute (CTSI); Dr. Kritchevsky is a Core Faculty member of the CTSI's KL2 program. The CTSI has a Translational Research Academy, a Mentor Academy, and a K and R Award Writer's Series, which provide added value to the REC through courses, facilitation of grants, navigating regulations, and evaluating competencies. All REC scholars are encouraged to participate in the Translational Research Academy to help optimize the relative contributions of the CTSI and REC programs. The REC co-leaders are Drs. Kritchevsky and Houston; Dr. Klepin, REC leadership intern, will specifically recruit and advise promising clinical faculty. Dr. Kritchevsky is a national leader in aging research, whose expertise spans the translational spectrum from basic science to policy formulation. Dr. Houston is a national leader in nutrition and aging research with expertise in both epidemiologic studies and clinical trials. Dr. Klepin is a national leader in geriatric oncology with expertise in conducting patient-oriented

research, including both pharmacologic and behavioral interventions. Each of the Core Leaders is accomplished in interdisciplinary and team-based research, and well positioned to assure that REC programs and activities are well integrated with other internal and external career development activities. All REC projects continue to utilize Pepper Core support to signify the integration of resources and disciplines. This includes: Ellen Quillen, PhD (Integrative Biology Core) and Atalie Thompson, MD, MPH (Biostatistics and Data Management Core and Clinical Research Core). The REC currently supports five REC scholars which includes two REC scholars that began in the summer/fall of 2021 (Quillen, Thompson) and three new REC scholars (Genesio Karere, PhD; Lindsay Reynolds, PhD; and Jaime Hughes, PhD) that started in April 2022. The three new REC scholars were selected in response to an RFA for REC scholars distributed across the institution in October 2021. Two REC developmental scholars (Chinenyenwa Usoh, MD, and Philip Kramer, PhD) were also selected with the purpose of helping them refine and develop their research ideas and strengthen their research portfolios.

Pilot and Exploratory Studies Core (PESC)

Leader 1:	Dalane Kitzman, MD	dkitzman@wakehealth.edu
Leader 2:	Tom Register, PhD	register@wakehealth.edu
Leader 3:	Tina Brinkley, PhD	tbrinkle@wakehealth.edu

Effective pilot and exploratory studies (PES) play a critical role in the development of successful, externally-funded research proposals, particularly for early stage investigators who often lack other means to obtain preliminary data. The Wake Forest OAIC Pilot and Exploratory Studies Core (WF PESC) proposes to continue our coordinated, multi-faceted group effort to promote PESs, and to further innovate to optimize our processes. Through support from the OAIC grants, Wake Forest University has been very active in efforts to enhance aging related research activities. These activities have focused on the mechanism, treatment and outcomes associated with functional decline and disability and have had a profound impact on the research culture at our institution with greater awareness and interest in addressing these important yet understudied issues of geriatric research.

The overall goal of the WF OAIC PESC is to develop key information needed for the design of definitive, externally funded, translational research studies that promote the WF OAIC mission of advancing our understanding of pathways influencing physical function and developing new approaches to disability prevention and treatment.

This will be achieved by executing the following Specific Aims to:

1) Identify and promote promising key areas of research
2) Identify and recruit talented investigators from complementary fields to focus on OAIC-themed aging research
3) Solicit and facilitate competitive research proposals and conduct peer review to select those with the best science and career development opportunities
4) Coach and mentor investigative teams to maximize the quality of research proposals and projects
5) Team with other WF OAIC cores to facilitate successful completion of the selected pilot projects and mentor junior early career investigators to advance their development as successful translational scientists

Continuously evaluate, refine, and optimize OAIC PESC processes and procedures.

Clinical Research Core (CRC)

Leader 1:	Barbara Nicklas, PhD	bnicklas@wakehealth.edu
Leader 2:	Jeff Williamson, MD	jwilliam@wakehealth.edu
Leader 3:	Kristen Beavers, PhD	beaverkm@wfu.edu
Leader 4:	Jack Rejeski, PhD	rejeski@wfu.edu
Leader 5:	Jason Fanning, PhD	fanning@wfu.edu

The Clinical Research Core (CRC) provides institution-wide guidance on the design and conduct of clinical research consistent with the WF OAIC theme (present and past) and involving older adults. The CRC also performs validated, standardized assessments of physical and cognitive function, strength, and disability. Assistance is provided to investigators at all levels of experience and all sizes of research studies with integration of these OAIC measures into their research involving older adults. The Core's scientific focus is the advancement of physical function based clinical research methods and the design, implementation, and evaluation of interventions designed to measure whether specific interventions developed in this or other cores preserve the independence of older adults. Functional assessment instruments and trial design encompass both community and clinic-based settings. Additionally, members of the core are involved in cross-disciplinary translational research with other cores within the center. The overall hypothesis for this CRC is that the inclusion of efficient, standardized measures of functional assessment will promote translation of the OAIC research into clinical research and care through improved understanding of function as both a risk factor and an outcome (see below). The Core also includes both 1) a recruitment unit and 2) a muscle and adipose tissue biopsy unit for OAIC supported studies. In addition, if including aging-related measures is required as part of specific studies, the Core supported staff will assist investigators by training them or their staff and/or collecting these assessments. Currently the standard assessment battery includes: 1. Anthropometry (Height, Body Mass, Abdominal Circumference) 2. Grip strength (Jamar hand grip dynamometer) 3. Lower extremity muscle power (Keiser knee extension and leg press) 4. The Short Physical Performance Battery (SPPB: three tests of physical function - standing balance, usual pace gait speed over 4 meters, time to rise from a chair and sit down five times) 5. 400 meter walk test (400MWT: study specific protocols for either usual or fast pace gait speed) 6. Pepper Assessment Tool for Disability (PAT-D: self-report instrument) 7. Mobility Assessment Tool – short form (MAT-sf: 10 or 12-item computer based self-report assessment of mobility using animated video clips) 8. Digit Symbol Substitution Test (DSST: validated cognitive assessment that is strongly correlated with walking speed) 9. Montreal Cognitive Assessment© (MoCA: global cognitive assessment that aids in interpreting DSST performance) The core also has the capacity to assess muscle strength of various muscle groups (Biodex isokinetic dynamometer), gait speed and spatiotemporal parameters of gait (GAITRite instrumented mat), and postural sway descriptors (AMTI portable force platform).

