Title: Time Restricted Eating Outcomes in Multiple Sclerosis (TREO MS)

NCT number: NCT04389970

Date: 5/5/2020

- 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; click checkboxes to check/uncheck.
- All responses should be Times New Roman, Bold, and Underlined.
- NOTES REGARDING VA RESEARCH: BVAMC research cannot be reviewed by an external IRB (only UAB IRB). Ensure you complete this form for any BVAMC research. BVAMC Research must be signed off by the BVAMC supervisor for scientific/scholarly review via PORF prior to submission of this form.

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: Time Restricted Eating Outcomes in Multiple Sclerosis (TREO MS)

2. Investigator and Contact Person

a. Name of Principal Investigator: **Brooks Wingo**
Degree(s)/Title: **PhD** BlazerID: **kbcotton**
Dept/Div: **Occupational Therapy** Mailing Address: **SHPB 385** UAB ZIP: **1212**
Phone: **4-5982** E-mail: **bcwingo@uab.edu**

b. Name of Contact Person: **Kathryn Green** Title: **Research Coordinator**
Phone: **205-319-14-24** E-mail: **kathryngreen@uabmc.edu**

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 submission 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:** **5-5-2020**

3. Protocol Personnel

a. Complete the **IRB PERSONNEL FORM to list all key personnel (each individual involved in the design and conduct of this protocol).**

b. Non-UAB Personnel Relying on UAB IRB - If you are requesting that the UAB IRB serve as the IRB of record for any non-UAB personnel, list these individuals below. Add additional rows as necessary.

Name and Degree	From Institution with or without own IRB?	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)

***** 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.***

VA Personnel: The VA Financial Conflict of Interest (fCOI) form must be submitted to the VA fCOI Committee Chair. Include in 3.a above any financial conflict of interest as submitted on that VA fCOI form. If there is a conflict, submit a copy of the management plan with this submission.

c. Are any of the investigators listed on the IRB PERSONNEL FORM students using this research for their thesis or dissertation? ☐Yes ☒No

If No, continue with Item 3d.

If Yes, provide the name of the student and the Thesis/Dissertation Title: _____

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: _____

Supervisor's Signature:_____

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

If Yes, who will provide the medical supervision?

☐ PI will provide ***-OR-***

☐ Other:

Name: _____ Telephone: _____

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

Signature _____

f. 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. Wingo will devote 10% of her time to this study. She will work with the research coordinator (K. Green) to oversee all aspects of participant recruitment, protocol development and data collection. She will oversee training of all study staff who will be directly involved with participants, and she will be responsible for quality control of data collection procedures.**

g. Describe your process for ensuring all key personnel are adequately informed about the protocol and their research-related duties and functions: **All persons assisting with the research will receive a copy of the study protocol where their roles are detailed. We will hold weekly meetings at the start-up of the study to ensure research-related duties and functions are understood. We will create a Manual of Operations which details duties and functions to be carried out during the study.**

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: **Time Restricted Eating Outcomes in Multiple Sclerosis (TREO MS)**

b. UAB PI of Grant, Contract, or Agreement: **Brooks Wingo**

c. Office of Sponsored Programs (OSP) Assigned Number: **NA (intramural award from UAB NORC)**
(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-sponsored, industry-initiated - Name: _____
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.
☐ Industry-sponsored, 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)**
☐ VA Funding —Specify: _____

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 NOTE: *Research may only be conducted by investigators who have a BVAMC appointment*
☐ Jefferson County Department of Health
☒ Other (i.e., any performance site not listed above, including those covered by subawards related to this protocol) - Describe: **UAB Wallace Research Lab at Lakeshore Foundation, School of Health Professionals Building, Webb Bldg.**
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):
UAB MS Clinics in TKC will assist with recruitment by placing flyers in the waiting rooms.
UAB Wallace Research Lab: All baseline and endpoint data collection will be conducted in the Wallace lab. Paper records will also be stored here until the study is complete. The research coordinator's office is also at Wallace.
SHPB: The PI's office is in SHPB. All paper study records will be moved here once the study is complete.

Webb: Blood samples will be stored and analyzed in the Webb Bldg.

c. Does this protocol require clinical services at one of the 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 Fiscal Approval Process (FAP)-designated unit 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 BVAMC consent form(s), if applicable. Attach any other applicable BVAMC forms (such as the Privacy and Information Security Checklist and The BVAMC FCOI forms).
NOTE: Investigators conducting research at BVAMC **must** have a BVAMC appointment.
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: **NCT04389970**
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? ☐Yes ☒No
b. Is the UAB Investigator the lead investigator? ☐Yes ☒No
c. Is this a multi-site study with a coordinating site? ☐Yes ☒No
d. Is this a multi-site study with UAB as a coordinating site? ☐Yes ☒No

If Yes to a, b, c, or d, 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 result; & 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.
If BVAMC, attached the completed BVAMC 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. **The protocol has been registered with OHS and has now approved the DXA protocol.**

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 biospecimens, 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) biospecimens from a repository? ☐Yes ☒No
If Yes, attach documentation of approval for use of biospecimens, and describe how existing biospecimens are labeled: _____

