Title: Effects of Dietary Protein Intake and Resistance Training on Retention of Fat Free Mass during Weight Loss in Adults over 50 with Obesity

ClinicalTrials.gov ID: NCT04014296

Document Date: September 27, 2023

Human Subjects Protocol (HSP)

Form Version: February 1, 2017

- You are applying for IRB review of the research described in this form.
- To avoid delay, respond to all items in order and include all required approvals and documents. For more tips, see the UAB IRB website.
- To complete the form, click the underlined areas and type or paste in your text; double-click checkboxes to check/uncheck.
- All responses should be Times New Roman, Bold, and Underlined.
- Submit all materials to AB 470, 701 20th Street South, Birmingham, AL 35294-0104.

Indicate the type of review you are applying for:

☒ Convened (Full) IRB ***-OR-***

☐ Expedited - See the Expedited Category Review Sheet, and indicate the category(ies) here:

☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

1. IRB Protocol Title: Effects of Dietary Protein Intake and Resistance Training on Retention of Fat Free Mass during Weight Loss in Adults over 50 with Obesity

2. Investigator and Contact Person

a. Name of Principal Investigator: **Drew Sayer**

Degree(s)/Title:PhD BlazerID: **sayerd**

Dept/Div: **Nutrition Sciences** Mailing Address: **Webb 634, 1675 University Blvd**

UAB ZIP: **35294**

Phone: **205-354-8950** Fax: **205-975-4065** E-mail: **sayerd@uab.edu**

b. Name of Contact Person: **Caroline Cohen** Title: **Clinical Trials Administrator**

Phone: **205-873-8241**

E-mail: **cwyoder@uab.edu** Fax: **205-975-4065**

INVESTIGATOR ASSURANCE STATEMENT & SIGNATURE

By my signature as Principal Investigator, I acknowledge my responsibilities for this Human Subjects Protocol, including:

- Certifying that I and all key personnel comply with reporting requirements of the UAB Conflict of Interest Review Board;
- Certifying that the information, data, and/or specimens collected for the research will be used, disclosed and maintained in accordance with this protocol and UAB policies;
- Following this protocol without modification unless (a) the IRB has approved changes prior to implementation or (b) it is necessary to eliminate an apparent, immediate hazard to a participant(s);
- Verifying that all key personnel listed on the protocol have completed initial IRB training and will complete continuing IRB training as required;
- Verifying that all personnel are licensed/credentialed for the procedures they will be performing, if applicable;
- Certifying that I and all key personnel have read the *UAB Policy/Procedure to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB, Institutional Officials, and Regulatory Agencies* and understand the procedures for reporting;
- Applying for continuing review of the protocol at least annually unless directed by the IRB to apply more frequently;
- Conducting the protocol as represented here and in compliance with IRB determinations and all applicable local, state, and federal law and regulations; providing the IRB with all information necessary to review the protocol; refraining from protocol activities until receipt of initial and continuing formal IRB approval.

Signature of Investigator: _____ **Date:** **10/16/19**

3. Protocol Personnel

Including the PI, list all key personnel (each individual involved in the design and conduct of this protocol). See the Key Personnel Flowchart.

Complete the UAB (3.a.) and non-UAB (3.b) tables, as applicable. Use the checkboxes to show each individual's role, whether the individual has financial interests as defined by the UAB CIRB, and briefly describe the individual's protocol responsibilities and qualifications to perform those responsibilities. **Insert additional rows as needed.**

FDA: For studies involving investigational drugs, list all investigators who will be listed on FDA Form 1572 and include a copy of the 1572. Send the IRB a copy of Form 1572 any time you update the form with the FDA.

a. UAB Personnel (includes UAB affiliates and Children's of Alabama personnel)

Name, Degree, and Dept.	Blazer ID	Role	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)
Name: **Drew Sayer** Degree: **PhD** Department: **Nutrition Sciences**	**sayerd**	Principal Investigator	☒No ☐Yes	**Dr. Sayer will have responsibility for directing and overseeing all aspects of the study. He will form and lead study team meetings of sub-investigators and other research staff. The study team will monitor all aspects of the of the study conduct including recruitment and enrollment, protocol execution, regulatory compliance, safety, and data collection. Dr. Sayer will have primary responsibility for submitting progress reports to the sponsor and IRB offices as well as decisions involving adjustments to the protocol and budget.**
Name: **James Hill** Degree: **PhD** Department: **Nutrition Sciences**	**hillj**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Hill will act as the primary mentor to the PI for this project (Dr. Sayer). Dr. Hill will be involved with data analysis, preparation of manuscripts and presentation of study results.**
Name: **Kenneth Saag** Degree: **MD, MSc** Department: **Clinical Immunology & Rheumatology**	**ksaag**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Saag will act as co-mentor to the PI of this project (Dr. Sayer). Dr. Saag will be involved with data analysis, preparation of manuscripts, and presentation of study results.**
Name: **Marcas Bamman** Degree: **PhD** Department: **Cell Development & Integrative Biology**	**mbamman**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Bamman will act as co-mentor to the PI of this project (Dr. Sayer). Dr. Bamman will be involved with data analysis, preparation of manuscripts, and presentation of study results.**
Name: **Barbara Gower** Degree: **PhD** Department: **Nutrition Sciences**	**bgower**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Gower will act as co-mentor to the PI of this project (Dr. Sayer). Dr. Gower will be involved with data analysis, preparation of manuscripts, and presentation of study results.**
Name: **Cynthia Brown** Degree: **MD** Department: **Gerontology, Geriatrics, & Palliative Care**	**cbrownmd**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Brown will act as co-mentor to the PI of this project (Dr. Sayer). Dr. Brown will be involved with data analysis, preparation of manuscripts, and presentation of study**

				results. Dr. Brown will also be acting as study physician. She will evaluate all safety endpoints and will make all safety-related medical decisions concerning study participants.
Name: **Tapan Mehta** Degree: **PhD** Department: **Health Services Administration**	**tapan**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Mehta is an obesity researcher and a data scientist with several years of experience in biostatistics. He has expertise in the design and analysis of adaptive clinical trials such as the SMART in the current project. He will assist Dr. Sayer with the analysis of research data and will contribute to the preparation of manuscripts and presentation of study results.**
Name: **Rob Motl** Degree: **PhD** Department: **Health Services Administration**	**robmotl**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Motl is an expert in the measurement of physical activity and physical functioning. His primary role in the study conduct will be to assist and train study team members with supervised exercise training programs, physical functioning tests (Time Up and Go and 6 Minute Walk), accelerometer data collection and analysis, and resting metabolic rate measurements.**
Name: **Irfan Asif** Degree: **MD** Department: **Family and Community Medicine**	**amasif**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Asif is the Chairman of the Dept. of Family and Community Medicine. Dr. Asif is an active collaborator with Drs. Sayer and Hill on a number of projects to enhance obesity treatment and research options within the UAB Family Medicine patient population. We anticipate that many participants for this project will be recruited from the UAB Family Medicine patient population. Patient recruitment letters will be sent from Dr. Asif.**
Name: **Caroline Cohen** Degree: **PhD, RD, LD** Department: **Nutrition Sciences**	**cwyoder**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Dr. Cohen will serve as the study coordinator and Study Dietitian. She will coordinate the recruiting of participants, obtaining informed consent, coordinating testing visits, and managing data. She will also coordinate and take primary responsibility for the delivery of the weight loss and weight loss maintenance interventions. Dr. Cohen will report to Dr. Sayer.**
Name: **Katherine (Katie) Ellison** Degree: **MS, RD, LD** Department: **Nutrition Sciences**	**vidya25**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Ms. Ellison will assist in recruiting participants, obtaining informed consent, and collecting data. She will assist Dr. Sayer and Dr. Cohen as needed. Katie will report to Dr. Sayer.**

Name: **Julianne Clina** Degree: **BS** Department: **Nutrition Sciences**	**jclina**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Ms. Clina will assist in recruiting participants, obtaining informed consent, and collecting data. She will assist Dr. Sayer and Dr. Cohen as needed. Julianne will report to Dr. Sayer.**

b. Non-UAB Personnel Relying on UAB IRB - If you are requesting that the UAB IRB serve as the IRB of record for anyone not affiliated with UAB, list these individuals below.

Name and Degree	From Institution with or without own IRB?	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)
Name: _____ Degree: _____ Institution: _____ Email: _____	☐Has own IRB but requests that UAB IRB serve as IRB of record?***-OR-*** ☐Does not have own IRB and needs to rely on UAB IRB.	☐No ☐Yes	_____

***Financial Interest** – for each individual listed above, answer **Yes** or **No** as to whether the individual or an immediate family member has any of the following:

- An ownership interest, stock options, or other equity interest related to the investigator's institutional responsibilities of any value.
- Compensation greater than $5,000 in the previous two years when aggregated for the immediate family
- Proprietary interest including, but not limited to, a patent, trademark, copyright, or licensing agreement.
- Board of executive relationship, regardless of compensation.
- Any other Financial Interest as defined by the UAB CIRB.

UAB Personnel: If the individual or his/her spouse or dependent child has a Financial Interest, a disclosure has to be made to the UAB CIRB. A completed CIRB evaluation has to be available before the IRB can complete its review.

Non-UAB Personnel: If the individual has a Financial Interest, ***include a copy of the report from his/her own institution's conflict of interest review with this submission to the UAB IRB.***

c. Do the investigators listed above include any students using this research for their thesis or dissertation?

☐ No, continue with Item 3.d.
☒ Yes, complete the following

Student Name	Thesis/Dissertation Title
Katherine Ellison	**Using the Multiphase Optimization Strategy and Sequential Multiple Assignment Randomized Trials to Treat Obesity**

d. Is the principal investigator a student, fellow, or resident? ☐Yes ☒No

If Yes, complete items below and obtain signature of faculty advisor or supervisor:

Supervisor's Name: _____
Degree(s) / Job Title: _____
Additional Qualifications pertinent to the protocol: _____
Telephone: _____
E-Mail: _____
Signature: _____

e. Describe the principal investigator's activities related to this protocol and provisions made by the PI to devote sufficient time to conduct the protocol: **Dr. Sayer will have responsibility for directing and overseeing all aspects of the study. He will form and lead study team meetings of sub-investigators and other research staff. Dr. Sayer will have primary responsibility for submitting progress reports to the sponsor and IRB offices as well as decisions involving adjustments to the protocol**

and budget. He will ensure that all members of the research team are following the protocol and that the UAB IRB standards are upheld.

f. Is medical supervision required for this research? ☒Yes ☐No

If Yes, who will provide the medical supervision?

☐ PI will provide ***-OR-***

☒ Other:

Name: **Cynthia Brown** Telephone: **(205) 934-9261**

If other than PI, obtain signature of person providing medical supervision:

Signature Cynthia J. Brown MD

g. Describe your process for ensuring all key personnel are adequately informed about the protocol and their research-related duties and functions: **All members of the investigative team have had active input into the protocol and their proposed roles and responsibilities, and have reviewed all written materials to this study (e.g. consent form, IRB application, etc). Upon Approval from the IRB, the protocol will be given to the research team at the beginning of the trial, and both the study protocol and everyone's responsibilities will be reviewed as a group before the study begins. Prior to beginning participant enrollment, Dr. Sayer will ensure that all staff are properly trained in their duties. Study team members will be updated if any changes are initiated to the protocol.**

4. Funding

Is this protocol funded? ☒Yes ☐No

If No, specify that costs of the protocol will be covered by funds from the UAB department or other source named: _____

If Yes, attach one copy of completed application or request for funding sent to sponsor, and complete a-d.

a. Title of Grant, Contract, or Agreement: **Effects of Dietary Protein Intake and Resistance Training on Retention of Fat Free Mass during Weight Loss in Postmenopausal Women with Obesity**

b. UAB PI of Grant, Contract, or Agreement: **Drew Sayer, PhD**

c. Office of Sponsored Programs (OSP) Assigned Number: **N/A, internal award**
(If not yet available, enter "Pending" and provide upon receipt from OSP.)

d. Sponsor, Funding Route:
(Check and describe all that apply)
(If subaward, list both the funding source and the institution receiving the direct award)

☐ Gov't Agency or Agencies—Agency name(s): _____
- ☐ Department of Defense (DoD): Identify DoD component: _____
- ☐ Department of Energy (DOE)
- ☐ Department of Justice (DOJ)
- ☐ Department of Education

☐ NIH Cooperative Group Trial - Group name: _____

☐ Private Nonprofit (e.g., Foundation) - Name: _____

☐ Industry, investigator-initiated - Name: _____
Describe the funding arrangement: _____
NOTE: The UAB IRB typically only reviews industry-sponsored protocols that are investigator initiated or when the protocol qualifies for expedited review or involves gene therapy.

☒ UAB Departmental/Division Funds—Specify: **UAB Nutrition Obesity Research Center (NORC), Dr. Sayer start-up account**

5. Locations Involved

a. Indicate all performance sites that will provide space, services, or facilities for the conduct of this protocol.

☒ UAB Hospital
☐ UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital
☐ The Kirklin Clinic at Acton Road
☐ UAB Callahan Eye Hospital
☐ UAB Clinical Research Unit
☐ Children's of Alabama
☐ Birmingham Veterans Affairs Medical Center
☐ Jefferson County Department of Health
☒ Other (i.e., any performance site not listed above, including those covered by subawards related to this protocol) - Describe:

Department of Nutrition Sciences (Webb Building)

UAB/Lakeshore Research Collaborative (Wallace Building)

NOTE: Documentation of IRB approvals from sites receiving subawards must be received by the UAB OIRB before funding will be released for that subaward.

b. Describe the space, service, or facilities available for the conduct of the research in the performance sites listed in Item 5.a (For research on UAB campus, include building names):

Department of Nutrition Sciences, University of Alabama at Birmingham (UAB), Webb Building
The UAB Department of Nutrition Sciences consistently ranks among the top human nutrition departments in the U.S. in terms of NIH research funding. The department's research portfolio spans basic, clinical, and translational research across a wide spectrum of chronic diseases, including diabetes, obesity, cancer, arthritis, and osteoporosis, and genetic diseases. The department has top-notch research capabilities in carbohydrate metabolism, body composition, energy metabolism, physiology, and the molecular and genetic basis of disease.