BioImaging

Leader 1:	Leon Lenchik, MD	llenchik@wakehealth.edu
Leader 2:	Christina Hugenschmidt, PhD	chugensc@wakehealth.edu
Leader 3:	Ashley Weaver, PhD	asweaver@wakehealth.edu

This core supports independently funded studies, pilot studies, and research development studies in the accurate in vivo measurement of body composition, specifically focusing on skeletal muscle mass and composition, fat mass and distribution, and bone mineral density. This core collaborates with other OAIC cores in the development of new, multidisciplinary, and translation research projects directed at elucidating the etiology, consequences, prevention and treatment of sarcopenia and its sequelae. The BRC has contributed to the success of the WF OAIC by helping to quantify structural and functional tissue-related measures, developing novel bio-imaging techniques, integrating imaging assessments with other OAIC cores, and using imaging technologies for studies of physical function and disability in older persons. The BRC has also provided early-career and experienced investigators access to a broad range of imaging methods relevant to disability and age-related physical decline including dual x-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasonography (US) as well as access to expertise and mentoring in bio-imaging including image acquisition, analysis, interpretation, archival, and dissemination. The Bioimaging Resource Core (BRC) has contributed to the success of the WF OAIC by helping to quantify structural and functional tissue-related measures, integrating imaging assessments with other OAIC cores, and using imaging technologies for studies of physical function and disability in older persons. The BRC has also provided early-career and experienced investigators access to a broad range of imaging methods relevant to age-related physical decline including dual x-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasonography (US) as well as access to expertise and mentoring in bio-imaging including image acquisition, analysis, interpretation, archival, and dissemination. Over the past year, the BRC has added an emphasis on expanding the imaging infrastructure. The infrastructure initiative has two parts: 1) updating hardware and software and harmonizing archiving with other OAIC and ADRC cores to increase access to data already collected and 2) adding new bone imaging capability to the suite of imaging techniques available to OAIC investigators. The BRC received an administrative supplement (in response to NOT-AG-17-008 and PA-16-287) to develop research on Alzheimer's disease and Alzheimer's-related dementias (ADRD). The goal was to harmonize imaging data workflow between the WF OAIC and WF ADRC. In the past year, the BRC made progress on: 1) archiving of past imaging studies using a newly acquired Vendor Neutral Archive (VNA), 2) harmonizing imaging data storage, processing, and archiving between the OAIC and ADRC, and 3) harmonizing imaging data request process between OAIC and ADRC. Such harmonization will allow investigators to ask cutting-edge questions about the brain-body integration including the trajectory of physical decline in people with ADRD and the trajectory of cognitive decline in older adults with mobility disability, obesity, and frailty.

Biostatistical Design and Analysis Core (BIC)

Leader 1:	Iris Leng, PhD	ileng@wakehealth.edu
Leader 2:	Nicholas Pajewski, PhD	npajewsk@wakehealth.edu
Leader 3:	Jaime Speiser, PhD	jspeiser@wakehealth.edu

The goal of the Wake Forest OAIC Biostatistics and Research Information Systems Core (BIC) is to build on our outstanding success in biostatistical collaboration and to expand a broad class of statistics/informatics tools tailored to research in aging. The BIC team has highly qualified investigators/staff with expertise in design and management of observational, pilot, and interventional studies; centralized and decentralized data management; forms design and data processing, psychometrics; statistical analysis of data from multiple study designs; and

development of novel statistical methods. The BIC team is committed to the WF OAIC's programmatic aims to: (1) discover new common pathways contributing to age-related declines in physical function and disability; (2) develop, evaluate, and refine strategies for disability treatment and prevention; (3) translate proven strategies beyond traditional research environments; and (4) train the next generation of research leaders focused on disability treatment and prevention. The BIC provides expertise and critical infrastructure essential to the mission of the WF OAIC, and promotes efficiency through centralized data management. BIC members will play a key role in study design, analysis, and interpretation for WF OAIC projects, will be integral members of mentoring teams for REC Scholars and early-stage faculty, and continue their intellectual contributions that strengthen research on aging through the development of novel measurement, statistical, and research informatics tools. During the past year, members of the Biostatistics and Research Information Systems Core (BIC) have continued to provide support for numerous studies performed within the WFU OAIC. Efforts include developing web-based data entry systems for individual studies, harmonizing common measurements taken across multiple studies, performing analyses of pilot/developmental studies and existing data bases, and collaborating on the development of pilot studies and grant submissions resulting from WFU OAIC pilot studies. In addition, faculty in the Core continue to be involved with mentoring committees for REC fellows, collaboration on career development award submissions, reviewing pilot studies and applications of prospective REC fellows. During the past year, members of the BIC collaborated with WFU OAIC investigators in the submission of several R01s, a U24, and a K76 grant. During the past year, members of the BIC collaborated with WFU OAIC investigators in the submission of several R01s, a U24, and a K76 grant. As of October 2021, the BIC has also undergone a planned change in leadership, with Drs. Miller and Ip stepping down from their roles.

Integrative Biology Core

Leader 1:	Jamie Justice, PhD	jjustice@wakehealth.edu
Leader 2:	Osvaldo Delbono, PhD	odelbono@wakehealth.edu
Leader 3:	Bumsoo Ahn, PhD	bahn@wakehealth.edu

Over the past year, the Integrative Biology Core (IBC) advanced the science of our OAIC by adding biological measures to facilitate translational research for OAIC investigators and by advising and mentoring REC scholars and early-career faculty. We also continued maintenance of our centrally collected and stored Biological Specimen Repository from aging-related studies. The Core provided resources and personnel in support of several externally-funded studies (SOMMA, HALLO-P, U01 Aging Biomarkers, SECRET2, VARIA, INVEST, UPLIFT, B-NET, HOPE and EMPOWER), and externally-funded and OAIC-supported pilots. Core Resource Use and Development of New Services: Repository, Biomarker, and tissue biopsy services—IBC personnel assist study investigators with the proper collection, transfer, and central storage of human biological tissue specimens and facilitate their later use in ancillary studies by other investigators. In the past year the Core supported labeling, tracking and storage of blood samples from participants enrolled in 6 externally-funded studies (INVEST, SOMMA, B-NET, SECRET2, HOPE, and UPLIFT), and assisted with collection, processing, and storage of muscle (SOMMA) and adipose tissue (SOMMA). The Core also expanded its biomarker services through purchase of two instruments for biomarker determination: Ella SimplePlex and Luminex LX200. Ella SimplePlex is a semi-automated device with integrated cartridge system used for targeted biomarkers – which will form the basis for an expanded 'Pepper Common Battery' for biomarkers, and Luminex LX200 has advanced multiplexing capability that permits a discovery-based biomarker approach. The two systems work well in tandem, providing industry-standard biomarker

multiplexing via Luminex LX200 which can be used to identify specific markers for analysis using Ella SimplePlex. Resources and personnel advanced the science of our OAIC theme by adding measures to externally-funded studies and pilots to facilitate translational research for OAIC investigators, and by advising and mentoring of the REC scholars. In the past year, the Integrative Biology Core (IBC) advanced the science of our OAIC by adding biological measures to facilitate translational research for OAIC investigators, and by advising and mentoring REC scholars and early-career faculty. We also continued maintenance of our centrally collected and stored Biological Specimen Repository from aging-related studies. The Core provided resources and personnel in support of several externally-funded studies (SOMMA, HALLO-P, U01 Aging Biomarkers, SECRET2, VARIA, INVEST, UPLIFT, B-NET, HOPE and EMPOWER), and externally-funded and OAIC-supported pilots.