11. Use of Biospecimens

Does this protocol involve the collection of biospecimens? ☒Yes ☐No
If Yes, complete 11.a-11.h.
If No, skip to Item 12.

a. How will biospecimens be obtained, processed, distributed, and stored? **A fasting blood draw of two (2) vials (7 mL or 1.4 teaspoons) via venipuncture (7 mL) will be collected to assess insulin, markers of inflammation, and a lipid panel. Serum samples will be stored in the Webb Bldg until the end of the**

study. Once all data collection is complete, samples will be analyzed by the NORC metabolism core in the Webb Bldg. There will be blood collected at baseline and at the follow up visit.

b. How will biospecimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)? **Unique study identifier, date, and assessment point will be the only information included on the label.**

c. How will clinical data associated with the biospecimens be collected and stored? **Clinical data will be stored on a password-protected computer on the UAB server.**

d. What participant-identifying information will be collected and linked to the biospecimens? **Unique study identifier will be the only participant-identifying information.**

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" biospecimens). **Documents connecting the participant with their associated identifier will be locked in a cabinet in the Wallace Research Lab and only the PI and research coordinator (K. Green) will have access to the files. Also, the information will be available through REDCap, which is password protected and only those on this project will have access to the information.**

f. Is genetic testing planned as part of this protocol? ☐Yes ☒No

If Yes, describe the planned genetic testing here. _____

i. Does this include whole genome sequencing? ☐Yes ☐No

ii. Will participants be informed of the results of any DNA testing? ☐Yes ☐No

g. Will biospecimens 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. In addition, indicate where the biospecimens will be banked _____

- If above is a BVAMC location, what IRB is responsible for overseeing the operations of the biospecimens bank (i.e., local IRB or other multi-site or central IRB?) _____

h. Will biospecimens be shared with other investigators in the future? ☐Yes ☒No

i. What identifiers, clinical information and demographic information will be shared; or will the biospecimens be stripped of identifiers (i.e., anonymized)? _____

NOTE: *Coding data is not considered anonymous.*

ii. Outline your procedure for assuring IRB approval for release and use prior to release of biospecimens. _____

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

i. Will specimens be destroyed after the project-specific use is completed? ☒Yes ☐No

j. Will specimens be used and/or shared for commercial profit? ☐Yes ☒No

k. Will specimens be destroyed after the project-specific use is completed? ☒Yes ☐No

l. Will participants be informed of the results of the specimen testing? ☐Yes ☒No

m. Are there any implications for family members based on specimen testing results? ☐Yes ☒No

(If yes, the family members may be participants.)

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
☐ Birmingham Veterans Affairs Medical Center
☐ 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 or BVAMC server - Describe: No information systems will be the sources of information for the protocol.

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

NOTE: For BVAMC research, the BVAMC HIPAA authorization form or UAB HIPAA waiver form must be completed and submitted with the HSP.

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 pilot study is to determine the preliminary efficacy, safety, and acceptability of time restricted feeding (TRF) among a sample of 12 adults with Relapsing-Remitting Multiple Sclerosis (RRMS). The specific aims of this study are: 1: To determine preliminary efficacy of TRF for reducing symptom burden, improving inflammatory markers, and reducing cardiometabolic risk among adults with RRMS. 2: To determine the safety and participant acceptability of TRF. Participants will be asked to consume all food during an 8-hour window each day and not eat for the remaining 16 hours. All participants will follow this eating pattern for 8 weeks.

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

I. Clinical outcomes of MS. We will use the Multiple Sclerosis Functional Composite (MSFC) and the Patient-Determined Disease Steps (PDDS) to measure clinical outcomes. The MSFC includes three components: a timed 25-foot walk, 9-hole peg test, and the symbol digit modalities test. The PDDS is a patient-reported measure of disability.

II. Patient-reported outcomes. Symptoms of depression, anxiety, fatigue, and pain will be measured by the Hospital Anxiety and Depression Scale (HADS), Modified Fatigue Impact Scale (MFIS), Fatigue Severity Scale (FSS), and short-form McGill Pain Questionnaire (SF-MPQ), respectively. We will measure sleep using the Pittsburg Sleep Quality Index. The HADS contains 14 items that measure the frequency of anxiety and depressive symptoms over the past week. The MFIS is a 21-item measure of physical, cognitive, and psychosocial impact of fatigue on daily life over the past 4 weeks. The FSS is a 9-item unidimensional measure of fatigue and its disabling consequences over the past week in medical populations including MS. The Fatigue Severity Scale is scored on a 7-point Likert scale, where 1 means strongly disagree and 7 means strongly agree. All items refer to the physical domain of fatigue, meaning it measures the effects of fatigue on a person's activities and lifestyle. **The SF-MPQ has a 15-item adjective checklist that captures sensory and affective dimensions of pain experienced over the past week. Participants will also be asked to record levels of hunger, fatigue, sleep quality and energy on a daily basis via the food journaling app used to record dietary intake.**

III. Cardiometabolic risks. We will measure cardiometabolic risks by anthropometrics (height, weight, and waist circumference), body composition, blood pressure, and lipid panel, fasting insulin.