UAB/Lakeshore Collaborative Research Center, Wallace Building
The UAB/Lakeshore Collaborative Research Center is located in the Wallace Building on the Lakeshore Foundation campus; the physical space is rented through a 10-year lease by the School of Health Professions at UAB. All exercise training programs and study testing will take place in this facility. The UAB/Lakeshore Collaborative Research Center is directed by Prof. Robert Motl and guided by a multidisciplinary executive steering committee of faculty members in the School of Health Professions at UAB. The UAB/Lakeshore Collaborative Research Center is a world class, shared space for dedicated research on exercise, nutrition, and emotional self-regulation (e.g., health behaviors) for improving health, function, and well-being among persons living with physical disability and chronic health conditions. The shared space provides an environment that facilitates inclusion and interaction of a range of scientists and clinicians including those in health professions (e.g., PT, OT, nutrition, and health services administration) as well as psychology, engineering, epidemiology, education, and medicine. This permits a collaborative, multidisciplinary interaction between UAB and Lakeshore that acts as an accelerator and incubator for research on health and wellness for optimizing programs, services, and outcomes critical for quality of life and independence. The UAB/Lakeshore Collaborative Research Center occupies ~15,000 square feet of dedicated research space that consists of three private, sound-dampened rooms for participant screening, neurological examinations, neuropsychological testing, and patient-reported outcomes; a body composition laboratory; an exercise testing laboratory; an exercise training laboratory; a tele-health laboratory; biostatics and qualitative research cores; and secured storage for data. The UAB/Lakeshore Collaborative Research Center further has offices for project/research coordinators, faculty members, and graduate students/post-doctoral

fellows, as well as a reception area for participants and dedicated locker-rooms for participant privacy. This space is leased and regulated by UAB, not Lakeshore Foundation, and all Internet services within the Center are overseen by UAB IT.

The Center contains a dedicated body composition lab that houses dual-energy x-ray absorptiometry (DXA) for objectively measuring anthropometric data, as well as a scale stadiometer for collecting height and weight. Phlebotomy services (blood draws and sample processing) are provided by trained phlebotomists at the adjacent Encompass Health Lakeshore Rehabilitation Hospital. The 2,000+ square foot exercise testing laboratory includes research-grade NuStep recumbent steppers, motor-driven treadmills, upright and recumbent cycle ergometers, and a wheelchair treadmill for measuring aerobic fitness outcomes. For muscular strength testing, the exercise testing laboratory houses a Biodex isokinetic dynamometer. The exercise testing laboratory has an open floor space for over-ground walking tests and a gait mat for analysis of ambulatory dysfunction. The space further includes several ParvoMedics True One metabolic systems for administering submaximal and maximal cardiopulmonary exercise tests. The 3,000+ square foot exercise training laboratory contains motor-driven treadmills, cycle ergometers, NuStep recumbent steppers, functional electrical stimulation cycles, and resistance training equipment. The exercise training laboratory houses stretching mats for yoga and other functional training. The tele-health laboratory consists of a dedicated, private office space for confidential one-on-one telecoaching appointments. There are three areas within this space that include three dedicated computers with web-cams and microphones for the implementation of tele-exercise and other tele-health interventions delivered remotely. The tele-health laboratory further houses dedicated iPads for remote behavioral interventions. The biostatistics and qualitative research cores have dedicated space for conducting data analysis and one-on-one private interviews and focus groups, respectively.

UAB Targeted Metabolomics and Proteomics Laboratory (TMPL)

The Barnes group began as the Comprehensive Cancer Center Mass Spectrometry Shared Facility in 1993. In 2009 it was renamed the Targeted Metabolomics and Proteomics Laboratory (TMPL). It typically serves the research of 60-80 UAB investigators on an annual basis. It is currently supported by a NIH P30 grant to the UAB Acute Kidney Injury Center and has collaborations with investigators with R01s, P01s and other federal grants. It also is part of the UAB Lung Health Center and the UAB Center for Free Radical Biology. A SCIEX 5600 Triple-Tof Plus mass spectrometer will be used for measurement and quantification of sex hormones for this research project. This is a powerful metabolomics instrument from SCIEX. It is effective for both discovery and targeted, quantitative analysis of drugs and their breakdown products and offers high mass resolution (30,000-40,000) and high mass accuracy (2-3 ppm) and comprehensive MSMS capability. It is operated with an Eksigent Ekspert 415 nanoLC system or a Shimadzu LC pump. It has been upgraded to do MSMSALL for comprehensive lipid analysis and SWATH-MS for quantitative metabolomics and proteomics analysis.

UAB Hospital

The UAB Hospital is a major center for clinical research and hosts some of the top medical programs in the U.S. The UAB Hospital is located in Birmingham's Medical District, a couple blocks away from the UAB's Department of Nutrition Sciences. It has 1,157 licensed beds and is among the 20 largest and best equipped hospitals in the nation. We plan to use the UAB Hospital electronic medical record to assist with our recruitment of participants.

c. Is this protocol a clinical trial requiring clinical services at one of the performance sites listed in Item 5.a above? ☒Yes ☐No

If Yes, will any of the services be billed to either participants/their insurance or to the study account through the Hospital Billing Office (PFS) or the HSF Billing Office (MSO)? ☒Yes ☐No

If Yes, submit a Full Fiscal Approval Process (FAP)-designated unit submission to s complete a FAP submission and send to fap@uab.edu. For more on the UAB FAP requirements, go to FAP - SiteMinder Processes.

d. Is this a field study? ☐Yes ☒No

If Yes, describe the community and include information about how the community will be involved in the design, implementation and analysis of the research. This would include focus groups, training local facilitators/community health advisors: _____

e. Has this protocol been rejected or disapproved by another review board (another IRB, similar review board, or departmental review committee(s)) that authorizes the use of its patient populations? ☐Yes ☒No

If Yes, provide name(s) of the review board(s) and reason(s) not approved: _____
Attach copies of the disapprovals.
NOTE: If this protocol is subsequently rejected or disapproved by another review board, promptly notify UAB IRB.

f. Will the protocol be conducted at or recruit participants from the Birmingham Veterans Affairs Medical Center (BVAMC)? ☐Yes ☒No

If Yes, describe the involvement of the BVAMC: _____
Attach the VA IRB approval and VA IRB-stamped consent form(s), if applicable.
NOTE: See the BVAMC section of the IRB Guidebook for more information.

g. Will the protocol be conducted at or recruit participants from the Jefferson County Department of Health (JCDH)? ☐Yes ☒No

If Yes, describe the involvement of the JCDH and list the JCDH clinics being used: _____
Attach the JCDH Research Review Panel approval, if applicable.
NOTE: Human subjects research conducted at certain JCDH clinics requires review by the JCDH Research Review Panel. See the JCDH section of the IRB Guidebook for more information.

6. Clinical Trial

Does this protocol meet the following definition of a clinical trial? ☒Yes ☐No

**A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. For more information, see the full definition of clinical trial here.*

If Yes, you will need to fulfill the following requirements (regardless of funding):

a. All key personnel must complete the Good Clinical Practices (GCP) training. For information on this requirement, visit the IRB website here.

b. This protocol must be registered on ClinicalTrials.gov. Provide the National Clinical Trial (NCT) identifier number: **NCT04014296**
If you have any questions regarding registering a study on ClinicalTrials.gov, email the UAB Center for Clinical and Translational Science at ccts@uab.edu.

7. Multi-Site Studies

a. Is this a multi-site study with the UAB investigator as the lead investigator? ☐Yes ☒No

b. Is this a multi-site study with UAB as a coordinating site? ☐Yes ☒No

c. If Yes to a or b, describe the management of information obtained in multi-site research that might be relevant to the protection of participants. Include, at a minimum, how the following items are managed:

- IRB approvals from other sites

- Unanticipated problems involving risks to participants or others. (For example, if there is an unanticipated problem involving risks to participants or others, which site is responsible for reporting it?)
- Interim results
- Protocol modifications

8. Drugs

Will any drugs or supplements be *used or studied* in this protocol? ☐Yes ☒No

If Yes, attach the completed Drug Review Sheet.

9. Devices

a. Will any devices be *studied* in this protocol? ☐Yes ☒No

b. Will any *not FDA-approved* devices be *used or studied* in this protocol? ☐Yes ☒No

If Yes to a or b, attach the completed Device Review Sheet.

10. Special Approvals

a. Does this protocol involve the use of radioisotopes? ☐Yes ☒No

If Yes, attach documentation of approval from the Radiation Safety Division.

b. Does this protocol include patients with contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis)? ☐Yes ☒No

If Yes, attach documentation of approval from the Infection Control Committee of the appropriate facilities.

c. Does this protocol involve obtaining remnant biopsy or surgical material from the Department of Pathology or any other source? ☐Yes ☒No

If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Anatomic Pathology Release of Pathologic Materials).

d. Does this protocol require obtaining any remnant clinical laboratory specimens, body fluids, or microbiological isolates from the Department of Pathology or any other source? ☐Yes ☒No

If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Laboratory Medicine Release of Pathologic Materials).

e. Does this protocol use stored (existing) specimens from a repository? ☐Yes ☒No

If Yes, attach documentation of approval for use of specimens, and describe how existing specimens are labeled: _____

11. Use of Specimens

Does this protocol involve the collection of specimens? ☒Yes ☐No

If Yes, complete 11.a-11.h.

If No, skip to Item 12.

a. How will specimens be obtained, processed, distributed, and stored? **Blood samples will be collected at the clinical research facility in the Wallace Building by a trained phlebotomist with Encompass Health Rehabilitation Hospital, which is directly adjacent to the Wallace Building. A total of approximately 2 tablespoons (30mL) will be collected from each participant per visit, for a total of 10 tablespoons (150 mL) across all study visits. Screening blood samples will include a comprehensive metabolic panel, lipid panel, complete blood count, and follicle stimulating hormone. Blood samples at screening, baseline, week 8, week 16, and week 52 will be transported in an appropriate biohazard container to UAB. Glucose, insulin, and lipids will be processed and analyzed by the CLIA-certified analytical laboratory managed by the Department of Pathology (Outreach Lab). Sex hormones (estradiol, estrone, and testosterone) will be analyzed at the UAB Targeted Metabolomics & Proteomics Laboratory (TPML). In order to measure very low**

concentrations of sex hormones that are expected in this study population, TPML research staff will dansylate the samples prior to quantification by mass spectrometry (SCIEX 5600 TripleTof Mass Spectrometer).

b. How will specimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)? **Blood samples will coded with a unique study ID number, study visit (baseline, week 8, week 16, and week 52), blood draw time point (e.g., 0 min, 30 min) if applicable, and the date of sample collection.**

c. How will clinical data associated with the specimens be collected and stored? **Blood sample assays will be performed by technicians in the Human Physiology Core and uploaded to the study database in REDCap. Other study outcome data (blood pressure, waist circumference, body weight, body composition, resting metabolic rate, physical functioning tests, accelerometry data, and questionnaire data) will be obtained by research staff and entered into the study database in REDCap and/or password-protected folders on encrypted computers in the Webb building. Data collected on paper forms will be kept in locked cabinets in locked offices in the Webb building.**

d. What participant-identifying information will be collected and linked to the specimens? **For the study, we will collect information on each participant's name, phone number, email address, mailing address, birth date, and social security numbers; this information will be protected in REDCap and restricted to authorized research staff and the IRB on a need-to-know basis. Upon entering the study, each participant will be assigned a unique study ID number. All data and specimens will be coded the participant's unique study ID number and the date of collection; no other participant-identifying information will appear on the labeled specimens.**

e. What steps will be taken to maximize the confidentiality of linked identifiers? For example, procedures could include using a password-protected computer database to link identifiers, with limited personnel knowledgeable of the password, or coded identifiers released without the ability to link to clinical data (also called "stripped" or "anonymized" specimens). **Confidential data in electronic form will be maintained in REDCap or password-protected files on encrypted computers in locked offices in the Webb building. Access to linked identifiers will be restricted to authorized research staff and the IRB on a need-to-know basis.**

f. Is genetic testing planned as part of this protocol? ☐Yes ☒No
If Yes, describe the planned genetic testing here. _____

g. Will specimens be stored for future use? ☒Yes ☐No
If Yes, indicate whether they will be used for the disease under study in this protocol or research on other diseases. . **Blood specimens from blood draws will be frozen and stored for future analyses of glucose, insulin, estrone, estradiol, testosterone, and lipid panel for the study.**

h. Will specimens be shared with other investigators in the future? ☐Yes ☒No
If Yes, answer i. and ii.
i. What identifiers, clinical information and demographic information will be shared; or will the specimens be stripped of identifiers (i.e., anonymized)? _____
ii. Outline your procedure for assuring IRB approval for release and use prior to release of specimens.

_____

NOTE: Investigators who receive and/or use these specimens must document approval from the appropriate IRB(s) before the specimens may be released.

12. Gene Therapy

Does this protocol involve gene therapy or administering recombinant materials to humans? ☐Yes ☒No
If Yes, submit the Gene Therapy Project Review Panel Report ***-OR-*** the Protocol Oversight Review Form For Clinical Vaccine Trials, as applicable.