CAREER DEVELOPMENT

REC Scholar, Research & Grants Funded During Pepper Supported Time	Years / Publications

Lindsay Reynolds, PhD 2022-2024 /
Assistant Professor / Department of Epidemiology and Prevention 1 (total)
Dietary Patterns and Biological Aging in the Women's Health Initiative 0 (1st/Sr)

To examine epigenetic aging measures as a mediator between adherence to healthy dietary patterns and incidence of frailty over ~ 10 years using existing data from the Women's Health Initiative.

- (Pending Funding) Title: MARVEL: A Multidisciplinary Assessment of Risks from Vaping during Early Life Project Number: P01CA269048-02 Name of PD/PI: Sutfin/Donny MPIs Source of Support: NCI/NIH Submission date: 5/19/2022 Role: Co-I (co-lead Project 3) Project/Proposal Start and End Date: 04/01/23 - 03/31/28
- Title: Epigenetics of COPD - SPIROMICS pilot Name of PD/PI: Reynolds, LM Source of Support: Wake Forest Tobacco Control Center of Excellence Year 03/01/2022 - 03/31/2023 1.80 Calendar months
- Title: Women's Initiative Health (WHI) - Regional Center (RC) Project Number: 75N92021D00005 Name of PD/PI: Vitolins, M. Source of Support: NHLBI Year 10/15/2022 - 10/14/2023 1.8 Calendar months

Genesio Karere, PhD 2022-2024 /
Assistant Professor / Department of Internal Medicine, Section on Molecular Medicine 1 (total)
0 (1st/Sr)
MicroRNA biomarkers and pathways underlying response to exercise intervention in older adults

To identify a panel of circulating miRNA biomarkers and coordinately regulated miRNA-gene networks and pathways indicative of response to exercise in older obese adults from prior WF OAIC supported intervention studies. Specific aims: Using stored samples from the IASDR, 1) Identify a panel of circulating miRNA biomarkers indicative of response to exercise intervention in older adults with obesity; and 2) Identify coordinately regulated miRNA-gene networks and pathways underlying response to exercise intervention in older adults with obesity.

Jaime Hughes, PhD 2022-2024 /
Assistant Professor / Department of Implementation Science 7 (total)
Promoting healthy sleep-wake behaviors across a 24-hour cycle in frail older adults 5 (1st/Sr)

1) describe frail older adults' sleep-wake behaviors across a 24-hour cycle and explore the association between co-occurring poor sleep and low activity with functional status; 2) explore older adults' and providers' attitudes towards a comprehensive sleep-wake intervention, including treatment knowledge and preferences as well as potential intervention and implementation barriers and facilitators; and 3) explore the feasibility and acceptability of daytime intervention components for a comprehensive sleep-wake intervention in frail older adults in a pilot trial.

Past Scholars

Kathryn Callahan, MD, MS, Gerontology and Geriatric Medicine (2014-2018)
Candace Parker-Autry, MD, Obstetrics-Gynecology (2015-2019)
Rita Bakhru, MD, MS, Pulmonary, Critical Care, Allergy and Immunologic Diseases (2016-2021)
Jamie Justice, PhD, Gerontology and Geriatric Medicine (2017-2018)
Amber Brooks, MD, Anesthesiology (2017-2018)

Sam Lockhart, PhD, Gerontology and Geriatric Medicine (2018-2019)
Hariom Yadav, PhD, Molecular Medicine (2019-2021)
Jason Fanning, PhD, Health and Exercise Science (2019-2021)
Ellen Quillen, PhD, Department of Internal Medicine, Section on Molecular Medicine (2021-2023)
Atalie Thompson, MD, MPH, Department of Ophthalmology, Section on Glaucoma (2021-2023)

PILOT/EXPLORATORY PROJECTS (4 Pilot Projects Listed)

1. **Project Title:** **PESC 2020.1 Application of the Novel D3Cr Dilution Method to Better Understand Weight Loss Associated Changes in Muscle Mass and Physical Performance Among Older Adults with Obesity**

   Leader: **Kristen Beavers, PhD (Health & Exercise Science)**

   The number of older adults living with obesity is growing at an unprecedented rate. Intentional weight loss (WL) can reverse obesity but concerns develop as WL decreases muscle mass. Counter-intuitively, despite decreased muscle mass; older adults can significantly improve muscle strength, physical performance, and mobility following intentional WL. We posit these paradoxical observations originate from indirect bioimaging methods commonly used to approximate muscle mass in clinical research. In contrast to these methods, the D3-Creatine (D3Cr) dilution method directly measures whole-body muscle mass. Consequently, D3Cr muscle mass displays stronger associations with physical function (i.e. strength, physical performance, and mobility) than dual energy x-ray absorptiometry (DXA) lean mass. However, given the novelty of this method, D3Cr muscle mass has not been examined in an intentional WL RCT; thus, the effects of intentional WL on changes in D3Cr muscle mass remain unclear. To address this knowledge gap, and as an appropriate next step in this line of research, we propose to add the D3Cr muscle mass measure to the ongoing NIA and Claude D. Pepper Older Americans Independent Center supported RCT (NCT04076618), Incorporating Nutrition, Vest, Education and Strength Training trial (INVEST). This pilot will leverage the current INVEST assessment schedule to add the D3Cr muscle mass measure at baseline and six-months. The primary objective of this pilot is to determine the feasibility of the D3Cr muscle mass measure as part of a clinical WL trial. We hypothesize this method for measuring muscle mass will be feasible among participants enrolled in INVEST. Additionally, our secondary objectives aim to (i) quantify the associations between six-month change in D3Cr muscle mass and change in 1) physical function, and 2) computed tomography (CT) muscle density and cross-sectional area (CSA), and DXA lean mass among 30 INVEST participants and (ii) examine the ability of baseline D3Cr muscle mass, CT muscle density and CSA, and DXA lean mass to predict six-month change in physical function among 90 INVEST participants. Overall, we hypothesize stronger associations will be observed between change in D3Crmuscle mass and physical function, compared to DXA and CT; and that baseline D3Cr muscle mass will predict intervention-related changes in muscle physical function; and, to a greater degree than DXA or CT parameters. These data will provide first of its kind data identifying the feasibility of the D3Cr method in a WL trial, support a prior R01 application (AG070169; 35%; MPIs: Cawthon/K. Beavers), and provide a unique training opportunity for Dr. Miller (T32 AG033534).The number of older adults living with obesity is growing at an unprecedented rate. Intentional weight loss (WL) can reverse obesity but concerns develop as WL decreases muscle mass. Counter-intuitively, despite decreased muscle mass; older adults can significantly improve muscle strength, physical performance, and mobility following intentional WL. We posit these paradoxical observations originate from indirect bioimaging methods commonly used to approximate muscle mass in clinical research. In contrast to these methods, the D3-Creatine (D3Cr) dilution method directly measures whole-body muscle mass. Consequently, D3Cr muscle mass displays stronger associations with physical function (i.e. strength, physical performance, and mobility) than dual energy x-ray absorptiometry (DXA) lean mass. However, given the novelty of this method, D3Cr muscle mass has not been examined in an intentional WL RCT; thus, the effects of intentional WL on changes in D3Cr