IV. Biomarkers of inflammation will include TNF-α, IL-6 and IL-17.

V. Participant acceptability will be measured by self-report questionnaire at midpoint (4 weeks) and end point (8 week).

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).

Multiple sclerosis (MS) is a chronic, immune-mediated neurodegenerative disease of the central nervous system. The disease manifests as symptoms (e.g. fatigue and depression) and impairments (e.g. walking and cognition) that compromise quality of life and participation. Over the last decade there has been an influx of evidence demonstrating the impact of lifestyle risk factors including physical inactivity, smoking, and poor diet on the progression of MS symptoms. Specifically, epidemiological studies consistently report that poor diet is associated with increased risk of disability in adults with MS. Diet may impact risk of disability by directly complicating the disease process through exacerbating inflammation or

impairing immune responses. It may also have an indirect impact by increasing risk for vascular and cardiometabolic diseases, which are common among adults with MS and are associated with worse prognosis of MS. Despite the evidence of the association between poor diet and MS, little research has explored dietary interventions that may reduce symptom burden of MS, or the mechanisms through which these interventions may work.

One dietary intervention that has shown particular promise in animal models of MS is intermittent fasting (IF), which is a dietary pattern characterized by cycles of eating and extended fasting (see attached for animal model literature). There are a number of protocols for IF, the most popular of which include alternate day modified fasting (cycling between days of substantially restricted caloric intake and days of unrestricted eating); and time restricted feeding (TRF), in which all food is consumed during a limited window of time each day (typically less than 10-12 hours). There is growing evidence that demonstrates IF reduces inflammation, improves immune function and improves cardiometabolic risk in animal models of MS, however, very little of this research has been translated into human trials of MS. In addition to the physiological benefits, we also believe that IF, and particularly TRF, will provide a behavioral benefit, as it addresses many of the barriers traditionally seen in dietary interventions by shifting the focus from restricting what participants can eat, to only focusing on meal timing.

An eight-hour eating window was chosen for this trial in an effort to balance efficacy with feasibility. TRF protocols of 4 and 6 hour eating windows have been tested without major adverse events, however this may be too short of a window for people to realistically stick with. Conversely, The median American eats over a 12.4-hour period, so using a longer window such as 10 hours may not confer as many benefits from a modest change. Safety and efficacy of an 8-hour window has been published in other populations (references attached).

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)? **12**

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: **Male and Female**

Race/Ethnicity: **All races/ethnic groups will be recruited**

Age: **18-65**

Health status: **Diagnosis of relapsing-remitting MS; stable on current disease modifying treatment (or not on treatment) for 6 months; no relapse within previous 30 days.**

c. From what population(s) will the participants be derived? **We will recruit participants through flyers posted at Lakeshore Foundation, UAB Neurology clinics, and the UAB MS Center, as well as direct mail to Lakeshore Foundation members who have noted interested in participating in research.**

Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants: **Dr. Wingo is actively involved with the UAB/Lakeshore Research Collaboration and has access to study participants from the Lakeshore Foundation. Lakeshore has over 5000 active and inactive members with disabilities. She also collaborates with physicians and research staff at the UAB Neurology clinics and MS center. Dr. Rinker will also inform potential patients who are treated in the MS clinics about the study.**

d. Describe the inclusion/exclusion criteria:

Inclusion Criteria:

1. **18-65 years old**
2. **Diagnosed with Relapsing-Remitting MS**
3. **If on disease-modifying medications, stable for 6 months.**

4. **If not on disease-modifying medication, no medication usage within previous 6 months.**
5. **BMI 18.5-50 kg/m^2**
6. **Able to walk 25 ft. with or without assistance**

Exclusion Criteria:

1. **Relapse within previous 30 days**
2. **Actively engaged in a weight loss program or unwilling to follow assigned dietary timing pattern**
3. **Regularly fasts >15 hours/day**
4. **Pregnant or breastfeeding**
5. **Current use of insulin or sulfonylurea agents**
6. **Score indicating low cognitive functioning on the Telephone Interview for Cognitive Status assessment**

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. **NA**

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 **NOTE**: For BVAMC Research <19 years old
☒ 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: **Adults with MS who are employees or students of UAB or Lakeshore Foundation may participate in this study. Participation for all study participants will be on a voluntary basis. Participants will be assured that all responses will be kept confidential and that participation will not be shared with their supervisor. Participants will not be anyone who is under the supervision of Dr. Wingo at UAB or Lakeshore.**

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. **Flyers will be posted in common areas around Lakeshore Foundation, UAB Neurology Clinic, and MS Center (see attached for flyer). The same flyers will be included in newsletters emailed and/or mailed to Lakeshore Foundation members. Lakeshore Foundation also maintains a database of members who are interested in participating in research and this database will be used for targeted recruitment. Lakeshore members are also aware of ongoing research and are welcome to visit the research office and lab at any time. Members who present to the research office and inquire about research opportunities will be made aware of the study.**