13. HIPAA Privacy and Security

Will the PI or others obtain, review, or make other use of participants' "protected health information" (i.e., information, whether oral or recorded in any form or medium that (a) is created or received by a health care provider and (b) relates to past, present, or future physical or mental health or condition of an individual; or provision of health care; or payment for provision of heath care)? ☒Yes ☐No

If Yes, complete Items 13.a-13.**f.**

If No, skip to 14.

a. Will the data/information be stored or managed electronically (on a computer)?

☒Yes ☐No

b. Is the principal investigator requesting that the UAB IRB waive patient HIPAA authorization from another institution or entity (e.g., insurance company, collaborating institution)? ☐Yes ☒No

If Yes, attach copies of the privacy notices from each institution/entity, and provide the name of each institution/entity: _____

c. Indicate which of the entities would provide health information for this protocol, maintain health information as it was collected for this protocol, and/or store health information after it has been collected for this protocol.

☒ UAB Hospital or UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital or Acton Road (and/or associated clinics)
☐ UAB Callahan Eye Hospital
☐ Children's of Alabama
☐ Jefferson County Department of Health
☐ School of Dentistry
☒ School of Health Professions
☐ School of Medicine
☐ School of Nursing
☐ School of Optometry
☐ University of Alabama Health Services Foundation
☐ UAB Health Centers
☐ Viva Health
☐ Ophthalmology Services Foundation
☐ Valley Foundation
☐ Medical West - UAB Health System Affiliate
☐ None - **If None, skip to Item 14.**

d. Indicate any information systems that will be the sources of information used for the protocol.

☒ A system maintained centrally by UAB Health System (these include the following: HealthQuest for registration, billing, and patient administration; PowerInsight (clinical data warehouse); Cerner IMPACT for PowerNotes for meds, Lab, Radiology, UED, Surgery

NOTE: If a researcher needs information in a specified format or a specified time, the researcher must confirm with the unit who can supply the information/service that the request can be met before writing the information/service into the research protocol. In addition, the researcher must be aware that these services may have a cost attached that should be considered in the research budget.

To request access to clinical systems for research purposes, visit https://www.oneuabmedicine.org/web/hsis/technical-support, click "Accounts Request" and complete the form indicating access for research purposed.

☐ Another system on a UAB server - Describe: _____

e. Indicate which of the listed identifiers will be accessed, associated and/or linked with the protected health information (PHI) used for this protocol.

☒ Names
☒ Geographic subdivisions smaller than a state
☒ Elements of dates (except year) related to an individual
☒ Telephone numbers
☒ Fax numbers
☒ Email addresses
☒ Social security numbers
☒ Medical record numbers
☐ Health plan beneficiary numbers
☐ Account numbers
☐ Certificate/license numbers
☐ Vehicle identifiers and serial numbers
☐ Device identifiers and serial numbers
☐ Biometric identifiers
☐ Web universal resource locators (URLs)
☐ Internet protocol address numbers
☐ Full-face photographic images
☐ Any other unique identifying number - Describe: _____
NOTE: Codes are not identifying as long as the researcher cannot link the data to an individual
☐ None - **If None, skip to Item 14.**

f. Choose one plan to describe your use of the personal health information:

☐ The data collected meet the specifications for a "limited data set" (LDS)
-If the LDS will leave the covered entity or will be received from another covered entity you will need a Data Use Agreement

☒ Research staff will obtain authorization from each participant to use the information
-Include the HIPAA Authorization form, complete except for participant name and IRB protocol number, as the final page of the consent form

☐ PI requests waiver of authorization to use the information
-Attach Waiver of Authorization and Informed Consent form

PROPOSED RESEARCH

- The IRB will not accept grant applications and/or sponsor's protocols in lieu of the items as outlined below.
- Do not separate responses from items. Instead, insert your response to each item below the item, keeping the information in the order of this form.

14. Purpose - in nontechnical, lay language

a. Summarize the purpose and objectives of this protocol in one short paragraph. **The purpose of this study is to examine the separate and combined effects of a high-protein (HP) diet and resistance training (RT) on body composition and potential biological moderators of body weight in men and women >50y. All participants will receive dietary physical activity guidance through our in-person, group-based weight loss program, State of Slim (SOS). These participants will be randomized to receive either a counseling-based HP diet plan or RT plan. Body composition assessments at 8 wk will identify responders and non-responders; the latter will be re-randomized to "augment" (HP: add protein supplements; RT: supervise RT) or "combine" (HP with protein supplements + supervised RT). We hypothesize that non-responders randomized to "combine" will demonstrate greater fat loss and fat-free mass (FFM) retention when compared to "augment."**

b. Describe how outcomes will be measured for this protocol.

Primary Outcome Measure:

Changes in body composition (via dual energy x-ray absorptiometry) from baseline to weeks 8 and 16.

Exploratory Outcome Measures:

Changes in body composition from week 16 to week 52.

Changes in glucose, insulin, insulinogenic index, disposition index from baseline to weeks 8, 16, and 52.

Changes in lipid profile from baseline to weeks 8, 16, and 52.

Changes in resting metabolic rate and respiratory exchange ratio from baseline to weeks 8, 16, and 52.

Changes in estimated aerobic fitness and measured physical activity and sedentary behavior from baseline to weeks 8, 16, and 52.

Changes in skeletal muscle mass (via D3 creatine dilution) from baseline to weeks 8, 16, and 52.

Questionnaire responses and other factors that may influence response to the weight loss program (e.g., daily appetite, physical activity, sleep, social and physical environment, stress, motivation for weight loss). See Study Visits and Procedures/Questionnaires for full list of measures.

15. Background - in nontechnical, lay language

Summarize in 2-3 paragraphs past experimental and/or clinical findings leading to the design of this protocol. Include any relevant past or current research by the PI. For drug and device studies, summarize the previous results (i.e., Phase I/II or III studies).

Obesity is one of society's most pressing public health concerns and is especially problematic for aging adults who experience profound biological and behavioral changes that are associated with the accrual of body fat and loss of skeletal muscle. This dangerous combination may result in a loss of functional capacity and lower engagement in physical activity, which creates a vicious cycle of increasing adiposity and loss of skeletal muscle. This cycle precipitates sarcopenic obesity and this condition forces clinicians to decide whether to treat their patients' obesity at the risk of further reducing skeletal muscle mass. The result is that relatively few interventions are currently available that specifically target the treatment of obesity in older adults. The majority of past research in this area has utilized high protein (HP) diets or resistance training (RT) to preferentially target fat loss and preserve FFM in older adults. However, relatively few studies have directly investigated the comparative effectiveness of HP and RT for FFM retention in older adults, and, to our knowledge, no studies have utilized an adaptive intervention design such as the SMART experimental approach as in the proposed research.

Verreijen et al. (*Nutrition Journal*, 2017) conducted one of the few randomized trials that manipulated both dietary protein (1.3 vs. 0.8 g/kg body weight/d) and RT (3 d/wk vs. no RT) in older adults with overweight/obesity. They found that combining a HP diet with RT increased FFM during the 10-wk intervention, but this study was limited by a relative inability to achieve recommended dietary protein targets (HP: 1.13 g/kg achieved vs. 1.3 g/kg recommended; normal protein: 0.98 g/kg achieved vs. 0.8 g/kg recommended) that resulted in a modest difference in dietary protein intake. Further, overall weight loss was only ~2 kg for all groups, which could be related to the short duration of the 10-wk trial. Work by Villareal et al. (*New England Journal of Medicine* 2011 and 2017) has demonstrated that combining exercise with weight loss is the most effective strategy for improving physical functioning and body composition in older adults with obesity. These interventions used a dietary protein prescription of 1 g/kg body weight/d for weight loss that resulted in 9-10% weight loss and ~3% reduction in FFM with combined dietary weight loss and exercise training compared to ~5% reduction with weight loss alone. With average FFM losses of this magnitude, many of the participants in both groups would have experienced large reductions in FFM that may have increased their risk for sarcopenia and/or impaired physical functioning. A major benefit of the SMART experimental approach is that participants losing too much FFM and/or too little fat mass will be re-randomized to 2nd stage interventions to increase the likelihood of achieving clinically significant weight loss while minimizing the loss (or gaining) of FFM.

We previously published data from the Beef WISE Study demonstrating ~10% weight loss in 16 weeks among adults aged 18-50 y using the State of Slim (SOS) weight management program. Importantly, changes in body weight resulted from reductions in body fat mass (22% mean reduction in fat mass) while FFM was virtually completely retained (1% mean reduction in FFM). SOS is a group-based program with a high protein (HP) diet (~40% of energy from protein or 1.8 g/kg body weight/d) and 420 min/wk of exercise training17. However, SOS has not been rigorously studied in adults aged ≥50 y, and whether the retention of FFM in Beef WISE was driven by the HP diet, exercise, or their combination is unknown. The proposed research seeks to build upon the work by Verreijn et al., Villareal et al., and Beef WISE by utilizing a SMART adaptive experimental approach to investigate the separate and combined effects of a dietary protein and exercise training on FFM retention during weight loss.

16. Participants (Screening and Selection)

a. How many participants are to be enrolled at UAB (if other sites relying on UAB IRB, list the number for each site)? **N=80 targeted**
If multi-site study, total number at all sites/institutions: _____

b. Describe the characteristics of anticipated or planned participants (if multiple groups, repeat list for each group).
Sex: **Female and Male**
Race/Ethnicity: **All**
Age: **≥50 years**
Health status: **BMI 30-50 kg/m^2 (≤350 lbs)**

c. From what population(s) will the participants be derived? **We will aim to recruit a study population from the general public that is reflective of local demographics in the greater Birmingham area: 67% Caucasian, 28% African-American, and 5% other.**

Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants: **As described in detail below, we will utilize a combination of recruitment strategies including flyers on the UAB campus and surrounding community and ads in UAB Reporter. However, we may rely on a search of the UAB Medicine electronic medical record using the i2B2 platform if we are unable to meet our recruitment goals via other methods.**

d. Describe the inclusion/exclusion criteria:

Inclusion criteria:

1. **Either sex**
2. **Age ≥50 years**
3. **BMI of 30-50 kg/m^2 (≤350 lbs)**

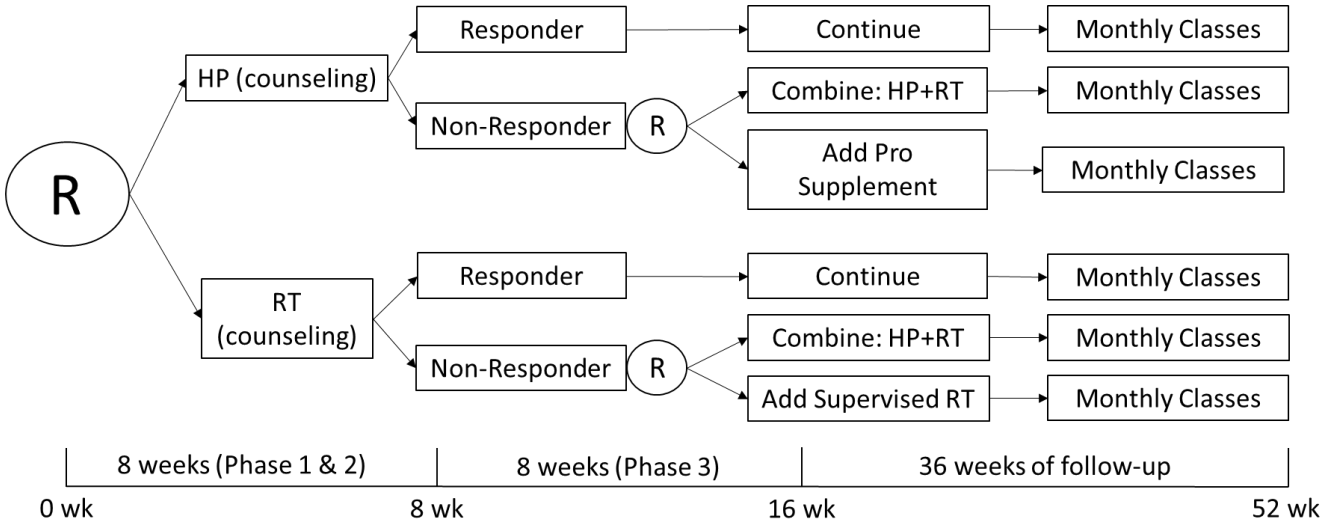
Exclusion Criteria:

1. **Untreated hyper or hypothyroidism.**
2. **Cancer (except basal cell).**
3. **Gastrointestinal disorders affecting food intake.**
4. **<6 months of stable use of medications that affect metabolism, body weight, energy expenditure or appetite.**
5. **Current eating disorder (e.g., binge eating disorder, anorexia, or bulimia).**
6. **Any medical condition for which following a HP diet and/or 70 minutes of exercise daily would be inadvisable.**

e. If participants will comprise more than one group or stratification, describe each group (e.g., treatment/intervention, placebo, controls, sham treatment) **and** provide the number of participants anticipated in each group.