muscle mass remain unclear. To address this knowledge gap, and as an appropriate next step in this line of research, we propose to add the D3Cr muscle mass measure to the ongoing NIA and Claude D. Pepper Older Americans Independent Center supported RCT (NCT04076618), Incorporating Nutrition, Vest, Education and Strength Training trial (INVEST). This pilot will leverage the current INVEST assessment schedule to add the D3Cr muscle mass measure at baseline and six-months. The primary objective of this pilot is to determine the feasibility of the D3Cr muscle mass measure as part of a clinical WL trial. We hypothesize this method for measuring muscle mass will be feasible among participants enrolled in INVEST. Additionally, our secondary objectives aim to (i) quantify the associations between six-month change in D3Cr muscle mass and change in 1) physical function, and 2) computed tomography (CT) muscle density and cross-sectional area (CSA), and DXA lean mass among 30 INVEST participants and (ii) examine the ability of baseline D3Cr muscle mass, CT muscle density and CSA, and DXA lean mass to predict six-month change in physical function among 90 INVEST participants. Overall, we hypothesize stronger associations will be observed between change in D3Crmuscle mass and physical function, compared to DXA and CT; and that baseline D3Cr muscle mass will predict intervention-related changes in muscle physical function; and, to a greater degree than DXA or CT parameters. In May 2022, baseline and six-month pre-dose/post-dose urine sample collect was completed on our target 24 participants, and samples were sent to Dr. Bill Evan's group (co-I) for processing. An abstract describing the quantification of total body muscle mass was submitted by Allison Avery (HES graduate student) accepted for presentation at the 2023 Southeastern American College of Sports Medicine (SEACSM) annual meeting (2.24.22; Greenville, SC). A second abstract describing associations between D3Cr muscle mass and DXA lean mass was submitted in December 2022 to the 2023 National American College of Sports Medicine (ACSM) annual meeting by Dr. Daniel Beavers. Collectively, data will serve the basis of Ms. Avery's thesis and corresponding manuscript (targeting submission to the Journal of Cachexia, Sarcopenia, and Muscle by April 2023).

2. Project Title: **PESC.2020.3 Real-world monitoring of limb loading for bone preservation during weight loss**

Leader: **Ashley Weaver, PhD, Katherine Hsieh, PhD (Biomedical Engineering)**

Obesity is a serious health concern among older adults that is associated with a loss of physical function and increased disability. Despite known medical complications that accompany obesity, there is reluctance to recommend intentional weight loss for older adults. This hesitation is partly due to reduced bone mineral density (BMD) that is observed with weight loss in this population, which can exacerbate the potential for development of osteoporosis and osteoporotic fracture. Reduced BMD because of weight loss is thought to occur due to less mechanical stress on the bone with reduced body weight. Although resistance training increases mechanical loading and attenuates BMD loss, compliance is challenging among older adults. A novel method to increase mechanical loading and improve BMD is through wearing weighted vests. This mode of increasing external load is currently being evaluated in an active OAIC-investigator led clinical trial (INVEST). However, the INVEST trial does not contain a direct measure of limb loading. The lack of direct limb loading metrics combined with uncertainty as to which loading metrics are associated with improved bone health likely contributes to observed variation in individual levels of preserved BMD with external loading interventions. Therefore, the overarching goal of this study is to evaluate the feasibility of using

innovative force-sensing insoles to compare limb-loading response between external loading during intentional weight loss and intentional weight loss alone. Force-sensing insoles are a portable, valid, and reliable wearable technology that measures force at the foot-shoe interface and provides an indicator of overall limb loading. These insoles can be used outside of a research or clinical setting and measures real-world activities for continuous hours. Leveraging the investigator's ongoing clinical trial, the primary goal of this study is to evaluate the feasibility of measuring daily limb loading using force-sensing insoles in 45 overweight or obese older adults (ages 60-85 years) in an intentional weight loss program combined with weighted vest use (VEST+WL) or resistance training (RT+WL) compared to intentional weight loss alone (WL). We hypothesize we will be able to recruit participants into the study with high adherence and satisfaction when wearing the insoles. We will also compare a) daily loading metrics with the insoles and b) femoral stress and strain between groups using CT imaging and finite element (FE) modeling. Last, we will identify associations and between limb loading metrics, changes in physical function and BMD change. The results of this study will expand the ability for remote home-based assessment and intervention delivery through force-sensing insoles, a necessity during the COVID-19 pandemic. Moreover, these findings will understand how to tailor external loading during weight loss for older adults to maximize their physical function and prevent disability associated with aging. Recent Updates: 44 participants have completed baseline insole assessment: 43 of those have been randomized, 37 participants have competed at-home wear, and 36 have completed follow up assessment. Data collection will be completed by the end of January 2023. Limb loading metrics (cumulative loading, loading rate, peak loading) are being processed and analyzed as data collection is on-going. Baseline data processing is completed, and at-home wear and follow-up data are currently being processed. Subject specific FE models of the dominant leg for randomized subjects have been generated. Simulations have been conducted using a well-validated full human body FE model in the mid-stance stance of the gait cycle to quantify how loads measured at the insole (foot) transfer to loading at the mid-femur level. From this, a translation value was derived to appropriately associate the insole forces to the mid-femur shaft of the isolated femoral FE model. Relationships derived from literature are being used to simulate the mid-femur in the maximal force configuration corresponding to each subject (i.e. heel strike or toe off), which was determined through visual inspection of the force v. time data. Subject-specific FE simulations are in progress, and virtual instrumentation is being developed for the FE models to extract strain metrics from the simulations. As data is being continuously processed, a feasibility paper (Aim 1 of the pilot) is currently drafted and will be submitted in Spring 2023.