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. **See attached.**

j. Describe the screening process/procedures for potential participants. **Participants will call the phone number listed on the study flyer or come by the research office to inquire about research possibilities. Study staff will give potential participants additional information about the study using attached script. If the person is interested in participating, the staff will ask a series of questions to assess eligibility. This will include age, self-reports of height and weight, disease-modifying medication use, dietary habits, cognitive screening (utilizing the Telephone Interview for Cognitive Status (TICS-m)), as well as primary mode of ambulation. If potential participant meets eligibility criteria, he/she will be scheduled for baseline data collection. Pregnant women will be excluded because it is not safe for them to have a DXA scan. Women who are currently breastfeeding will be excluded due to hormone differences and fluctuations which can impact diet. These impacts could skew results on metabolic outcomes of the diet.**

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. **Twelve adults with relapsing-remitting multiple sclerosis (RRMS) will be recruited. Participants will take part in an 8-week trial in which they will eat all food during an 8-hour window each day. They will be asked to consume only water, unsweetened tea, or black coffee during the remaining 16 hours of each day.**

At the baseline visit, study staff will administer and review the consent forms with the participant and the participant will sign them before any data collection or intervention begins. After signing the consent forms, all baseline measures will be collected. Baseline measures include:

1. **Anthropometric measures: Waist circumference will be measured twice al at the level of the umbilicus after normal expiration, with participants standing. If the two values differ by >1 cm, a third measurement will be taken and the results of the two or three trials averaged. Height will be measured with participants standing against the wall. Weight will be assessed using a digital scale. BMI will be calculated using the formula weight/height^2 (kg/m^2). Blood pressure will be obtained and participants will also be asked to inform study staff of all current medications and supplements being taken.**
2. **Blood work: Fasting insulin, lipid panel, TNF-α, IL-6 and IL-17 will be collected on all participants. Two (2) vials of blood will be drawn (7 mL or 1.4 teaspoons) via venipuncture.**
3. **DXA: Total and regional body composition will be measured on a Lunar Prodigy with enCORE software version 13.6 (GE Healthcare, Chicago, IL). Participants will undergo a total body scan requiring about 20 minutes, while lying on their back on a padded table with metal objects removed. The scan provides estimates of soft tissue attenuation ratios, fat and lean tissue mass, and bone mineral density. Individuals who are too large to scan in a single scan will be scanned twice (one scan for the left half of body, one for the right). The software is able to merge the two scans to assess total body composition. All women of child-bearing age will be required to complete a pregnancy test in the lab prior to DXA scan.**
4. **Patient-reported outcomes: Participants will complete the following questionnaires: Demographics, Hospital Anxiety and Depression Scale (HADS), Modified Fatigue Impact Scale (MFIS), Fatigue Severity Scale (FSS), short-form McGill Pain Questionnaire (SF-MPQ), and Pittsburg Sleep Quality Index. Copies of each are attached.**
5. **Accelerometer: Participants will wear an Actigraph accelerometer Version 6.13.3 on the waist for 7 days. We will classify activity counts into sedentary behavior, light, moderate and vigorous activity. We will record total minutes of activity in each category.**
6. **Dietary adherence: The UAB CCTS will perform three 24 hour dietary phone recalls with each participant over a 14 day period. These calls will be unannounced and participants will be informed that they will be asked to recall all they consumed within the last 24 hours at the time of the call. They will receive two of the three recall phone calls during the week, and one on a Monday morning to capture a weekend recall. CCTS staff will follow standard protocols for performing a 24 hour**

food recall and study staff will provide participants with materials at baseline to help them answer the food recall questions. Participants will receive three more 24 hour dietary recall phone calls at the 8 week mark.

7. **Timed 25-Foot Walk (T25-FW): The T25-FW is a quantitative mobility and leg function performance test based on a timed 25-foot walk. The participant is directed to one end of a clearly marked 25-foot course and is instructed to walk 25 feet as quickly as possible, but safely. The time is calculated from the initiation of the instruction to start and ends when the participant has reached the 25-foot mark. The task is immediately administered again by having the participant walk back the same distance. Participants may use assistive devices when doing this task. Assistive devices may include braces, a cane, or a walker.**
8. **9-Hole Peg Test (9-HPT): The 9-HPT is a brief, standardized, quantitative test of upper extremity function. Both the dominant and non-dominant hands are tested twice. The participant is seated at a table with a small, shallow container holding nine pegs and a wood or plastic block containing nine empty holes. On a start command when a stopwatch is started, the participant picks up the nine pegs one at a time as quickly as possible, puts them in the nine holes, and, once they are in the holes, removes them again as quickly as possible one at a time, replacing them into the shallow container. The total time to complete the task is recorded. Two consecutive trials with the dominant hand are immediately followed by two consecutive trials with the non-dominant hand.**
9. **Symbol Digit Modalities Test (SDMT): The SDMT is a five-minute assessment that quickly screens the participant for any kind of cerebral dysfunction using a simple substitution task. When undertaking the SDMT, a participant is given a reference key that they must use to help them connect basic Arabic numerals (1-9) to a series of geometric shapes (i.e. reference key= key showing which number aligns with each symbol). Responses can be verbal or written, and the entire test should be finished in 90 seconds. Scoring and evaluation of the test takes a further five minutes to complete. Because responses can be written or spoken, it can be used with a broad spectrum of participants, including those suffering from motor disabilities and speech impediments.**
10. **Patient-determined disease steps (PDDS): The PDDS is a patient-reported measure of disability.**
11. **Participant Satisfaction with the meal timing plan will be measured by questionnaire (see attached).**

At the end of the baseline visit, the research coordinator will give the participant an accelerometer to wear around their waist for 7 days, along with a stamped envelope to return the accelerometer at the end of the week. She will also provide detailed instructions on the 24 hour food recalls that will be conducted over the next 14 days. The baseline visit is about 2 hours. The coordinator will explain the meal timing protocol in detail, introduce them to the food journaling app that will be used to record food intake and daily symptoms, and answer any questions the participant may have. Finally, the coordinator will schedule a time for the first weekly check in call.