Randomization and Cohort Details

This study will use a Sequential Multiple Assignment Randomized Trial (SMART) experimental approach with a targeted accrual of 80 adults with obesity. Subjects will be randomly assigned to either the HP diet or RT study arm using a computer-generated randomization program on SAS. At week 8, participants will be classified as Responders or Non-Responders based on changes in fat mass and FFM by dual x-ray absorptiometry (DXA). We will define Responders as those individuals achieving both a ≥7.5% reduction in fat mass AND ≤1.5% reduction (or gain) in FFM. Non-Responders will be defined as anyone with <7.5% reduction in fat mass OR >1.5% reduction in FFM. Responders will continue with their 1st stage SMART intervention group (HP or RT) for the remainder of the study. Non-Responders will be re-randomized to a 2nd stage SMART intervention of either "augment" (HP: add protein supplements; RT: supervise RT) or "combine" (HP with protein supplements + supervised RT) for the remainder of the intervention. A figure illustrating the SMART experimental design is included below:



f. Indicate which, if any, of the special populations listed below will be involved in the protocol. Include the Special Populations Review Form (SPRF) if indicated.

☐ Pregnant Women: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Fetuses: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Neonates/Nonviable Neonates: SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Prisoners: Attach SPRF—Prisoners
☐ Minors (<18 years old): Attach SPRF—Minors
☒ Employees or students at institution where research conducted
☐ Persons who are temporarily decisionally impaired
☐ Persons who are permanently decisionally impaired
☐ Non-English Speakers

For each box checked, describe why the group is included **and** the additional protections provided to protect the rights and welfare of these participants who are vulnerable to coercion: **UAB employees and students are included because they may interested in losing weight. All potential participants will be informed of alternate options for losing weight (e.g. clinical and commercial programs, self-directed weight loss). UAB employees and students will be clearly informed that their participation in the study is in no way related to their employment/student status at UAB. The following language is included in the informed consent and will be abided by: "If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research."**

g. List any persons other than those directly involved in the protocol who will be at risk. If none, enter "None": **None**

h. Describe the recruitment process (e.g., medical record review, referrals, letter of invitation, existing patients) that will be used to seek potential participants (e.g., individuals, records, specimens). Research recruitment by non-treating physicians/staff may require completion of Partial Waiver of Authorization for Recruitment/Screening.

Recruitment

Subjects will be recruited using by multiple methods including 1) community and campus recruitment by flyers, local newspaper, local TV, and online advertisements, and/or campus email newsletters (UAB Reporter), 2) referral from physicians at UAB Family Medicine Clinics, the UAB Obesity Medicine Clinic, and UAB Comprehensive Diabetes Center, 3) review of the UAB Medicine electronic medical records (EMR) using the i2B2 platform.

If we are unable to meet our recruitment goals using methods 1 and 2, potentially eligible patients in the Birmingham area will be identified by a systematic search of the UAB Medicine EMR via i2B2. Once potentially eligible patients are identified, they will contacted by secure email (myUABMedicine) or in person or by phone or by a mail to inform them of the study and provide the investigators' contact information. Patients identified by the EMR search will first be contacted by a "Dear Patient" letter sent through myUABMedicine. The "Dear Patient" letter was created using a previously IRB-approved letter from IRB-300002928 as a template. Patients identified as potentially eligible in the EMR will be contacted by a person already involved in their medical care (e.g., health care professionals or administrative staff).

i. If you will use recruitment materials (e.g., advertisements, flyers, letters) to reach potential participants, attach a copy of each item. If not, identify the source (e.g., IRB Protocol Number for approved databases) from which you will recruit participants. **Copies of recruitment materials are attached.**

j. Describe the screening process/procedures for potential participants.

Screening

All subjects will be screened by phone first. Subjects who pass phone screening and are interested in participation will be asked to sign a consent form at a screening visit and prior to any study assessments being performed. Subjects will be sent a Study Intake Form by email or regular mail prior to the screening visit and asked to bring the completed form to the in-person screening. The Study Intake Form contains a detailed, self-reported medical history and will not be reviewed by research staff until informed consent is obtained. During the phone screening process, potential participants will be informed of the potential risks of using unencrypted email including the potential for unauthorized parties to intercept and view emails. Once the risks are explained, potential participants will be asked to give or deny their permission to receive the Study Intake Questionnaire by email. If the participant does not give her/his permission, the Study Intake Questionnaire will be delivered by traditional mail.

Subjects passing the phone screen will be evaluated at the in-person screening visit to determine if they meet study eligibility. These visits will be scheduled within approximately 3 weeks of completing and passing the screening by phone. Screening laboratory analyses will include a a comprehensive metabolic panel, complete blood count, a lipid panel, and follicle stimulating hormone (FSH) to confirm post-menopausal status. Dr. Brown will review screening laboratory results for potential underlying disease that may affect study participation. The baseline visit will be scheduled following this visit and will vary in timing depending on participant accrual. The time between the screening and baseline visits is not expected to exceed 8 weeks.

17. Protocol Procedures, Methods, and Duration - in nontechnical, lay language

a. Describe the procedures for all aspects of your protocol. Tell us what you are doing.

Overview of the State of Slim Weight Management Program

All study participants will be enrolled in the State of Slim (SOS) weight management program. SOS is a 16-week group-based behavioral weight loss program (up to 20 per group). The usual SOS diet plan is HP, low in fat and emphasizes non-starchy vegetable and whole-grain carbohydrates. The diet is plan is structured into 3 distinct phases with phase-specific food choices from which participants can chose to eat in defined portions rather than counting calories. Phase 1 is 2 weeks long, Phase 2 is 6 weeks, and Phase 3 is 8 weeks, and additional foods are added to the food choices as participants complete each phase. The SOS diet plan utilizes 5 'Diet Rules' through all 3 phases of the diet to encourage weight loss: (i) Eat 6 times per day; (ii) Have breakfast within 1 h of waking; (iii) Don't count calories, measure portions; (iv) Have the right carbohydrate and protein mix at every meal (1 carbohydrate and 1 protein at every meal, vegetables as only carbohydrate source at 3 meals); and (v) Eat a healthy fat twice a day. SOS also includes a strong exercise component with a prescription to exercise on 6 d/wk and to progressively increase exercise duration from 10 min/d to 70 min/d. Participants in the commercial SOS program are encouraged to reach the goal of 420 weekly minutes of exercise through any combination of aerobic, strength, and alternative (e.g., yoga, Pilates, flexibility, balance) exercise training.

Research Modifications to State of Slim

For this study, participants will be randomly assigned to either SOS with an energy-restricted HP diet that uses the unmodified diet plan in the published book (HP) or SOS with 3 d/wk of prescribed RT that will contribute ~135 min/wk (45 min/session) to the 420 min/wk exercise goal (RT) The 1st and 2nd stage SMART interventions for each group are described below.

All subjects will also have access to the online SOS community during the entire study where they can interact/connect with other individuals from their class and also have access to the class coach who will be available to provide information and answer questions. The SOS community is a private Facebook group that is only open to participants in that specific SOS class.

1st Stage SMART Interventions

Dietary Intervention

Prior to initiating the SOS program, participants assigned to HP will complete a session with the SOS coach to select and prepare high protein foods from the SOS food lists. The estimated macronutrient distribution of the HP diet is 40% protein (or ~1.8 g/kg body weight/d), 32% carbohydrate, and 28% fat. In order to control for the overall degree of dietary energy restriction, participants assigned to RT will be prescribed a modified SOS diet that is lower in protein (20% of energy or ~0.9 g/kg body weight/d), proportionally higher in carbohydrate (53% of energy), and approximately equivalent in fat (26% of energy), but using the same overall food sources. Specific SOS Diet Rules will be altered to achieve targeted differences in macronutrient composition between the diet plans. In the HP diet (usual SOS diet plan), suggested protein portion sizes are 4-6 ounces, and vegetables are the only carbohydrate source at 3 meals. These Diet Rules will be modified for participants assigned to RT to achieve a lower protein, higher carbohydrate diet plan by reducing the protein portion size to 2-3 ounces and requiring non-vegetable carbohydrate foods at all 6 meals.

Resistance Training Program

The 1st stage SMART RT program will utilize resistance bands that will be provided to participants at no cost for the duration of the study. Prior to initiating the SOS program, participants assigned to RT will complete a RT orientation session with a personal trainer to demonstrate proper technique for exercises and develop a plan for RT progression (e.g., increase number of sets). Participants will be counseled to complete 3 d/wk of RT using the provided resistance and consisting of up to 3 sets of 8-12 repetitions of 8 exercises (squat, heel raise, overhead press, chest press, row, arm curl, triceps push-

down, and abdominal flexion). Participants will be counseled to begin with 1 set of each exercise and to add additional sets once s/he is able to achieve 12 repetitions of all exercises.

2nd Stage SMART Interventions

At week 8, participants will be classified as Responders or Non-Responders based on changes in fat mass and FFM by DXA. We will define Responders as those individuals achieving both a ≥7.5% reduction in fat mass AND ≤1.5% reduction (or gain) in FFM. Non-Responders will be defined as anyone with <7.5% reduction in fat mass OR >1.5% reduction in FFM. Responders will continue with their 1st stage SMART intervention group (HP or RT) for the remainder of the study. Non-Responders will be re-randomized to a 2nd stage SMART intervention of either "augment" (HP: add protein supplements; RT: supervise RT) or "combine" (HP with protein supplements + supervised RT) for the remainder of the intervention.

The protein supplements and a shaker cup will be provided to participants at no cost for weeks 8 – 16. The protein supplement will be a whey-based protein isolate (Optimum Nutrition Gold Standard) and is available in a variety of flavors from which the participants can choose. Each serving of the protein supplements provides 24 grams of protein and 110 kilocalories when mixed with water. Participants will be instructed to consume the supplement 2x per day until week 16. Because the SOS food lists include whey protein powder, participants will be instructed that they can continue to consume the whey protein for weeks 17-52 of the study, but the supplement will no longer be provided by the research team.

Supervised RT will be led by a personal trainer in a group setting (up to 4 participants per group) on 2 days per week for weeks 8 – 16. The participants will be counseled to continue completing 1 day of RT on their own. Exercises for the supervised RT will be the same as those prescribed for the 1st stage RT intervention. Continued RT will be encouraged for weeks 17-52 of the study, but RT will no longer be supervised by personal trainers.

Weeks 17-52

After completion of the 16-week SOS program, subjects will be enrolled in the *Next Steps* weight loss maintenance program for an additional 8 months. In-person *Next Steps* meetings will be delivered once a month, and will focus on sustaining the lifestyle changes learned in the foundation SOS program and specific to the participants' intervention assignments.

Study Visits and Procedures

Subjects will be followed for 52 weeks and will be seen for 5 research study visits: at screening, baseline, week 8, week 16, and week 52. Subjects will meet weekly for the SOS classes for weeks 1-16 and monthly for *Next Steps* classes for weeks 17-52. In the study consent form, participants will be asked to opt-in or out of receiving limited participant communications by email including scheduling of study visits and reminders of study visits (see ICF and participant email templates). If the participant opts-out of receiving emails, study visits and reminders will be completed by phone. The following measures will be completed at baseline, week 8, week 16, and week 52 unless otherwise noted:

- **Body weight, waist circumference, and body composition (fat and lean mass and percent) by dual x-ray absorptiometry (DXA).**
- **D3-creatine dilution to assess muscle mass.**
- **Fasting blood draw: sex hormones (estrone, estradiol, testosterone) and lipid panel (triglycerides, total cholesterol, low-density lipoprotein cholesterol [calculated], and high density lipoprotein cholesterol).**
- **Oral glucose tolerance test: serum glucose and insulin measured just prior to a 75g glucose load and at 30 minutes after glucose ingestion.**
- **Systolic and diastolic blood pressure.**

- **6 minute Walk Test to estimate aerobic fitness.**
- **Resting metabolic rate measured by indirect calorimetry using the ventilated hood technique.**
- **Objectively measured physical activity and sedentary behavior for 7 days using accelerometry.**
- **Questionnaires (can be completed outside of research visit). These questionnaires will be used for measuring self-reported behaviors related to eating, physical activity, sedentary time, and sleep as well as for investigating potential moderators/predictors of weight loss during the study (Exploratory Aim 5).**
    - **Diet History Questionnaire III (past month with portion sizes)**
    - **International Physical Activity Questionnaire**
    - **Munich Chronotype Questionnaire for self-reported sleep behavior**
    - **Sallis Social Support and Important Others Questionnaire for social support**
    - **Visual Analog Scales for Daily Appetite (hunger, fullness, and cravings). Will be completed at the end of the day for 7 days at each time point.**
    - **Reward-Based Eating Drive Scale**
    - **Palatable Eating Motives for emotional eating**
    - **Perceived Stress Scale**
    - **Treatment Self-Regulation Questionnaire for motivation for weight loss**
    - **Behavior Rating Inventory of Executive Function**
    - **Short form of Psychological Well-Being for resilience of centered identity**
    - **Diet Satisfaction Questionnaire**

Table of Assessments	**Screen**	**Baseline**	**Wk 8**	**Wk 16**	**Wk 52**
Informed consent	X				
Study Intake Questionnaire	X				
Height	X				
Weight	X	X	X	X	X
Waist circumference		X	X	X	X
Body composition by DXA		X	X	X	X
D3 creatine dilution		X	X	X	X
6 Minute Walk Test		X	X	X	X
Resting metabolic rate		X	X	X	X
Blood draw	X	X	X	X	X
Oral glucose tolerance test (OGTT)		X	X	X	X
Blood pressure	X	X	X	X	X
Accelerometry for 7 days		X	X	X	X
Questionnaire packet		X	X	X	X
Assess for adverse events		X	X	X	X
Document concomitant medications	X	X	X	X	X

Anthropometrics:
Height, body weight, and waist circumference will be measured by trained research staff. Height will be measured at baseline using a stadiometer. Body weight will be measured using a calibrated electronic scale accurate to ± 0.1 kg. Waist Circumference will be measured in triplicate at the superior border of the iliac crest and averaged in accordance with NIH recommendations.