3. Project Title: PESC.2020.4 (Ignition Pilot) MicroRNAs biomarkers and miRNA-gene networks associated with exercise-modulated weight loss

Leader: Genesio Karere, PhD (Internal Medicine)

The prevalence of overweight and obesity is increasing in the US and the world-wide. Obesity is associated with comorbidities, including cardiovascular disease, diabetes and hypertension. Exercise is a proven approach to weight loss and is accompanied by physiological changes in skeletal muscles. Identification of skeletal muscle miRNAs associated with weight loss and measured in circulating biofluids is important for elucidating molecular indicators of weight loss and exercise-modulated molecular mechanisms underlying the weight loss. MicroRNAs (miRNAs) are post-transcriptional regulators of gene expression that results in alteration of mRNA and protein abundance, impacting diverse biological processes including cell growth, proliferation, differentiation and apoptosis. These processes are fundamental to maintenance of

tissue cellular homeostasis. miRNAs expression is responsive to external stimuli, including exercise. Consequently, miRNAs are emerging potential biomarkers because are readily dateable in biofluids, including plasma/serum, saliva and urine, and potential therapeutic targets. Dysregulation of a few specific miRNAs (miR375. 126-3p, 663, 30c-p, 100-5, 27-3p, and 590-5p) has been implicated in weight loss after bariatric surgery (Doyon L et al. 2020). Inhibition of miR-324-5p resulted in reduction of adipose tissue and overall body weight loss in juvenile mice (Li D et al 2019). Other studies have revealed miRNAs dysregulated after exercise. For example, the expression of skeletal muscle-specific miRNAs (miR-1, miR-133a and b, miR-208b and miR-206) measured in plasma increased after chronic exercise (Banzet et al. 2013). In another study, serum circulating levels of miR-486 decreased after chronic versus acute exercise, and the expression was negatively correlated with VO2 max (Aoi et al. 2013). Together these studies separately suggest that miRNAs are responsive to weight loss and exercise. However, a comprehensive study revealing miRNA biomarkers of and molecular mechanisms underlying weight loss due to exercise is lacking. The objective of the proposed pilot study is to evaluate the feasibility of using miRNAs to predict weight loss after exercise and to provide potential mechanistic insights. We hypothesize that miRNAs are potential biomarkers predicative of weight loss after exercise, providing potential insights to molecular mechanisms underlying exercise outcomes.

We will test the hypothesis using the following specific aims:

1. Identify circulating miRNAs in plasma that correlate with weight loss after exercise. We will use small RNA Seq to assess miRNAs in plasma at baseline and post intervention in two groups: a group that showed weight loss after exercise (n= 5 pairs) and another group that exhibited no change (n= 5 pairs). Outcomes will be identification of miRNAs differentially expressed between baseline and post interventions in each group and miRNAs that are differentially expressed between the groups post intervention.

2. Identify skeletal muscle miRNA-gene regulatory networks associated with weight loss. We use the same study design in Aim 1 and small RNA Seq to identify differentially expressed miRNAs. In addition, we will identify miRNA-gene regulatory networks by integrating miRNA data and existing skeletal muscle transcriptomic data from the same individuals. Outcomes will be identification of skeletal muscle differentially expressed miRNAs and miRNA-gene networks dysregulated in exercise-modulated weight loss, providing potential biomarkers and insights to molecular mechanisms underlying weight loss after exercise.

4. Project Title: **PESC.2021.1 Epigenetics of an intensive lifestyle intervention: the Look AHEAD study.**

Leader: **Lindsay Reynolds, PhD (Epidemiology and Prevention), Mark Espeland, PhD (Gerontology and Geriatric Medicine), Timothy Howard, PhD (Biochemistry), Carl Langefeld, PhD (Biostatistics)**

Diabetes and obesity increase the risk of age-related health deficits and may accelerate epigenetic aging. Lifestyle interventions promoting weight loss, such as the Action for Health in Diabetes (Look AHEAD) trial intervention, can potentially buffer against decline in age-related health status in overweight or obese adults with type 2 diabetes. However, significant variation exists among who benefits from intensive lifestyle intervention (ILI) programs. Better understanding of the biological impact of ILI could help lay the foundation for personalized

medicine approaches to predict individual responses to ILI. Epigenetic aging measures (the difference between a DNA methylation-based measure of biological age vs. chronological age) capture aspects of biological aging, and have potential as biomarkers of impact of ILI. We hypothesize that an ILI is more beneficial for participants with higher baseline measures of epigenetic aging, and that changes in epigenetic aging mediate benefits of ILI on accumulation of health deficits over time. To test our hypothesis, we are proposing to test epigenetic aging measures as predictors and biomarkers of the impact of the Look AHEAD ILI in adults with diabetes and obesity. We will assess baseline epigenetic age acceleration as a predictor of impact of an ILI on frailty in adults with diabetes and obesity. The goal of this pilot study is to generate preliminary data establishing feasibility and estimates for sample size calculations for an R01 application. We will generate epigenomic data and DNA methylation-based estimates of epigenetic aging in samples from a subset (n=32) of participants of the Look AHEAD trial at baseline and ~16 years after baseline. We will generate descriptive statistics for baseline epigenetic aging measures (epigenetic age acceleration and rate of aging) and for the change in epigenetic aging measures from baseline to Year 16 visit. Baseline epigenetic aging and change in epigenetic aging from baseline to Year 16 visit will be compared between intervention arms: ILI (n=16) vs. diabetes support and education (control condition; n=16). We will also compute associations of baseline epigenetic aging measures with change in frailty index from baseline to Year 16 visit (n=32). Our experienced and multi-disciplinary team, led by an Early Career Investigator, is well-positioned to perform the proposed pilot study, and future studies aiming to better understand the biological basis of benefit of an intensive lifestyle intervention for aging adults with diabetes who are overweight or obese. Most recently the pilot study has received the samples, DNA extracted, methylation arrays run, methylation data generated, DNAm GrimAge has been calculated, and data analysis has begun to generate the pilot data to support planned R01 proposal to be submitted in the fall of 2023.

DEVELOPMENT PROJECTS (0 Development Projects Listed)

No development projects.