Participants will be instructed to eat all meals in an 8 hour window. Participants will be allowed to choose the times in which they eat in an effort to maximize adherence, but must start no later than 11:00 am (e.g. participants who typically wake early may choose to eat from 8:00 am- 4:00 pm, while those who typically eat later in the day may choose to eat from 11:00 am- 7:00 pm). During the 16-hour fasting period, participants will be instructed to drink only water, unsweetened tea, or black coffee, and not eat any food. Participants will be provided with an electronic food journal (HealthWatch 360), and instructed to record all food and beverages consumed daily, along with the time of day consumed. The HealthWatch 360 platform includes a HIPAA-compliant research portal, which allows the research staff to view participants' entries in real-time. It is accessible via a mobile app and desktop version, so participants have multiple ways to enter data depending on their preference.

Participants will receive daily caloric prescription intended to maintain baseline weight (i.e. an isocaloric diet based on Harris-Benedict estimation equation), but will not have any other restriction on intake. This will allow for analysis of the impact of food timing independent of calorie restriction or weight loss.

All participants will receive weekly calls from the study coordinator. During these calls, the coordinator will review food records with the participant, conduct weekly adverse event screening, and answer any questions from the participants. She will also help participants who are having trouble adhering to the prescribed feeding plan problem solve ways to increase adherence.

At the mid-point of the study (4 weeks) participants will be sent a link to a REDCap survey to complete the mid-point participant satisfaction survey. They will not need to come to the lab to complete this. If they do not have access to the internet, we will mail a hard copy along with a stamped/addressed return envelope for them to return the survey.

After 8 weeks, participants will return to the Wallace research lab to repeat the same data collection protocol as they did at baseline, with the exception of PDDS, which will only be completed at baseline.

b. What is the probable length of time required for the entire protocol (i.e., recruitment through data analysis to study closure)? **12 months**

c. What is the total amount of time each participant will be involved? **12 weeks (2 week baseline measures, 8 weeks intervention, 2 week follow-up measures).**

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
Anthropometrics	**15 minutes**	**Baseline and follow up**	☒Res ☐Routine
Bloodwork	**10 minutes**	**Baseline and follow up**	☒Res ☐Routine
DXA	**20 minutes**	**Baseline and follow up**	☒Res ☐Routine
Questionnaires	**~30 minutes**	**Baseline and follow up**	☒Res ☐Routine
Timed 25-Foot Walk (T25-FW)	**1-5 minutes**	**Baseline and follow up**	☒Res ☐Routine
9-Hole Peg Test (9-HPT)	**10 minutes or less**	**Baseline and follow up**	☒Res ☐Routine
Symbol Digit Modalities Test (SDMT)	**5 minutes**	**Baseline and follow up**	☒Res ☐Routine
Patient-Determined Disease Steps (PDDS)	**20 minutes**	**Baseline**	☒Res ☐Routine

24 Hour Glucose Monitoring	**24 hours**	**Baseline and follow up**	☒Res ☐Routine
24 Hour Dietary Recall	**3 days**	**Baseline and follow up**	☒Res ☐Routine
Accelerometer	**7 days**	**Baseline and follow up**	☒Res ☐Routine
Participant Satisfaction Survey	**15 minutes**	**Midpoint, follow up**	☒Res ☐Routine
Dietary intervention	**8 weeks**	**One time only**	☒Res ☐Routine
Symptom Rating	**2 minutes**	**Daily during intervention**	☒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. _____

h. Will participants be compensated? ☒Yes ☐No

If Yes, complete i-v.

i. Type: (e.g., cash, check, gift card, merchandise): **Check**

ii. Amount or Value: **$100**

iii. Method (e.g., mail, at visit): **Mail**

iv. Timing of Payments: (e.g., every visit, each month): **$50 at completion of baseline measures, $50 at completion of study.**

v. Maximum Amount of Compensation per Participant: **$100**

18. Benefits

Describe the potential benefits of the research. **The potential benefit of this study is that individuals with RRMS may have improved health (cardiometabolic risk reduction) and reduced symptoms of RRMS (pain, fatigue). There is also a potential that we will learn more about the way TRF impacts RRMS, which will allow more information on which to base future larger trials.**

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.