Dual X-Ray Absorptiometry:
DXA scans will be performed to measure any changes in fat-mass and fat-free mass. Scans will be performed using an iDXA whole-body scanner (GE-Lunar Radiation Corporation, Madison, WI). The radiation dose is less than 1 mrem. Scans will be analyzed using CoreScan software, and muscle mass will

be estimated using published equations. The maximum allowable weight for measurement by the scanner is 350 lbs, and the eligibility criteria have been set in accordance with this limit.

D3 Creatine Dilution:
This method quantifies muscle mass using deuterium, a naturally-occurring, stable, and non-radioactive isotope of the element hydrogen that is contained within creatine. Almost all (98%) creatine in the body is contained within skeletal muscle, and its conversion to creatinine provides a convenient and accurate method of measuring total muscle mass. The extent to which labeled creatinine is diluted in the urine provides the basis for this measurement. This method is safe and has been used for testing in infants, children and the elderly. We will provide all materials required for this test to the participants at the time of their testing appointments. Three days prior to the testing appointment, participants will receive a reminder to take the D3-creatine capsule. On the morning of the appointment, participants will provide a urine sample (second void of the day). A test strip will be dipped into the sample and be shipped to the University of California, Berkeley for analysis.

Aerobic Fitness Testing:
VO2max will be estimated from the 6 Minute Walk Test using equations from the American College of Sports Medicine. The test starts with the participant sitting in a chair for at least 5 minutes during which time blood pressure, resting heart rate, and Borg ratings of perceived exertion will be measured. The participant will be instructed to complete as many laps on a 30-meter marked corridor as possible by walking (but not jogging or running). After 6 minutes, the research staff will instruct the participant to stop walking and will mark the location where the participant stopped. The participant will then be asked to sit in a chair and blood pressure, heart rate, and Borg ratings of perceived exertion will be measured again.

Resting Metabolic Rate:
Resting energy expenditure and respiratory exchange ratio (measurement of macronutrient oxidation) will be measured by indirect calorimetry using the ventilated hood technique.

Blood draw:
Blood samples will be analyzed for fasting-state estrone, estradiol, testosterone, total cholesterol, low-density lipoprotein cholesterol (LDL; calculated), high-density lipoprotein cholesterol (HDL) triglycerides, and circulating microRNA.

Oral Glucose Tolerance Test:
Participants arrive at the study visits in a fasted state and a blood sample is obtained prior to the consumption of a 75 g oral glucose solution. An additional blood sample (4 mL) will be drawn at 30 minutes following initiation of glucose ingestion. An OGTT-derived insulinogenic index and disposition index (DI_{OGTT}) will be calculated from these measures using the ratio of 0 to 30 minute changes in insulin divided by changes in glucose (i.e., $\Delta insulin_{0\text{-}30}$/ $\Delta glucose_{0\text{-}30}$).

Blood Pressure:
Blood pressure will be measured at the left upper arm by trained research staff using an electronic sphygmomanometer after the participant rested quietly in a seated position for ≥5 min with his/her legs uncrossed and back and arms supported.

Accelerometry:
Physical activity, sedentary time, and time spent laying down will be measured using accelerometry for 7 consecutive days at baseline, week 8, week 16, and week 52. The device (activPAL4) is worn on the front of the thigh and secured and waterproofed using a waterproof sleeve and medical tape. The device is to be worn for the entire 7-day assessment periods including while showering/bathing, but participants will

be asked not to swim during this time. Participants will be asked return the accelerometer after the 7-day wear period.

Questionnaire Packet:
Questionnaires (except the Diet History Questionnaire III [DHQ III]) will be delivered to participants using an emailed link that will direct participants to a REDCap interface for completing questionnaires unless the participant opts-out of receiving emails during the study. In the case of a participant opting-out of email receipt, the participant will be given the questionnaire packet (except the DHQ III) as a hardcopy and to complete at home. Data from the questionnaires will be transferred to the study database in REDCap. The DHQ III will be completed directly on the web-based tool that was developed and maintained by the National Institutes of Health/National Cancer Institute/Division of Cancer Control & Population Science. Secure login information and a web link will be created for each participant to complete the DHQ III. There is no mechanism to complete the DHQ III by paper and pen due to the extensive branching logic of the tool. If the participant declines to receive email notification of the questionnaire packet, she/he will need to complete the DHQ III on a computer during a study visit.

Other Procedures:
Subjects will be asked to complete State of Slim logs documenting their consumption of State of Slim-recommended foods and exercise. These logs will be dispensed and returned at SOS classes and/or study visits. These logs are usual component of the State of Slim program and will not be used to generate research data. Food intake and physical activity behaviors will be measured using the Diet History Questionnaire III and International Physical Activity Questionnaire and accelerometry, respectively. The baseline visit will take place within 14 days that subjects start their participation in the SOS class. The week 8, 16, and 52 study visits will take place in a ±7 day period of the corresponding SOS class.

Home and work/school addresses will be collected for research purposes to determine if the participants' food and physical activity environment, neighborhood crime rate, and neighborhood socioeconomic status influence weight loss and/or behaviors related to energy balance regulation (physical activity and diet).

Data Analysis Plan:
Results from the SMART intervention will be analyzed in accordance with recommendations for the analysis of adaptive interventions. The differential proportion of participants identified as Responders at week 8 between the HP and RT groups will be determined using the Chi-Square statistic. The main effect describing the comparative effectiveness of the 1st stage interventions (HP vs. RT) will be assessed by pooling and comparing week 16 changes in body weight and composition for all participants initially assigned to HP and RT. This analysis is completed using a linear mixed model that controls for 2nd stage intervention assignment. The comparative effectiveness of 2nd stage intervention options (Augment vs. Combine) for Non-Responders will be assessed using a linear mixed model that controls for 1st stage intervention assignment. Exploratory analyses of embedded adaptive interventions within the SMART design and quantitative ranking of all intervention subgroups will also be completed for potential hypothesis-generating purposes.

Associations of fasting-state sex hormones as well as fasting and 30 min glucose and insulin and the DI_{OGTT} with changes in body weight and composition will be assessed using Pearson's Correlation Coefficients and multiple linear regression. At week 16, participants will also be dichotomized as high (≥15% fat loss AND ≤2.5% reduction in FFM) and low responders. Linear mixed models controlling for 1st and 2nd stage intervention types and sex will be used to compare these biological variables among high and low responders.

Changes in body weight and composition during the weight loss maintenance period (weeks 17-52) will be compared among Responders, Non-Responders assigned to 'Augment,' and Non-Responders assigned to 'Combine' using linear mixed models.

b. What is the probable length of time required for the entire protocol (i.e., recruitment through data analysis to study closure)? **Up to 10 years**

c. What is the total amount of time each participant will be involved? **52 weeks for all participants, optional additional research for long-term follow-up by EMR search for up to 10 years. No in-person interactions will occur during the optional follow-up period.**

d. If different phases are involved, what is the duration of each phase in which the participants will be involved? If no phases are involved, enter "None." **None**

e. List the procedures, the length of time the procedure takes, the total # of times the procedure is performed, and indicate whether each is performed solely for research or would already be performed for treatment or diagnostic purposes (routine care) for the population.
-Insert additional table rows as needed.
-If procedure is sometimes research and sometimes routine care, include on separate lines with number of times as each.

Procedure	Length of Time Required of Participants	Total # of Times the Procedure is Performed	Research (Res) –OR- Routine Care
Phone Screen	**20 minutes**	**1**	☒Res ☐ Routine
Study Intake Questionnaire	**30 – 60 minutes**	**1**	☒Res ☐ Routine
Informed Consent	**30 minutes**	**1**	☒Res ☐ Routine
Blood Draw	**5 minutes**	**5**	☒Res ☐ Routine
Oral Glucose Tolerance Test	**45 minutes**	**4**	☒Res ☐ Routine
Anthropometrics	**5 minutes**	**5**	☒Res ☐ Routine
Blood Pressure	**5 minutes**	**5**	☒Res ☐ Routine
Resting Metabolic Rate	**45 minutes**	**4**	☒Res ☐ Routine
DXA	**30 minutes**	**4**	☒Res ☐ Routine
D3 Creatine Dilution	**5 minutes**	**4**	☒Res ☐ Routine
Physical Function Tests	**30 minutes**	**4**	☒Res ☐ Routine
VAS for appetite	**1 minute**	**28**	☒Res ☐ Routine
Questionnaires	**90 - 120 minutes**	**4**	☒Res ☐ Routine
Accelerometry	**7 days**	**4**	☒Res ☐ Routine
State of Slim Classes	**1 hour**	**16**	☒Res ☐ Routine

Next Steps Classes	**1 hour**	**8**	☒Res ☐ Routine

f. Will an interview script or questionnaire be used? ☒Yes ☐No

If Yes, attach a copy.

g. Will participants incur any costs as a result of their participation? ☒Yes ☐No

If Yes, describe the reason for and amount of each foreseeable cost. **Participants will have to pay for their own transportation to and from UAB and the Lakeshore Foundation Campus. This is stated in the informed consent.**

h. Will participants be compensated? ☒Yes ☐No

If Yes, complete i-v.

i. Type: (e.g., cash, check, gift card, merchandise): **Check for non-UAB employees. Direct deposit for UAB employees.**

ii. Amount or Value: **Up to $300**

iii. Method (e.g., mail, at visit): **Mail for non-UAB employees. Direct deposit for UAB employees.**

iv. Timing of Payments: (e.g., every visit, each month):): **$50 after the week 8 study visit. $100 after the week 16 study visit. $150 after the week 52 study visit.**

v. Maximum Amount of Compensation per Participant: **$300**

18. Benefits

Describe the potential benefits of the research. **Participants may directly benefit from the study because they will enrolled in a program designed to produce weight loss. However, no benefit to participants is guaranteed. This study seeks to build upon previous research that has shown that exercise combined with weight loss is the most effective strategy for improving physical functioning and body composition in older adults with obesity.**

19. Risks - in nontechnical, lay language

a. List the known risks for participants as a result of participation in the research. This should not include the minimal risk of loss of confidentiality. However, it should include any physical, psychological, social, economic, and/or legal risks. If there is a greater than minimal risk of loss of confidentiality describe why this is so. Do not list risks associated with the standard-of-care procedures.

NOTE: Risks included here should be included in the consent form or information sheet, as applicable.

There is a risk of being randomized to one of the groups that is less effective or that has more side effects. Feelings of hunger, hypoglycemia (low blood sugar), dizziness, and weakness are possible with weight loss diets. With blood draws and OGTT, there is the possibility of discomfort, pain, bruising, and bleeding where the needle is inserted. There is also a very small risk of infection at the site of the blood draw. The DXA procedure involves exposure to very low levels of radiation (x-rays), which may be harmful during pregnancy. However, because post-menopausal status is among the inclusion criteria listed in item 16.d, pregnancy testing is not necessary prior to conducting DXA scans. The D3 Creatine Dilution procedure requires providing a urine sample, which some participants might find embarrassing or inconvenient. Participants may have feelings of claustrophobia during the resting metabolic rate measurements. Participants may perceive discomfort and inconvenience from wearing the accelerometers for 7 days and the restrictions on swimming during this time.

Common discomforts and risks associated with the 6 Minute Walk Test include sweating, fatigue, feeling out of breath, and muscle soreness after the test; these tests also present the risk of falling. Less common risks include risk of musculoskeletal injuries, headache, dizziness, nausea/vomiting, high or low blood pressure, and wheezing. There is a small, but serious, risk of abnormal heartbeats, chest pain, passing out, heart attack, stroke, or death. These risks are reduced by 1) allowing the participant to walk at their chosen pace (rather than on a motor-driven treadmill)

and 2) instructing participants that they can either take a break or stop the test at any time during the 6-minute testing period.

Participants will be asked to attend all study visits after having fasted for 8 hours. Risks of fasting include lightheadedness, dizziness, weakness and hypoglycemia. In order to mitigate this risk, subjects are only asked to fast for 8 hours and are instructed to take all of their medications except for rapid acting insulins (which are exclusionary per this protocol) and sulfonylureas, which should be withheld until just before eating. If a participant should experience significant symptoms of hypoglycemia they will be instructed to eat and the assessments which require fasting will be rescheduled.

Participants in both groups will be counseled to progressively increase their exercise level to 420 min/wk per the State of Slim program. In this study, participants will be assigned to either a supervised resistance training program on 3 days per week (Resistance Training Group) or a supervised flexibility and balance training program on 3 days per week (High Protein Diet Group). The primary risks associated with beginning an exercise program are likely to be fatigue, shortness of breath, or muscle soreness during or after the training sessions. It is expected that when these symptoms occur, they will be minor and brief. During exercise there is a very small risk participants will experience cardiovascular symptoms such as chest pain, shortness of breath, dizziness, syncope, or lower extremity claudication.

There is a very small but unlikely risk of a loss of confidentiality.

b. Estimate the frequency, severity, and reversibility of each risk listed. **Participants will be exposed to potential risks from the blood draw 5 times (screening, baseline, week 8, week 16, and week 52) and all other study procedures 4 times (baseline, week 8, week 16, and week 52). These risks are all minimal, mild in severity, and are expected to be reversible, with the exception of serious risks described for the 6 minute walk test. However, the likelihood of a serious event during the 6-minute walk test is very low.**

c. Is this a therapeutic study or intervention? ☒Yes ☐No

If Yes, complete i.-iii.

i. Describe the standard of care in the setting where the research will be conducted: **Obesity is usually treated first with behavioral/lifestyle therapy to change dietary and physical activity behaviors. If unsuccessful, some patients with obesity may be prescribed medications or bariatric surgery.**

ii. Describe any other alternative treatments or interventions: **Participants can choose this or other lifestyle approaches for weight loss. They could also choose to use medications for weight loss or choose to have bariatric surgery if recommended by their physician. They could also choose not to lose weight. Participants are not permitted to join any other weight loss programs or take weight loss medications for the duration of the study (16 weeks).**

iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: **Participants will be asked to follow the SOS program for weight loss and not participate in weight loss interventions. Any medication changes during the study should be completed under the direction of their usual physician and be reported to the study coordinator as soon as feasible.**

d. Do you foresee that participants might need additional medical or psychological resources as a result of the research procedures/interventions? ☐Yes ☒No

If Yes, describe the provisions that have been made to make these resources available. _____

e. Do the benefits or knowledge to be gained outweigh the risks to participants?