RESEARCH (0 Projects Listed)

PUBLICATIONS

2024

2023

1. **Semaglutide in HFpEF across obesity class and by body weight reduction: a prespecified analysis of the STEP-HFpEF trial.**
   Borlaug BA, Kitzman DW, Davies MJ, Rasmussen S, Barros E, Butler J, Einfeldt MN, Hovingh GK, M?ller DV, Petrie MC, Shah SJ, Verma S, Abhayaratna W, Ahmed FZ, Chopra V, Ezekowitz J, Fu M, Ito H, Lelonek M, Melenovsky V, N??ez J, Perna E, Schou M, Senni M, van der Meer P, Von Lewinski D, Wolf D, Kosiborod MN
   Nat Med, 2023 Sep, 29(9): 2358-2365
   https://doi.org/10.1038/s41591-023-02526-x | PMID: 37635157 | PMCID: PMC10504076
   Citations: 1 | AltScore: NA
2. **Targeting Obesity to Optimize Weight Loss in Cardiac Rehabilitation: A PILOT STUDY.**
   Brinkley TE, Hsu FC, Bowman BM, Addison T, Kitzman DW, Houston DK
   J Cardiopulm Rehabil Prev, 2023 Jan 1, 43(1): 39-48
   https://doi.org/10.1097/HCR.0000000000000750 | PMID: 36441136 | PMCID: PMC9797431
   Citations: NA | AltScore: 0.25
3. **A Randomized, Controlled Trial of Resistance Training Added to Caloric Restriction Plus Aerobic Exercise Training in Obese Heart Failure With Preserved Ejection Fraction.**
   Brubaker PH, Nicklas BJ, Houston DK, Hundley WG, Chen H, Molina AJA, Lyles WM, Nelson B, Upadhya B, Newland R, Kitzman DW
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   https://doi.org/10.1161/CIRCHEARTFAILURE.122.010161 | PMID: 36314122 | PMCID: PMC9974606
   Citations: 6 | AltScore: 46.8
4. **Is an MRI-derived anatomical measure of dementia risk also a measure of brain aging?**
   Casanova R, Anderson AM, Barnard RT, Justice JN, Kucharska-Newton A, Windham BG, Palta P, Gottesman RF, Mosley TH, Hughes TM, Wagenknecht LE, Kritchevsky SB
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   Citations: 1 | AltScore: 13.2
5. **Assessment of an embedded primary care-derived electronic health record (EHR) frailty index (eFI) in older adults with acute myeloid leukemia.**
   Cheng JJ, Tooze JA, Callahan KE, Pajewski NM, Pardee TS, Reed DR, Klepin HD
   J Geriatr Oncol, 2023 Sep, 14(7): 101509
   https://doi.org/10.1016/j.jgo.2023.101509 | PMID: 37454532
   Citations: NA | AltScore: 23.05
6. **Risedronate use may blunt appendicular lean mass loss secondary to sleeve gastrectomy: Results from a pilot randomized controlled trial.**
   Flores LE, Beavers KM, Beavers DP, Greene KA, Madrid DA, Miller RM, Ard JD, Bilek LD, Weaver AA
   JCSM Rapid Commun, 2023 Jan-Jun, 6(1): 18-25
   https://doi.org/10.1002/rco2.72 | PMID: 37273449 | PMCID: PMC10236921

Citations: 1 | AltScore: NA

7. **Impact of Geroscience on Therapeutic Strategies for Older Adults With Cardiovascular Disease: JACC Scientific Statement.**
   Forman DE, Kuchel GA, Newman JC, Kirkland JL, Volpi E, Taffet GE, Barzilai N, Pandey A, Kitzman DW, Libby P, Ferrucci L
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   https://doi.org/10.1016/j.jacc.2023.05.038 | PMID: 37389519 | PMCID: PMC10414756
   Citations: NA | AltScore: 22.75
8. **Serum factors mediate changes in mitochondrial bioenergetics associated with diet and exercise interventions.**
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9. **Vitamin D Supplementation and Muscle Power, Strength and Physical Performance in Older Adults: A Randomized Controlled Trial.**
   Houston DK, Marsh AP, Neiberg RH, Demons JL, Campos CL, Kritchevsky SB, Delbono O, Tooze JA
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   https://doi.org/10.1016/j.ajcnut.2023.04.021 | PMID: 37084814 | PMCID: PMC10447505
   Citations: NA | AltScore: 25.75
10. **Effect of Baseline BMI and IL-6 Subgroup Membership on Gait Speed Response to Caloric Restriction in Older Adults with Obesity.**
    Hsieh KL, Neiberg RH, Beavers KM, Rejeski WJ, Messier SP, Nicklas BJ, Beavers DP
    J Nutr Health Aging, 2023, 27(4): 285-290
    https://doi.org/10.1007/s12603-023-1909-1 | PMID: 37170436
    Citations: NA | AltScore: 2.1
11. **Factors associated with falls in older adults: A secondary analysis of a 12-month randomized controlled trial.**
    Hsieh KL, Speiser JL, Neiberg RH, Marsh AP, Tooze JA, Houston DK
    Arch Gerontol Geriatr, 2023 May, 108: 104940
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    Citations: 1 | AltScore: 2
12. **Rate-Adaptive Pacing for Heart Failure With Preserved Ejection Fraction.**
    Kitzman DW, Upadhya B, Pandey A
    JAMA, 2023 Mar 14, 329(10): 797-799
    https://doi.org/10.1001/jama.2023.1053 | PMID: 36871286 | PMCID: PMC10265352
    Citations: 2 | AltScore: NA
13. **Associations of physical function and body mass index with functional brain networks in community-dwelling older adults.**
    Laurienti PJ, Miller ME, Lyday RG, Boyd MC, Tanase AD, Burdette JH, Hugenschmidt CE, Rejeski WJ, Simpson SL, Baker LD, Tomlinson CE, Kritchevsky SB
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    https://doi.org/10.1016/j.neurobiolaging.2023.03.008 | PMID: 37054493 | PMCID: PMC10227726
    Citations: NA | AltScore: NA
14. **Associations of interleukin-6 with functional trajectories in older adults with cancer: Findings from the Health, Aging, and Body Composition Study.**

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Exp Gerontol, 2023 Jun 15, 177: 112185
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Citations: NA | AltScore: NA