1. **Fasting prior to bloodwork: Participants may experience a drop in blood sugar causing lightheadedness, dizziness, nausea, sweating, and shakiness as a result of fasting before their baseline and follow up visits.**

2. **Blood draw: Participants may experience pain and/or bruising during venipuncture.**

3. **24 hour glucose monitor: Participants may experience discomfort, pain, swelling, and bruising from the needle insertion and also a chance of skin irritation from the adhesive. In rare cases, the sensor may fracture, or the insertion site may become infected.**

4. **DXA: A DXA scan is an x-ray scan that uses a very low-level of radiation. The radiation dose received from the 1 to 2 scans is equivalent to about 8 days natural background radiation. Background radiation is radiation normally received from sources such as cosmic rays and natural radioactivity in building materials and the ground. A small risk of cancer and other radiation effects, which may not be known at this time, may develop from each scan you receive.**

5. **Loss of confidentiality: The potential risk to subjects involves loss of confidentiality regarding exposure to information obtained through a secure internet website, although our hosting environment is HIPAA compliant.**

6. **There is the possibility that MS could get worse over the duration of the study.**

b. Estimate the frequency, severity, and reversibility of each risk listed.

1. **Fasting prior to bloodwork: Risks associated with fasting are typically rapidly reversible upon ingesting food and drink or lying down and should not result in severe harm to the participant.**

2. **Blood draw: Discomfort associated with venipuncture is rapidly reversible. Bruises from venipuncture will heal in several days.**

3. **24 hour glucose monitor: All the expected risks are minimal, mild in severity, and expected to be reversible.**

4. **Loss of Confidentiality: We expect the potential loss of confidentiality to be low given the security and privacy provisions at the Wallace research lab.**

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: _____

ii. Describe any other alternative treatments or interventions: _____

iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: _____

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.

Data Security: All data will be entered into RERCap, and stored on the UAB REDCap secure server. Only Dr. Wingo and the study coordinator will have access to download the data from REDCap.

The intervention and measurement protocols pose minimal risk to participants. Participants will be asked a set of questions each week to assess their general health (see attached Adverse Event form). If a participant reports any notable changes for 2 consecutive weeks, that information will be given to Dr. Rinker for review.

Any serious adverse events will be promptly reported to the Institutional Review Board at UAB. Safety reports will be sent to the PI from the intervention staff, or data collection staff if the event occurs during baseline/follow up testing. The PI will be responsible for reviewing the data with Dr. Rinker. The adverse event weekly check and referral to Dr. Rinker is the safety plan.

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. **The PI will monitor protocol adherence. Throughout the study, study staff will inform the PI of adverse events. Events determined by the PI and Dr. Rinker to be unanticipated serious problems involving risks to subjects will be reported by the PI to the IRB and the directors of the UAB NORC Pilot and Feasibility Grant Program, within 5 working days of becoming aware of the event. Non-serious adverse events will be reported per IRB policy at the time of continuing review. If any protocol changes are needed as a result of an adverse event, the PI will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval.**

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. **If the risks involved in participating appear to exceed the benefits during review of occurrences of serious adverse events, the PI will consult with the complete investigator team, as well as the directors of the NORC Pilot and Feasibility Grant program to decide to terminate the study. If the study is terminated, participants will be given information related to the study risks that may have affected them or their health.**

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.

*For research being conducted at the BVAMC, the UAB Consent waiver form must be completed and submitted with the HSP.

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? **When a potential participant is interested in the study, the study coordinator will provide a detailed description of the study, screen the participant for eligibility, answer any questions, and if appropriate, schedule their first visit. At the beginning of the first visit, consent will be obtained prior to any testing. The consent will be completed in duplicate so that subjects can retain one copy of the document.**

d. Who will conduct the consent interview? **The research coordinator**

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

f. What steps will be taken to minimize the possibility of coercion or undue influence? **Participants will be self-referred. As described above, the consent form will be carefully reviewed with participants. Further, they will have at least 24 hours to consider participation in the study.**

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. **24 hours or more**

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. **Any interested individuals who are screened for eligibility in person, will be screened in a private room one-on-one. Consent will be obtained in a quiet space, and all assessments will only involve the necessary staff needed to perform the testing. Furthermore, all weekly participant phone calls will be performed in privacy behind closed doors.**

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. **All pre and post-test data will be entered into a secure server maintained by UAB (REDCap).**

Participants will be assigned a unique identification code. The file including subjects' identification and code numbers will be kept in the REDCap study database. Any paper with identifying information will be destroyed at the earliest possible time following completion of the study. All data will be analyzed according to group information, with no possibility of disclosing individual subject identity. All publications and presentations of the findings of the study will not contain personal, identifying information of study subjects.

Emails will be used to send appointment reminders. Emails will not contain any PHI, they will only include appointment reminders. Emails will only be sent from Dr. Wingo's lab email address (hbdlab@uabmc.edu). All participants will consent to using email as a form of communication. There will also be a disclaimer at the end of all the emails stating that they are unencrypted emails.

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? **The funding agency- Nutrition Obesity Research Center**

ii. What data will be shared? **Aggregate data on baseline characteristics and outcomes of the sample will be reported.**

iii. How will the data be identified, coded, etc.? **No identifiable or individual-level data will be given.**

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." **None**

Sample size and statistical analysis plan

The goals of this study were to determine the feasibility of TRE and to collect exploratory pilot data. A sample of n = 10−12 per group has been reported to be adequate for a pilot study when there are no existing data available. Given the lack of previous data on TRE in adults with MS, a sample size of n = 12 was determined to be adequate. An a priori cut point for feasibility was set at 80% of participants completing all pre- and post-intervention measures.