☒Yes ☐No

If No, provide justification for performing the research: _____

20. Precautions/Minimization of Risks

a. Describe precautions that will be taken to avoid risks and the means for monitoring to detect risks.

Randomization:

Participants will be assigned to one of the two groups by random chance. Each participant's assigned group may prove to be less effective or may have more side effects than the other study group. Participants are welcome to try either the other diet plan that they are not assigned to on their own but only after they have finished participating in the study. Both diet plans are designed to produce weight loss and include many healthy food options including fruits/vegetables, whole grains, low/non-fat dairy, and lean meats.

Weight Loss Intervention:

Increased hunger is a normal response to a reduced-calorie diet for weight loss. The SOS meal plan encourages participants to eat 5-6 meals throughout the day as a method for managing hunger.

Exercise Intervention:

The risks associated with either exercise intervention are expected to be minimal for most participants. Risks are reduced by ensuring all participants meet the specific inclusion/exclusion criteria. Participants will have previously undergone a medical screening including medical history interview, physical exam, and screening labs. If participants experience muscle soreness, we will prescribe light stretching, and hot/cold therapy to reduce the soreness. If these approaches do not alleviate the soreness, we will advise the use of OTC pain relievers (e.g. aspirin, acetaminophen, ibuprofen), unless contraindicated. It is anticipated that some participants will experience soreness during the first few days of exercise, but since the recommended intensity is moderate we expect the symptoms will be minor and transient. Although some minor to moderate orthopedic injuries may occur during the exercise program (primarily lower body musculoskeletal injuries such as muscle sprains, tendonitis, shin splints) given the moderate intensity and gradual increase of the exercise prescription we do not expect any severe injuries. Participants who experience minor to moderate orthopedic injuries will be allowed to remain in the study and return to exercise as tolerated.

DXA:

The amount of radiation used for this procedure is very small. The radiation dose from each DXA scan is equivalent to 4 days of exposure to ambient radiation that people are naturally exposed to in the environment.

D3 Creatine Dilution:

Risks associated with this procedure include feelings of embarrassment and the inconvenience of collecting a urine sample. Participants will be informed well in advance of their testing appointment that this sampling will occur and will be provided all the materials needed so as to make the urine collection as simple and comfortable as possible.

Accelerometry:

The risks associated with wearing the accelerometer are minimal, and include skin irritation where the device is secured with the medical tape. Participants will be instructed to contact research staff in the case of irritation/itching. Sleep disturbances and general discomfort are also possible while wearing the accelerometers, but these risks are minimal.

6 Minute Walk Test:

Risks associated with this test are expected to be minimal for most participants. Risks are reduced by 1) allowing the participant to walk at their chosen pace (rather than on a motor-driven treadmill) and 2) instructing participants that they can either take a break or stop the test at any time during the 6-minute testing period.

In the unlikely event of a cardiac emergency, research staff will implement the approved Adverse Event Protocol for the Wallace Building. The building is equipped with a Cardiac A3 AED that is mounted on the wall in the area where 6 Minute Walk Tests are completed and all staff (personal trainers and technical staff) at Wallace are trained in CPR/AED. Ms. Ellison and Ms. Clina are also CPR/AED certified and Drs. Cohen and Sayer will renew their certifications prior to study initiation. Lastly, the Wallace Building is physically connected to the Encompass Hospital, which could provide emergency medical situations. Thus, we feel as though our research team and the Wallace Building are well-equipped to handle potential medical emergencies.

Resting Metabolic Rate:

Risks for this measurement include possible feelings of claustrophobia while the hood is covering the participants' faces. Participants will be given the opportunity to try the hood prior to beginning the measurement and can request that the measurement be stopped at any time.

Phlebotomy:

A peripheral blood draw is associated with minimal risk due primarily to the possibility of pain, bleeding, infection, and injury at the injection site. These risks are minimized by the use of generally accepted phlebotomy practices (e.g. injection site preparation, sanitary practices, and trained phlebotomists).

Questionnaires:

Some of the questionnaires included in the packet may be sensitive to some individuals. Participants may experience discomfort and/or anxiety while completing these questionnaires. To minimize this risk, participants will be given the opportunity to complete these questionnaires in private by providing a link to the REDCap interface and participants will also be informed that they can skip any question or questionnaire that makes them feel uncomfortable. The time burden associated with completing the questionnaire packet is another potential discomfort that is minimized by allowing participants to save their work on the linked website and complete the packet over multiple sessions if desired.

Fasting:

Risks of fasting are generally minimal but will be further mitigated by allowing participants to bring a snack of their choosing to consume following the outcome measures that require the participant to be fasted (blood draw and resting metabolic rate).

Data Collection Tools:

Study visit-specific source documents will be created to capture data for each study visit. Research data will be collected/entered and stored using REDCap. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Adverse Events:

Participants will be instructed to report adverse events as they occur, as well as will be given emergency contact information. In addition, we will formally query all participants about adverse events once a month.

Handling Incidental Findings:

If any clinically abnormal result or illness is uncovered, or if participants exhibit signs of depression or mental illness, the affected participant will be notified and referred to his/her physician or an

appropriate health professional for treatment. Participants will be offered copies of any tests or incidental findings.

Non-Compliance:

Clear and verifiable cases of non-compliance to the study protocol including failure to attend SOS classes, resistance training sessions, or study visits will result in the participant being withdrawn from the study. Because this study is purposely designed as a pragmatic and counseling-based weight loss intervention (rather than a controlled feeding trial), adherence to the dietary and exercise recommendations will be assessed as potential mediators of study results but no attempts will be made to use non-adherence the prescriptions as a criteria for study withdrawal.

If the protocol involves drugs or devices skip Items 20.b. and 20.c. and go to Item 21. Instead include this information in the Drug Review Sheet or Device Review Sheet, as applicable.

b. If hazards occur to an individual participant, describe (i) the criteria that will be used to decide whether that participant should be removed from the protocol; (ii) the procedure for removing such participants when necessary to protect their rights and welfare; and (iii) any special procedures, precautions, or follow-up that will be used to ensure the safety of other currently enrolled participants. **This is a minimal risk trial and behavioral weight loss is commonly recommended to people with obesity. We do not expect any significant hazards. Nonetheless, should any hazards occur, Dr. Brown will evaluate the situation and determine (i) what medical follow-up is necessary to ensure the participant's safety and (ii) whether there are any risks to participant safety or data validity that merit withdrawing the participant from the trial. Any withdrawals will be documented.**

c. If hazards occur that might make the risks of participation outweigh the benefits for all participants, describe (i) the criteria that will be used to stop or end the entire protocol and (ii) any special procedures, precautions, or follow-up that will be used to ensure the safety of currently enrolled participants. **Dr. Brown will review adverse event data regularly. This is a minimal risk trial. However, should the risks outweigh the benefits, the trial will be stopped. The IRB may also be consulted to ensure the safety of the enrolled participants.**

21. Informed Consent

a. Do you plan to obtain informed consent for this protocol? ☒Yes ☐No

If Yes, complete the items below.

If No, complete and include the Waiver of Informed Consent or Waiver of Authorization and Informed Consent, as applicable.

b. Do you plan to document informed consent (obtain signatures) for this protocol? ☒Yes ☐No

If Yes, complete the items below.

If No, complete the items below **and** include the Waiver of Informed Consent Documentation.

c. How will consent be obtained?

Consent Procedures.

Study staff obtaining informed consent will thoroughly understand all aspects of the research study and have completed IRB required training as directed by institutional requirements. The study coordinator (Dr. Cohen) or other research staff (Katherine Ellison or Julianne Clina) will provide and have the subject read the consent and discuss the study fully with the subject before obtaining written informed consent. All questions will be answered. If the subject wishes to participate in the study, a signature will be required and a copy of the consent form will be given to the subject.

d. Who will conduct the consent interview? **Dr. Cohen, Ms. Ellison, and Ms. Clina will conduct consent interviews.**

e. Who are the persons who will provide consent, permission, and/or assent? **Participants only**

f. What steps will be taken to minimize the possibility of coercion or undue influence? **Applicants will have ample opportunity to have all their questions answered and may discuss their participation in the trial with whomever they want. Also, applicants will be informed of all risks and benefits of participation, that their participation is voluntary, and that they may choose to end their participation in the study at any time.**

g. What language will the prospective participant and the legally authorized representative understand? **English**

h. What language will be used to obtain consent? **English**

i. If any potential participants will be, or will have been, in a stressful, painful, or drugged condition before or during the consent process, describe the precautions proposed to overcome the effect of the condition on the consent process. If not, enter "None." **None**

j. If any protocol-specific instruments will be used in the consenting process, such as supplemental handouts, videos, or websites, describe these here and provide a copy of each. If not, enter "None." **None**

k. How long will participants have between the time they are told about the protocol and the time they must decide whether to enroll? If not 24 hours or more, describe the proposed time interval and why the 24-hour minimum is neither feasible nor practical. **We will give all participants at least one week to decide.**

22. Procedures to Protect Privacy

Describe how you will protect the privacy interest of the participants. Include how you will make sure others cannot overhear your conversation with potential participants and that individuals will not be publicly identified or embarrassed. **The Webb and Wallace building has private interview rooms in which study visits will be conducted. No sensitive conversation will take place in public areas where the discussion may be overheard. Clinic staff will not make any statement where others can hear that might reveal personal information about the participant.**

23. Procedures to Maintain Confidentiality

a. Describe how you will store research data to maintain confidentiality (both paper records and electronic data), including how access is limited. If data will be stored electronically anywhere other than a server maintained centrally by UAB, identify the department and all computer systems used to store protocol-related data. **Paper records will be stored in a locking file cabinet in the locked offices of the study staff in the Webb building. Electronic data (including recorded videos) will be stored in REDCap and/or on computers which are firewall-protected, encrypted, and password-restricted. The servers are monitored at all times for outages. Secured login IDs, granted on a need-to-know basis, will be required to access confidential information.**

b. Will any data from this protocol be given to any person, including the subject, or any group, including coordinating centers and sponsors? ☒Yes ☐No

If Yes, complete i-iii.

i. Who will receive the data? **All participants will be offered copies of their own data if requested.**

ii. What data will be shared? **Data will be shared with participants through secure email, fax, or print-outs—as requested by the participant. For participants who want their test results sent to them via email, we will be encrypt their data using the encryption software 7-Zip. A fully de-identified complete dataset will be posted publicly in spreadsheet form online for other researchers to use. Any limited data sets that we share with others will be transmitted securely via encrypted methods and through password-protected files.**

iii. How will the data be identified, coded, etc.? **Data sent to participants will be coded with the visit dates and their names. The limited data sets will contain only the date of data collection, age, and the unique study ID numbers.**

24. Genomic Data Sharing (GDS)

Researchers who collect genomic data as part of a NIH grant funded after January 25, 2008 may be required to submit those data to a NIH database for broad scientific sharing. See Genomic Data Sharing in the IRB Guidebook for more information.

a. Does this protocol involve the proposed submission of genetic data into genomic repositories created to share genetic information for research purposes? ☐Yes ☒No

b. Will UAB be uploading the final genomic data to the central repository (e.g., dbGaP)? ☐Yes ☒No

If Yes to both a and b, submit a Detailed Data Sharing Plan to the IRB for review. This plan should include any known data use limitations and indicate whether aggregate-level data are appropriate for general research use. For guidance see the NIH Genomic Data Sharing Policy.

c. Submit a copy of the NIH Institutional Certification Form.

To determine which certification form to include, answer i-ii.

i. Was this protocol funded prior to January 25, 2015? ☐Yes ☐No

- **If yes,** and consent will be obtained, submit the Extramural Institutional Certification - Before January 25 - With Consent.
- **If yes,** and consent will not be obtained, submit the Extramural Institutional Certification - Before January 25 - Without Consent.

ii. Was this protocol funded after January 25, 2015? ☐Yes ☐No

- **If yes,** submit the Extramural Institutional Certification - After January 25.

25. Additional Information

In the space below, provide any additional information that you believe may help the IRB review the proposed research, or enter "None." **Please note that we made additional changes to the study protocol based on the review of an extramural grant using a similar experimental design. These changes include recruitment of men and women (rather than women only), increasing the length of the study from 16 to 52 weeks, and modifications to the delivery of the dietary and exercise programs. Dr. Irfan Asif, Chairman of the Department of Family and Community Medicine has also been added as a sub-investigator. The recruitment letter from the MD to patients has been modified with Dr. Asif's signature and contact information because we anticipate that many participants for this protocol will be obtained from patients at the UAB Family Medicine Clinic.**

Statistical Analysis Plans:

Recruitment: For this study, we would consider 16 weeks to be the feasible amount of time required to recruit 40 participants into the proposed research. In our experience, some potential participants become either disinterested or experience changes in inclusion/exclusion criteria once recruitment periods extend beyond 16 weeks. In the event that recruitment requires >16 weeks, we will modify the study design of the full-scale SMART and/or dedicate additional financial and personnel resources to study recruitment to reduce the recruitment period.