15. **Effect of exercise modality and weight loss on changes in muscle and bone quality in older adults with obesity.**
Madrid DA, Beavers KM, Walkup MP, Ambrosius WT, Rejeski WJ, Marsh AP, Weaver AA
Exp Gerontol, 2023 Apr, 174: 112126
https://doi.org/10.1016/j.exger.2023.112126 | PMID: 36796657 | PMCID: PMC10033433
Citations: NA | AltScore: 29.5
16. **A Liquid Biopsy-Based Approach to Isolate and Characterize Adipose Tissue-Derived Extracellular Vesicles from Blood.**
Mishra S, Kumar A, Kim S, Su Y, Singh S, Sharma M, Almousa S, Rather HA, Jain H, Lee J, Furdui CM, Ahmad S, Ferrario CM, Punzi HA, Chuang CC, Wabitsch M, Kritchevsky SB, Register TC, Deep G
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https://doi.org/10.1021/acsnano.3c00422 | PMID: 37224410
Citations: NA | AltScore: 1.5
17. **Dual Roles of Cardiorespiratory Fitness and Fatigability in the Life-Space Mobility of Older Adults: The Study of Muscle, Mobility and Aging (SOMMA).**
Moored KD, Qiao YS, Rosso AL, Toledo FGS, Cawthon PM, Cummings SR, Goodpaster BH, Kritchevsky SB, Glynn NW
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https://doi.org/10.1093/gerona/glad037 | PMID: 36715332 | PMCID: PMC10395561
Citations: NA | AltScore: 2.6
18. **Physical activity and relationship to physical function, quality of life, and cognitive function in older patients with acute decompensated heart failure.**
Nelson MB, Shiroma EJ, Kitzman DW, Duncan PW, Reeves GR, Whellan DJ, Mentz RJ, Chen H, Pastva AM
Am Heart J, 2023 Feb, 256: 85-94
https://doi.org/10.1016/j.ahj.2022.11.002 | PMID: 36372251 | PMCID: PMC9840656
Citations: NA | AltScore: 21.3
19. **Role of a Novel Self-Reported Questionnaire for Frailty Assessment in HFpEF.**
Pandey A, Kitzman DW
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https://doi.org/10.1016/j.jchf.2023.01.026 | PMID: 37019556 | PMCID: PMC10283081
Citations: NA | AltScore: 10
20. **Frailty and Effects of a Multidomain Physical Rehabilitation Intervention Among Older Patients Hospitalized for Acute Heart Failure: A Secondary Analysis of a Randomized Clinical Trial.**
Pandey A, Kitzman DW, Nelson MB, Pastva AM, Duncan P, Whellan DJ, Mentz RJ, Chen H, Upadhya B, Reeves GR
JAMA Cardiol, 2023 Feb 1, 8(2): 167-176
https://doi.org/10.1001/jamacardio.2022.4903 | PMID: 36598761 | PMCID: PMC9857661
Citations: 7 | AltScore: 89.1
21. **Associations between skeletal muscle energetics and accelerometry-based performance fatigability: Study of Muscle, Mobility and Aging.**

Qiao YS, Santanasto AJ, Coen PM, Cawthon PM, Cummings SR, Forman DE, Goodpaster BH, Harezlak J, Hawkins M, Kritchevsky SB, Nicklas BJ, Toledo FGS, Toto PE, Newman AB, Glynn NW
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https://doi.org/10.1111/acel.14015 | PMID: 37843879
Citations: NA | AltScore: NA

22. **An Examination of Whether Diabetes Control and Treatments Are Associated With Change in Frailty Index Across 8 Years: An Ancillary Exploratory Study From the Action for Health in Diabetes (Look AHEAD) Trial.**
Simpson FR, Justice JN, Pilla SJ, Kritchevsky SB, Boyko EJ, Munshi MN, Ferris CK, Espeland MA, Look AHEAD Research Group
Diabetes Care, 2023 Mar 1, 46(3): 519-525
https://doi.org/10.2337/dc22-1728 | PMID: 36542537 | PMCID: PMC10020016
Citations: 4 | AltScore: NA
23. **Performance of Cox regression models for composite time-to-event endpoints with component-wise censoring in randomized trials.**
Speiser JL, Ambrosius WT, Pajewski NM
Clin Trials, 2023 Oct, 20(5): 507-516
https://doi.org/10.1177/17407745231177046 | PMID: 37243355 | PMCID: PMC10524851
Citations: NA | AltScore: NA
24. **Association Between Contrast Sensitivity and Physical Function in Cognitively Healthy Older Adults: The Brain Networks and Mobility Function Study.**
Thompson AC, Chen H, Miller ME, Webb CC, Williamson JD, Marsh AP, Hugenschmidt CE, Baker LD, Laurienti PJ, Kritchevsky SB
J Gerontol A Biol Sci Med Sci, 2023 Aug 2, 78(8): 1513-1521
https://doi.org/10.1093/gerona/glad060 | PMID: 36800312 | PMCID: PMC10395565
Citations: NA | AltScore: 0.25
25. **The relationship between visual function and physical performance in the Study of Muscle, Mobility and Aging (SOMMA).**
Thompson AC, Johnson E, Miller ME, Williamson JD, Newman AB, Cummings S, Cawthon P, Kritchevsky SB
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https://doi.org/10.1371/journal.pone.0292079 | PMID: 37756354 | PMCID: PMC10529600
Citations: NA | AltScore: NA
26. **Mechanisms of Exercise Intolerance in Chronic Heart Failure With Preserved Ejection Fraction: Challenging the Traditional Hypothesis.**
Upadhya B, Kitzman DW
Chest, 2023 Sep, 164(3): 574-577
https://doi.org/10.1016/j.chest.2023.06.019 | PMID: 37689469
Citations: NA | AltScore: NA

EXTERNAL ADVISORY BOARD MEMBERS

Nir Barzilai
Albert Einstein College of Medicine
Serving since 2012 (12 years)

Heather Whitson
Duke University
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Kirk Erickson
University of Pittsburgh
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Nathan LaBrasseur
Mayo Clinic
Serving since 2018 (6 years)

RECOGNITION AND AWARDS (2023-2024)

Recognition and Awards not specified.

MINORITY RESEARCH

General Brief Description of Minority Activities:

The Maya Angelou Research Center for Health Equality (MA-RCHE) has been established by the WFUSM to address issues related to racial and ethnic health disparities. Its overarching goal is to enhance wellness, improve quality of life, and reduce the burden of disease in underrepresented minorities through a comprehensive program in four core areas: health education, career/leadership development, research, and dissemination/application of new research findings for more effective and efficient health care approaches.

A key feature of the MA-RCHE is its model campus/community partnership involving WFUSM, the Reynolda Campus of Wake Forest University, Winston-Salem State University (a historically Black college/university) and the Forsyth County community at-large. This partnership brings the vast experiences, knowledge base and resources of each partner to bear on health problems of underrepresented minorities.