Feasibility variables were assessed with descriptive statistics, specifically frequency and mean and standard deviation. Secondary outcomes were explored descriptively and with single-group paired samples t-tests. Significance values are presented, and results are highlighted whenever either the changes were clinically meaningful and/or $p<.20$, a standard threshold used for pilot studies; however, due to the exploratory nature of these analyses, the study was not powered to find significance among changes in these variables. Cohen's *d* was calculated to determine the effect size of changes between baseline and follow-up. Given the small sample and exploratory nature of the study, all paired-samples analyses included only those participants who completed the study. All statistical analyses were conducted with SPSS v 27 (IBM Corporation; Armonk, NY).

CONSENT FORM

Title of Research: Time Restricted Eating Outcomes in Multiple Sclerosis (TREO_MS)

UAB IRB Protocol #: IRB-300005334

Principal Investigator: Brooks C. Wingo, Ph.D.

Sponsor: UAB Nutrition Obesity Research Center

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 test the initial effects, safety, and acceptability of time-restricted eating in adults with Relapsing-Remitting Multiple Sclerosis (MS).
Duration & Visits	You will come to the UAB Wallace Research Lab on the Lakeshore Foundation campus a total of two times over a 12 week time period (one time at the start of the study and one time at the end) The visit at the start, and the visit at the end will last about 2 hours.
Overview of Procedures	You will come to a beginning visit that includes a physical exam, blood draw, physical and cognitive assessments measuring the disability and symptoms of MS, and completion of surveys related to symptoms of MS. For two weeks after the first visit, you will wear an activity monitor on your waist and complete 3 food recalls with a registered dietitian. Once you have completed the two weeks of testing, you will follow the study diet for 8 weeks. The study diet entails eating all of your meals within an 8 hour period each day. You will have access to a food journaling app to record all your food intake, and the time of your first and last meal each day. You will also receive a call from the study dietician each week. You will come back to Wallace Research Lab after completing the 8-week program to complete the same testing you completed at the beginning.
Risks	The most common risks include dizziness or lightheadedness while fasting for testing, pain or bruising from the blood draw, and loss of confidentiality. Additionally, a small risk of cancer and other radiation effects, which may not be known at this time, may develop from each DXA scan you receive. Some people also report hunger and fatigue when starting a new diet pattern, however these typically resolve after a few days.
Benefits	You may or may not benefit from participating in this study.
Alternatives	If you do not want to take part in the study, the alternative is to not participate in this study.

Purpose of the Research

We are asking you to take part in a research study. The purpose of this research study is to test if the time of day that you eat impacts symptoms of MS such as pain and fatigue, clinical

outcomes of MS such as hand/leg function and cognition, and risk for diabetes and heart disease.

People who enter the study will eat all of their food over an 8 hour window each day. This is a pilot study, and this is the first study of daily meal timing patterns in people with MS. In addition to the effect of meal timing, we are also testing for safety of this eating pattern, and how well people tolerate and enjoy the pattern. There will be 12 participants enrolled in this study.

Explanation of Procedures

Before you can begin the intervention, you will complete baseline assessments at the UAB Wallace Research Lab at Lakeshore Foundation. The visit will take approximately 2 hours.

***Baseline Visit 1*:** During this visit, we will measure your height, weight, waist circumference, and blood pressure. We will also measure body composition and collect blood work using tests explained below.

- **Blood Work –** We will draw 2 vials of blood (7 mL or 1.4 teaspoons) via venipuncture to measure your insulin, and lipids (cholesterol and triglyceride levels), as well as markers of inflammation (TNFα, IL-6, IL-17). You will be asked to not eat or drink anything after 12:00 am the morning of your blood draw.
- **Body Composition –** We will measure your body composition (body fat percentage, fat mass and muscle mass) using a DXA scan. The DXA uses very low level radiation to measure your total body composition including fat mass and bone density. To complete the DXA, you will lie on a table and a machine will pass over your body. Prior to completing the scan, all women of child bearing potential will undergo a urine pregnancy test to ensure that there is no risk of undue harm to the child. Pregnant women will not be enrolled in the study. In the event that your whole body does not fit into a single scan, we will conduct 2 scans- one of the right half of your body and one of the left half.
- **MS symptoms and functional limitations-** You will be asked to complete a series of assessments including brief walking tests and tests of cognitive function, which will be performed by our trained research staff. These assessments are intended to measure the disability and symptoms of MS.
- **Questionnaires-** You will also be asked to complete a series of questionnaires related to symptoms of MS such as pain and fatigue.

***14 days after baseline*:**

- **24 Hour Food Recalls:** During these 14 days you will be asked to participate in 3 phone interviews to complete 24-hour food recalls. A research staff person from UAB will call you on three different days and review what you had to eat on the previous day.
- **Accelerometer:** At the end of the baseline visit, you will be given an accelerometer to wear around your waist for 7 days, along with instructions for use. You will also be given a pre-stamped envelope in order to return the accelerometer.