Retention: The proposed K01 research will continue with monthly weight loss maintenance classes to encourage continued engagement in the study. For this study, retention rates of 90% at week 8, 85% at week 16 and 80% at week 52 would indicate that the study is feasible as is. Week 8 and week 16 retention rates are consistent with our past trials using SOS. An 80% retention rate at week 52 would represent a marked improvements in past research using SOS, but is in line with other research using a 1 year behavioral intervention for obesity. We also believe these retention rates are achievable due to the adaptive structure of the SMART, which may improve adherence and/or study retention rates because the 2nd stage intervention provides an alternative for participants who are not responding to their initial group assignment.

Class Attendance: The proposed K01 study will involve 16 weekly SOS classes for weight loss followed by 8 monthly *Next Steps* classes for weight loss maintenance. For this study, an average class attendance rate of ≥87.5% for both SOS (14 of 16 classes) and *Next Steps* (7 of 8 classes) would indicate that this portion of the study is feasible as is.

Treatment Credibility: Participants will report their expectations regarding the effectiveness of 1st and 2nd stage interventions by completing the Credibility/Expectancy Questionnaire (CEQ). The CEQ will be modified for weight loss expectations and credibility. Participants will be aware of their intervention assignments at the time of survey completion, but will not have begun the intervention. The CEQ consists of two scales to assess treatment credibility and expectancy. The first scale is focused on participant *thoughts* about treatment credibility and expectancy whereas the second scales is concerned with participants *feelings* on these same constructs. Credibility is assessed by answering 4 questions and using a 9-point Likert scale with values ranging from 1: Not at all logical/useful/confident to 9: Very logical/useful/confident. Participants rate their thoughts and feelings of treatment expectancy by selecting the percentage improvement in their body weight they expect by the conclusion of the study. The scales are delivered in 10% increments from 0% to 100%. Participants will be instructed that 100% improvement would indicate they have reached their own personal "goal weight." From these items, separate composite scores are calculated for treatment credibility and expectancy. Independent *t*-tests will be used to compare 1st stage intervention credibility and expectancy (all participants) as well as 2nd stage intervention credibility and expectancy (Non-Responders only). If differences in these constructs are likely (type-1 error rate of 10%), linear mixed models will be used to investigate effects of perceived effective/preferred interventions on changes in body weight and composition while including factors for 1st and 2nd stage intervention assignments. These models will test for main effects of credibility and expectancy as well as their interaction with 1st and 2nd stage intervention assignment on changes in body weight and composition. Linear correlations of credibility and expectancy with changes in body weight and composition will also be investigated using Pearson's correlation coefficients and multiple linear regression.

Intervention Preference: All participants will complete a 2-item Intervention Preference questionnaire at baseline that assesses preference for the adaptive intervention approach of the SMART vs. a parallel design randomized trial as well as 1st stage interventions of HP vs. RT. Non-Responders will complete an additional Intervention Preference Questionnaire at week 8 to assess preference for Intensify vs. Combine 2nd stage interventions. The questionnaire uses a 5-point Likert scale with "1" and "5" representing a strong preference for either intervention and "3" representing no intervention preference. Intervention preferences for 1st and 2nd stage interventions will be assessed at the baseline and week 8 visits, respectively, prior to informing participants of their intervention assignments. First, we investigate potential differences in preference for the SMART vs. parallel design trial, HP vs. RT, and Intensify vs. Combine. The Chi-Square statistic will used to quantify potential differential proportions of participants reporting intervention preferences (1+2, or 4+5 on Likert scale) and no preference (3 on the scale). Participants will then be classified as being assigned to their preferred or non-preferred interventions. A single factor analysis of covariance with 3 levels will be used to compare changes in body weight and composition among 1) participants with no preference, 2) those assigned to preferred interventions, and 3) those assigned to non-preferred interventions.

Main Effect of 1st and 2nd Stage Interventions: The main effect describing the comparative effectiveness of the 1st stage interventions (HP vs. RT) will be assessed by pooling and comparing week 16 and week 52 changes in body weight and composition for all participants initially assigned to HP and RT. This analysis is completed using a linear mixed model (Analysis of Covariance [ANCOVA]) that controls for 2nd stage intervention assignment. The comparative effectiveness of 2nd stage intervention options (Intensify vs. Combine) for Non-Responders will be assessed using a linear mixed model (ANCOVA) that controls for 1st stage intervention assignment. Both models are identical to single factor models with 2 levels (1st stage: HP vs. RT; 2nd stage: Intensify vs. Combine) that would be used to analyze data from a two-arm parallel design randomized trial.

Embedded Adaptive Interventions: Linear mixed model approaches are also be used to compare the 2 or more embedded adaptive interventions that arise in in a typical SMART. However, a weighted regression approach must be employed because Responders are only randomized once in the SMART while Non-Responders are randomized twice. Therefore, their chances of following a particular intervention sequence are different, which results in Non-Responders being relatively underrepresented in the data in terms of 2nd stage interventions offerings. Specifically, a Responder has a 1/2 chance of following the sequence of interventions available whereas a Non-Responder has a 1/4 chance of following any particular intervention sequence. Weights are inversely proportional to the probability of being assigned to a particular intervention sequence, which requires that Non-Responders are assigned a weight of 4 and Responders are assigned a weight of 2. With the weights included in the model, we can pool data from Responders to 1st stage HP and Non-Responders assigned to Intensify HP for comparison to pooled data from Responders to 1st stage RT and Non-Responders assigned to Intensify RT. This analysis provides an estimation of comparative effectiveness of adaptive intervention **#1:** initiate with counseling to consume a HP diet and, if unsuccessful, intensify the HP diet by providing a protein supplement vs. **#3:** initiate with counseling to engage in RT and, if unsuccessful, intensify RT by supervising exercise sessions.

UAB IRB
Approved
21-Mar-2023
until
27-Sep-2023

CONSENT FORM TO BE PART OF A RESEARCH STUDY

Title of Research: Effects of Dietary Protein Intake and Resistance Training on Retention of Fat Free Mass during Weight Loss in Adults over 50 with Obesity

UAB IRB Protocol #: IRB-300003818

Principal Investigator: Drew Sayer, PhD

Sponsor: UAB Nutrition Obesity Research Center, UAB Department of Nutrition Science

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to compare two approaches to weight loss for body composition and other aspects of health.
Duration & Visits	You will be in this study for 52 weeks (1 year). There will be 5 study visits including screening to determine your eligibility for the study and visits at baseline, week 8, week 16, and week 52. You will also participate in weekly group weight loss classes via video conference for 16 weeks and monthly group weight loss maintenance classes via video conference for 8 months. Depending on your results in the study and the group you are assigned to, you may also complete supervised exercise sessions 2 times per week for weeks 9-16 of the study.
Overview of Procedures	This study will include a screening visit that includes a physical exam and a blood draw. If you are eligible to enroll in the study, you complete a weight loss program called State of Slim and will be randomly assigned (like a coin toss) to either a high-protein diet with flexibility training or standard-protein diet with resistance training. Study visits at baseline, week 8, week 16, and week 52 will include a physical exam, blood draw, and tests of your physical health. You will also be asked to complete a packet of surveys at baseline, week 8, week 16, and week 52, which can be completed at home.
Risks	The most common risks include pain or bruising from the blood draws, the possibility of injuries during the weight loss program or physical health tests, discomfort from wearing an accelerometer and other metabolic tests, and loss of confidentiality. There is also risk from exposure to low-level radiation from x-rays during body composition testing.
Benefits	You may benefit from study by losing weight in the State of Slim program, but you may not benefit from this study. Weight loss is not guaranteed.
Alternatives	Instead of participating in this study, you could choose to lose weight on your own, by using a different program, or choose not to lose weight at all.

Purpose of the Research Study

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the

information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
Previous research has shown that diets high in protein and exercise programs that include resistance training (e.g., weight lifting or strength training) can be beneficial for older adults with obesity. However, more research is needed to determine how different diets and types of exercise might impact body composition (the amount of muscle and fat you have). Specifically, this study will study the effects of consuming a high protein diet, engaging in a resistance training program, and their combination on changes in body composition. In addition, this study plans to learn more about the factors that are related to how much weight people lose during the study.

You are being asked to be in this research study because you have expressed an interest in losing weight.

Other people in this study
Up to 90 people from the Birmingham, AL area will be in the study.

Study Participation & Procedures

After you expressed interest in the study, you were contacted by a research staff member to complete a phone screening to assess your potential eligibility for and interest in the study. After phone screening, you will be invited to participate in an online group-based orientation session that provides an overview of the study procedures, frequency of online sessions and study visits, in addition to potential benefits and risks. During the orientation session, you will also meet the study team who will answer any questions you may have. If you are interested and decide to participate, you will be provided with a website link by email to complete the Study Intake Questionnaire prior to your in-person screening visit. This questionnaire includes information about your medical history and will be reviewed by the study team to confirm your eligibility to participate. If you are deemed ineligible for the study or decide not to participate, your completed questionnaire will be destroyed. The screening visit includes reviewing and signing the consent form for the study and, if you agree to participate, a physical exam (body weight, height, and blood pressure), and a blood draw.

If you are deemed eligible and decide to join the study, you will be assigned to a weight loss program with counseling to either consume a diet with a higher amount of protein or to start a resistance training (weight lifting) program. We will use a method of chance (like the flip of a coin) to determine which group you will be in for at least the first 8 weeks of the study. You have an equal chance of being assigned to either program. We will measure your progress after 8 weeks, and we may make changes to your diet or exercise to help you lose weight and limit your loss of muscle. If it is determined from these tests that you might benefit from additional interventions, you will be randomly assigned (like a coin toss) to receive a whey protein powder supplement, initiate a supervised resistance training program with a personal trainer, or both.

If you are assigned to the whey protein powder supplement, you will be provided with the supplement and a shaker cup at no cost to you and asked to consume the supplement twice per day for weeks 9-16 of the study. If you are assigned to initiate a supervised resistance training program, you will meet 2 times per week with a personal trainer and up to 3 additional study participants to exercise with the trainer's supervision and support. These personal training sessions will also be completed via video conference.

The study will last 52 weeks. After your baseline study visit, you will participate in a resistance training orientation session with a personal trainer and receive a resistance training rubber band if you are assigned to

the resistance training group. If you are assigned to the higher protein group, you will also participate in an orientation session with a personal trainer for balance and flexibility exercises. All participants will participate in the State of Slim weight loss program, which will consist of 16 weekly meetings via video conference with up to 14 other participants and a State of Slim weight loss coach. The weight loss coach will provide you with resources, support, and educational materials to help you follow your prescribed diet and/or exercise plan to lose weight. After 16 weeks and for the remainder of the study, all participants will continue with monthly meetings via video conference with the same participants and State of Slim weight loss coach (8 classes).

Regardless of which weight loss program you are assigned to, you will be followed in the study for 52 weeks. In addition to the virtual classes for the State of Slim program and the exercise sessions, there will be 5 study visits over the course of the 52 weeks. Study visits will occur today at screening, baseline, week 8, week 16, and week 52. The procedures performed at the study visits are for research purposes only. Any changes to your medical care should be done with guidance from your doctor. We ask that you let us know if your doctor recommends any changes to your medical care during the study.

Study Visits and Procedures.
You will complete the following measures after an overnight fast (no food or beverages except water for 8 hours) during study visits at baseline, week 8, week 16, and week 52 unless otherwise noted:

Body Measurements:
We will measure your height, weight, and waist circumference.

Body Composition Testing:
You will have your body composition (amount of fat mass and fat free mass) measured by Dual Energy X-Ray Absorptiometry (DXA) on 4 occasions. You will be asked to lie still on a table for 10 to 15 minutes while the scanner takes data. These scans will expose you to a low level of radiation. Your natural environment has some radiation in it.

Body composition (fat mass and lean mass) will be measured with an InBody S10 and H20N via bioelectrical impedance analysis on 4 occasions. You will be asked to lay in a supine position for 10-15 minutes prior to the test. The body composition test takes 2 minutes to complete and is obtained by placing electrodes on your finger, thumb, and ankle. A small, undetectable electric charge is sent through the body and the length of time required for the charge to pass through the body is used to determine body composition.

Blood Draw:
We will collect blood samples from you 5 times (at screening, baseline, week 8, week 16, and week 52). The total amount of blood we will collect will be approximately 10 tablespoons or 2 tablespoons at each study visit. We will get blood by putting a needle into one of your veins and letting the blood flow into a tube.

Finger Stick:
We will collect a finger stick blood sample from you 4 times (at baseline, week 8, week 16, and week 52). The total amount of blood we collect will be approximately 41.5 micrograms at each study visit. We will get blood by sticking your finger (usually the ring finger of your non-dominant hand) with a lancet and drawing the blood into a capillary tube.

Oral Glucose Tolerance Test:

For this test, you will consume a sugary drink, and 30 minutes later, we will measure your blood sugar and insulin by taking a small blood sample. This test is designed to determine how your body responds when you consume sugar.

Blood Pressure:
We will measure your blood pressure by placing a cuff on your upper arm. We will measure this on 5 occasions.

Fitness Testing:
You will do five physical fitness tests. The first is called a 3 Minute Step Test where you will be asked to step onto a 12-inch box for 3 minutes. Your heart rate and blood pressure will be taken before and after the test. The step test will be completed in a patient room within the clinic.

Second, you will be asked to hold a plank position for as long as you can. A plank position involves holding the trunk part of your body in a straight line off the ground by positioning yourself on your hands and toes.

Third, you will be asked to jump vertically off a mat three consecutive times to measure your jump height.