Minority Trainee(s):

- Gagan Deep, PhD, Associate Professor, Cancer Biology
  PESC Pilot 2019.1 Isolation and molecular characterization of exosomes secreted by visceral adipose tissue
- Genesio Karere, PhD, Assistant Professor, Department of Internal Medicine, Section on Molecular Medicine
  Current REC scholar Project title: MicroRNA biomarkers and pathways underlying response to exercise intervention in older adults
- Raghunatha Yammani, PhD, Associate Professor, Internal Medicine, Molecular Medicine
  PESC 2019.2 Is Restoring Protein Homeostasis A Viable Therapy For Age-Related Osteoarthritis?

Minority Grant(s):

1. Project Title: **PROSOCIAL BEHAVIOR AND EXERCISE AMONG OLDER ADULTS**

Leader(s): **FOY, CAPRI G**
WAKE FOREST UNIVERSITY HEALTH SCIENCES
NIH R21AG027413 / (2008-2011)

DESCRIPTION (provided by applicant): Regular physical activity has been shown to enhance physical function and health-related quality of life and reduce morbidity and mortality among older adults. Unfortunately, compliance rates to physical activity programs are distressingly low, even among asymptomatic populations. Many traditional exercise interventions do not provide the self-regulatory skills necessary for long-term behavioral change. These issues become more prominent as the population of older Americans continues to increase. Although only a small percentage of older adults engage in habitual physical activity, there are episodic charity events involving moderate physical activity that attract large numbers of participants of all age ranges. These actions are a form of prosocial behavior, defined as voluntary, intentional behavior that results in benefits for another. The opportunity to help others seems to be a motive to inspire these individuals to at least engage in acute moderate physical activity. In previous

pilot work (Section 4.1.a), we found that participants randomized into a prosocial behavior physical activity group demonstrated increased physical activity at 3 months compared to those in a standard exercise group. Our current research question contemplates whether prosocial behavior may be implemented as a viable behavioral incentive for long-term physical activity. Therefore, the primary aim of this investigation is to determine the feasibility of conducting a 9-month prosocial behavior intervention to increase physical activity among 80 underactive older adults. To our knowledge, the use of prosocial behavior as a motivational tool for physical activity has not been investigated, and represents a novel approach. The PBPA program will allow participants to earn boxes of food for donation to the Second Harvest Food Bank of Northwest North Carolina based upon their weekly physical activity. Other specific aims include determining the ability to successfully recruit participants into the study, the ability of participants to adhere to the PBPA program, and the ability to retain participants throughout the study. If successful, preliminary data from this study will be used to seek R01 funding to conduct a fully powered, longitudinal trial.

2. Project Title: **MOBILE INTERVENTION TO REDUCE PAIN AND IMPROVE HEALTH (MORPH) IN OBESE OLDER ADULTS**

Leader(s): **BROOKS, AMBER K ; FANNING, JASON ;**
WAKE FOREST UNIVERSITY HEALTH SCIENCES
NIH R21AG058249 / (2017-2020)

PROJECT SUMMARY Chronic pain has emerged as an urgent age-related health issue that significantly compromises physicalfunctioning and quality of life, with the adverse effects amplified by both obesity and sedentary behavior. The annualcost of pain in the United States is nearly 30% higher than the combined costs of cancer and diabetes. In 2016, the NIHcalled for a National Pain Strategy to: 1) expand non-pharmacological treatment options in older adults, who areparticularly susceptible to the side effects of opioid and other pain medications; 2) develop accessible treatments that aretailored to individuals; and 3) increase the development of self-management programs for chronic pain. The purpose ofthis R-21 is to develop and test the feasibility and acceptability of a novel, patient-centered intervention to reducechronic pain and improve physical functioning in older adults, leveraging the combination of telecoaching andindividually-adaptive mHealth tools to decrease both body mass and sedentary behavior. The proposal consists oftwo phases. The first phase will use an iterative user-centered design process to develop the mHealth application, to adaptthe weight loss and sedentary behavior components of the intervention to a telecoaching model, and to evaluate theusability and feasibility of the intervention for obese, older adults with chronic pain. In the second phase we will conducta pilot randomized controlled trial to provide initial evidence for effect sizes (pain and physical function) associated withthe proposed intervention, and to estimate the sample size needed for a full scale randomized controlled trial design thatcompare the effects of the intervention versus usual care on pain ratings and physical function in overweight/obese olderadults with chronic pain.

3. Project Title: **THE ENRGISE STUDY**

Leader(s): **PAHOR, MARCO ; AMBROSIUS, WALTER T ;**
UNIVERSITY OF FLORIDA
NIH U01AG050499 / (2015-2019)

DESCRIPTION (provided by applicant): Growing evidence from our group and others shows that low-grade chronic inflammation, characterized by elevations in plasma C-reactive protein, tumor necrosis factor alpha, and particularly Interleukin-6 (IL-6), is an independent risk factor o disability, impaired mobility, and lower walking speed. Low-grade chronic inflammation is a modifiable risk factor. However, it is unknown whether interventions that reduce the levels of inflammatory markers per se improve mobility, or avert decline in mobility in older persons. To address this gap in evidence we propose the randomized clinical trial ENRGISE (ENabling Reduction of low-Grade Inflammation in SEniors) to test the ability of anti-inflammatory interventions for preventing major mobility disability by improving or preserving walking ability. We have maximized the public health impact of our proposed interventions by selecting interventions that are safe, tolerable, acceptable, and affordable for vulnerable older persons. Based on an extensive literature review, we propose to test the efficacy vs. placebo of the angiotensin receptor blocker losartan and omega-3 polyunsaturated fatty acids in the form of fish oil, alone and in combination. Both angiotensin receptor blockers and omega-3 polyunsaturated fatty acids have shown to reduce IL-6 in clinical trials and preliminary data suggest that they may improve physical function. We plan to recruit older persons who are at risk for, or with, mobility impairment, as measured by slow gait speed and self-reported mobility difficulty, and who have elevated levels of IL-6, the marker most consistently associated with mobility limitations. Preliminary data regarding feasibility need to be gathered before such a tria can be effectively designed and implemented. We propose to conduct a feasibility phase that includes performing meta-analyses of existing trials and cohorts, and conducting a pilot trial to assess the effects of the interventions on several inflammatory markers and walking speed. This will allow us to refine the design, recruitment yields, target population, adherence, retention, tolerability, sample-size, and cost for the main ENRGISE trial. We will assemble the multicenter research infrastructure needed for the ENRGISE pilot and main trials, including the biorepository, and we will develop the materials needed for implementing the trials, including the protocol, manual of operations, data and safety monitoring plan, forms, quality control and quality assurance plan, and recruitment and retention materials.