- We will call you at the end of this 14 day period as a reminder to mail in your accelerometer, check on food recall completion, and to schedule your first weekly check-in call.

During the Intervention:

- You will eat all of your food over an 8 hour period each day. You will not be told what to eat, but you will be given a calorie level that you should not go over each day.
- You will be asked to log all your food, and the time you eat it, onto a website called HealthWatch 360.
- You will receive prompts from HealthWatch360 each day to rate your level of hunger, fatigue, energy and sleep.
- You will receive a call once each week from the study coordinator. This call is intended to review how you are doing with staying on your meal timing schedule, and answer any questions you have about the program. During this call, the study coordinator will also ask you about any adverse events (side effects, health problems) you have experienced that week.

Midpoint of the Intervention (4 weeks)

- You will complete a brief mid-point satisfaction survey to tell us about your experiences in the first month of the study. This will be completed on-line, so you do not have to come into the lab to complete it. If you do not have access to a computer with internet, we will mail you a copy of the survey.

Follow up Measures:

- At the end of the 8-week program, you will be scheduled to return to the lab to complete the same 1 time visit you completed at baseline, plus a few additional questionnaires about your experience with the diet. The visits will be the same as those you completed at the beginning of the study, with the visit lasting approximately 2 hours.
- During the 14 days after the follow up visits, you will again be given an accelerometer to wear. You will also complete 3 additional 24-hour food recall phone interviews. At the end of the 14 days, you will return the accelerometer using the pre-stamped, pre-addressed envelope provided to you at your follow up appointment.

The clinical results (including individual research results) will not be returned to you.

Incidental Findings

We are performing imaging solely for the research purposes described above. It is not a clinical scan intended for diagnostic or therapeutic purposes. Under no circumstance will the investigator, research staff, or imaging staff interpret the scan as normal or abnormal. They are unable to make any medical comments about your scan. The scan will not be looked at or read for any healthcare treatment or diagnostic purpose. If you want your scan to be reviewed by a physician to look for medical issues, you can request a copy of your scan. We will provide an electronic copy at no charge.

Risks and Discomforts

Fasting Prior to Testing: You may experience a drop in your blood sugar causing lightheadedness, dizziness, nausea, sweating, and shakiness. If you experience any of these symptoms prior to or during testing, please notify the researcher or technician so they may assist you.

Bloodwork: You may experience pain, bruising, and/or fainting during venipuncture.

DXA: A DXA scan is an x-ray scan that uses a very low-level of radiation. In this study you will be exposed to a very low level of radiation during the DXA scan. The radiation dose received from the 1 to 2 scans is equivalent to about 8 days of natural background radiation. Background radiation is radiation normally received from sources such as cosmic rays and natural radioactivity in building materials and the ground. A small risk of cancer and other radiation effects, which may not be known at this time, may develop from each scan you receive.

Changing diet habits: There is a potential risk of hunger when you make changes to your diet. We will attempt to reduce this risk by providing options for healthy foods that will not leave you hungry.

Loss of Confidentiality: There is a potential risk of loss of confidentiality regarding exposure of personal information obtained by our researchers. All information we obtain about you will be kept in a database on a secure UAB server. While using this type of server reduces your risk of loss of confidentiality, some risk does remain.

Questionnaires: There are minimal risks associated with completing the questionnaires with this study. One foreseeable risk may be psychological in that participants may experience feelings of discomfort or embarrassment when reporting on their symptoms or experiences of MS.

Benefits

You may have changes in body composition and may reduce your risk of heart disease and diabetes. You may also have improved physical function and reduced symptoms of pain and fatigue. However, it is possible that you will not benefit from this research.

Alternatives

If you choose not to participate in this research, you may still change your diet on your own. If you decide to participate in another research study, you should contact the investigator as this may affect your dietary intake related to this study.

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 investigators 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.

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 investigator 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.

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
All tests and materials will be provided to you at no cost during the study. You should check with your internet and cell phone provider to see about any extra costs.

Payment for Participation
You will be paid $50 after you complete all baseline measures and $50 when you complete all follow up measures. If you complete the entire study, you will be paid a total of $100. Ask the study staff about the method of payment for this study (e.g. check, cash, gift card, etc.).

Payment for Research-Related Injuries
UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

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

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

Questions
If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the Primary Investigator. You may contact Dr. Wingo at 205-934-5982 or by emailing her at bcwingo@uab.edu.

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.

Email Communication

During this study, we may offer the option to have appointment reminders sent to you by unencrypted email. There is a potential risk of loss of confidentiality when communicating via unencrypted email. Unencrypted email communication is considered a non-secure method of sharing information. There is no guarantee that such communication (and any other data associated with it) is private and will only be viewed by the intended recipient. By using unencrypted email, you acknowledge and accept this risk.

Please initial your choice below:

_____ I would like to communicate via unencrypted email.

_____ I do not wish to communicate via unencrypted email.

Signatures

Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed document.

Signature of Participant	Date
Signature of Investigator or Other Person Obtaining Consent	Date