Fourth, you will be asked to sit on the floor so that your legs are fully extended, and your feet are flat against the front board of the sit and reach box. You will then reach forward with one hand on top of the other so that your fingers are aligned. Study personnel will measure how many inches you extend forward as a test of your linear flexibility.

Fifth, your forearm strength and upper body strength will be tested by a device called a hand grip dynamometer. For this test, you will be asked to sit comfortably and grip the hand dynamometer for several seconds as hard as you can (three times with each hand, alternating between hands), and then relax for 10-20 seconds between tests.

Activity Monitoring:
The amount of time you spend being physically active, sedentary/sitting, and lying down will be measured using a small device called an accelerometer. If you are ambulatory, the accelerometer will be attached to your upper thigh with medical tape. You will wear the accelerometer for 7 consecutive days at 4 different times (7 days at baseline, week 8, week 16, and week 52). The accelerometer will be placed inside a waterproof sleeve and covered with waterproof medical tape. You can shower/bathe while the accelerometer is attached, but we ask that you do not swim during this time.

If you are a wheelchair user, the accelerometer will be attached to your chair to count wheel revolutions. The accelerometer will be placed on your chair for 7 consecutive days at 4 different times (7 days at baseline, week 8, week 16, and week 52). If you regularly use more than one chair, we will ask that you bring the additional chair(s) to the study visit so we can attach an accelerometer to each.

Questionnaires:
You will be asked to complete a series of questionnaires that are related to weight loss and your diet, physical activity (exercise and sitting), stress, and sleep behaviors. We are collecting this information from you to see how these behaviors might change during the study and to see if your answers are related to how much weight you lose during the study. The amount of time required to complete the questionnaires will be different for each person, but it is estimated to take approximately 90 to 120 minutes. You will be provided with a website link by email to complete the questionnaires so you can complete them at home, unless you

have opted-out of receiving study-related emails. You will also be able to save your work and complete the questionnaires over multiple sessions if desired. Questionnaires to be completed include:

- Rapid Eating Assessment for Participants
- Nutrition Knowledge Questionnaire
- Nutrition Skills Questionnaire
- Mindfulness Scale
- Growth and Voyager Mindset Questionnaire
- Quality of Life Scale
- Oxford Happiness Scale
- Satisfaction with Life Scale
- Modified Satisfaction with Food-Related Life Scale
- Satisfaction with Exercise-Related Life Scale
- Satisfaction with Body-Related Life Scale
- Satisfaction with Mindset-Related Life Scale
- Modified Weight Bias Internalization Scale
- Adult Food Security Survey Module
- Daily appetite (hunger, fullness, and cravings) ratings will be completed at the end of the day for 7 days.
- Perceived Stress Scale
- Brief Resilience Scale
- Treatment Self-Regulation Questionnaire
- Intervention Preference Questionnaire
- Credibility/Expectancy Questionnaire

You will also be asked to complete State of Slim food and exercise logs documenting your food consumption and exercise; these logs will be dispensed and returned at study visits.

You will also be asked to provide your home, work, and/or school addresses, which may be used for research purposes.

See table below of assessments by visit:

Table of Assessments	**Screen**	**Baseline**	**Wk 8**	**Wk 16**	**Wk 52**
Informed consent	X				
Study Intake Questionnaire	X				
Height	X				
Weight	X	X	X	X	X
Waist circumference		X	X	X	X
Body composition by DXA scan		X	X	X	X
Body composition by InBody S10		X	X	X	X
Body composition by InBody H20N		X	X	X	X
3 Minute Step Test		X	X	X	X
Plank Time Test		X	X	X	X
Vertical Jump Test		X	X	X	X
Sit and Reach Test		X	X	X	X
Handgrip Strength Test		X	X	X	X

Blood draw	X	X	X	X	X
Finger stick		X	X	X	X
Oral glucose tolerance test		X	X	X	X
Blood pressure	X	X	X	X	X
Activity monitoring for 7 days		X	X	X	X
24-hour dietary recalls		X	X	X	X
Questionnaire packet		X	X	X	X
Assess for adverse events		X	X	X	X
Document concomitant medications	X	X	X	X	X

Your de-identified private information (private information with all identifiers removed) may be used for future research studies or distributed to another researcher for future research studies without additional informed consent.

The data obtained from you in this research, which may or may not include your identifiable private information, may be used for commercial profit. There are no plans to provide financial compensation to you should this occur.

Your individual results obtained during the study can be given to you at the end of the study if you request them.

Risks and Discomforts

Discomforts or possible risks you may experience while in this study are detailed below.

- Randomization: You will be assigned to a weight loss program by chance, which may prove to be less effective or to have more side effects than the other program or alternatives.

- Confidentiality: There is a risk that people outside of the research team will see your research information, including information that identifies you personally. We will do all that we can to protect your information, but it cannot be guaranteed.

- State of Slim Weight Management Program: You may not like or may find it difficult to follow the State of Slim program. You may experience anxiety or dissatisfaction with your prescribed diet and recommended food items and exercise goals. You may find it inconvenient to follow your prescribed diet and to complete the daily compliance logs. You may experience bodily aches, pains, and possibly injuries as a result of increasing your exercise.

- Resistance Training: By beginning a new exercise program, there is a risk for fatigue, shortness of breath, or muscle soreness during or after the training sessions. If these symptoms occur, it is likely that they will be minor and brief. During exercise there is a very small risk that you may have symptoms such as chest pain, shortness of breath, dizziness, fainting, or cramping.

- Body Composition Testing: In this study, you will be exposed to a very low level of radiation during the DXA scan. Each DXA scan will give you about the same amount of radiation that you would get from your environment in 4 days; thus, 4 DXA scans will give you about the same amount of radiation that you would get from your environment in 16 days. Radiation from the environment or "background

radiation" is radiation normally received from sources such as cosmic rays and natural radioactivity in building materials and the ground.

- Blood Draws, Finger Sticks, and Oral Glucose Tolerance Test: Taking blood from the arm vein or finger may cause some minor discomfort. You may feel some pain when the needle goes into your vein or finger. A day or two later, you may have a small bruise where the needle went under the skin. The puncture site will be cleaned prior to inserting the needle to minimize the risk of infection.

- Fitness Testing: Common discomforts and risks associated with the physical fitness testing include sweating, tiredness, feeling out of breath, and muscle soreness after the test; these tests also present the risk of falling. Less common risks include risk of injuries to your muscles or joints, headache, dizziness, nausea/vomiting, high or low blood pressure, and wheezing. There is a small, but serious, risk of abnormal heartbeats, chest pain, passing out, heart attack, stroke, or death. You will be allowed to rest or stop the test at any time during , the 3 Minute Step Test, Plank Time Test, the Vertical Jump Test, the Sit and Reach Test and the Handgrip Strength Test.

- Activity Monitoring: Minimal risks are associated with wearing an accelerometer, such as skin irritation from the medical tape at the attachment site and possible sleep disturbances due to discomfort from the device. You may also find it inconvenient to wear the accelerometer for 7 days and to refrain from swimming.

- Fasting: You will be asked to arrive at study visits (screening, baseline, week 8, week 16, and week 52) after an 8-hour overnight fast. During the fasting time, you will be asked not to consume any foods or beverages except water. You should take all of your regular medications as usual prior to each visit with the exception of any sulfonylureas, which should be withheld until just before eating. Risks of fasting include lightheadedness, dizziness, weakness and low blood sugar. You will be allowed to bring a snack of your choosing to consume after completing the fasting-state blood draw and resting metabolic rate measurement.

- Questionnaire Packet: Possible risks for completing the questionnaires include discomfort or anxiety while completing the questionnaires. You may skip any question(s) or questionnaire(s) that make you feel uncomfortable. If some responses from these questionnaires are concerning or make you feel anxious, you should follow up with your primary care physician.

- Email Communication: We are requesting your permission to use email for limited communications related to the study. We would like to send you emails to 1) schedule study visits, 2) send you reminders about study visits, and 3) to deliver the questionnaire packet at baseline, week 8, and week 16. The main risk of using unencrypted email is a potential risk of an unauthorized party intercepting and viewing the email communication. We will attempt to reduce the risk by including as little personal information in the email as possible (for example, information about your medical history and diagnoses). You can opt-in or opt-out of email communications below. If you choose to opt-out of receiving emails, we will schedule your study visits and remind you of study visits by phone. For completion of questionnaires, most of these can be delivered to you by traditional mail and completed using pen and paper. The exception is the Diet History Questionnaire III, which must be completed online. If you choose not to receive emails during the study, we will ask you to complete this questionnaire on a computer during the study visits at baseline, week 8, week 16, and week 52. Please

note that the Diet History Questionnaire III takes approximately 1 hour to complete, which would be in addition the remainder of the study visit.

Initial your choice below:

___ I agree to allow research staff to contact by unencrypted email.

___ I do not agree to allow research staff to contact by unencrypted email.

There may be risks related to this study that are unknown.

UAB has made no provision for compensation in the event of injury or harm resulting from the research. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Benefits

You may not benefit from being in this study. It is possible that you will not lose weight and receive no medical benefit by participating. There is no guarantee that your health will improve if you join this study. Also, there may be risks from being in the study as discussed in the section describing the discomforts or risks.
It is possible that you may lose weight during this study, which may be associated with some health benefits.

Alternatives

There are other weight loss options available, including other weight loss behavioral programs and weight loss medications and surgery. You could also choose not to lose weight. You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you. If you agree participate in this study, however, you may not join any other weight loss programs or take any weight loss medications until the study has been completed (total of 52 weeks).

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g.,

treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System or Children's of Alabama. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator.

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

Results of research tests or procedures may be placed in your medical record. All information within your medical record can be viewed by individuals authorized to access the record.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who may use and give out information about you?
Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in it. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact the study doctor if you want to withdraw from the study.

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, if you are not following the study rules, or for any other reason. Also, the sponsor may stop the study at any time.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

You will be responsible for paying for your own transportation to and from all study visits and training sessions during the study. The State of Slim program, study procedures, and parking will be provided at no cost to you.

The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

Payment for Participation

You will be paid $100.00 after completing your week 8 visit, $50 after your week 16 visit, and $150.00 after your week 52 visit. This will equal $300.00 for your participation in the study. The payment will be sent after you have completed all of the visit activities, including the questionnaires and returning the accelerometer. If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit). Additionally, you will be provided with a body weight scale that you may keep after completion of the study.

New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Co-enrollment in the International Weight Control Registry Study

The International Weight Control Registry (IWCR) is a new research project managed by Tufts University and the University of Alabama at Birmingham. The aim of this project is to determine how people from different cultures can lose weight and keep it off. Your participation will help us identify factors associated with successful weight loss and will be used to support weight management and the health of individuals worldwide.

Whether or not you have lost a significant amount of weight since the age of 18, we would love to hear about your experiences. If eligible, you will complete questionnaires on factors related to weight management. We will also ask you to complete a smaller number of questions once a year so we can track your experiences over time. Each questionnaire will be a slightly different length, and you can stop and save your work at any time and return as often as you need. If you consent, your research data from the current trial (IRB-300003818) will be linked to the IWCR and available to the UAB and IWCR research teams.

Your participation is voluntary, and you may stop participating at any time without penalty. Also, your participation in the IWCR does not affect your ability to enroll in the current study.

Initial your choices below:

___ If eligible, I agree to co-enroll in the International Control Weight Registry study

___ I do not agree to co-enroll in the International Control Weight Registry study

Optional Research

Future Research Use of Research Data

We would like your permission to keep the data collected from you in this research for future research. This data would include all outcomes of the current study that are listed in the table above, the information you provide in the Study Intake Questionnaire, and the addresses for your home, work, and/or school. The future research may be similar to this study or may be completely different. Additionally, we would like to do a limited search of your electronic medical record once per year for up to 10 years after the study is completed to gather long-term clinical measurements of the metabolic syndrome. Metabolic syndrome is a cluster of clinical measurements related to heart disease risk including body weight, waist circumference, blood glucose (sugar), blood lipid and cholesterol, and blood pressure. The data we collect from the study and the long-term follow-up will be kept indefinitely. Information in electronic format will be kept in password-protected files or on encrypted computers in locked offices. Information in paper format will be kept in locking filing cabinets in locked offices.

It is possible that future research may require access to your private identifiable information and/or blood samples. Results of any future research will not be given to you or your doctor.

You can take part in this study even if you decide not to let us use your data for future research or participate in the long-term follow-up.

If you give us permission now to keep and use your study data, you can change your mind later and ask us to destroy it. However, once we have analyzed your data, we may not be able to take it out of our future research.

We may share your data, so that others can use it in their research. All data would be fully de-identified prior to posting it publicly in an online spreadsheet form. Their research may be similar to this study or may be completely different. Once we have shared your data with other researchers, we will not be able to get it back.

Future research use of data will be conducted in compliance with applicable regulatory requirements. You will not find out the results of future research on data. Allowing us to do future research on your data will not benefit you directly.

The data used for future research may be used for commercial profit. There are no plans to provide financial compensation to you should this occur.

Initial your choices below:

Data for future use:

___ I agree to allow research data collected from me to be kept and used for future research on obesity.

___ I do not agree to allow research data collected from me to be kept and used for future research.

Long-term follow-up:

___ I agree to allow the research staff to conduct a limited annual search of my electronic medical record for up to 10 years following the completion of the study and be kept for future research.

___ I do not agree to allow the research staff to conduct a limited annual search of my electronic medical record for up to 10 years following the completion of the study and be kept for future research.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Drew Sayer, PhD on his office phone at (205) 354-8950, by email at sayerd@uab.edu, or after hours by calling him at (720) 357-2495.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date