Protocol title: Time-restricted eating to address persistent cancer-related fatigue: The Fatigue REDuction After cancer (FREDA) trial

PI: Amber Kleckner, PhD

NCT number: NCT05256888

Original approval date: July 28, 2022

UNIVERSITY of MARYLAND BALTIMORE

Date: Thursday, June 13, 2024 3:38:27 PM Print Close

HP-00099067 Introduction Page_V2

Introduction Page

1 * Abbreviated Title:
Time-restricted eating to address persistent cancer-related fatigue

2 * Full Title:
Time-restricted eating to address persistent cancer-related fatigue: The Fatigue REDuction After cancer (FREDA) trial

3

* Select Type of Submission:

- (●) **IRB Application**
- ( ) Humanitarian Use Device (for FDA approved Indication & non-research purposes ONLY)
- ( ) Single Patient Expanded Access (pre-use)
- ( ) Single Patient Emergency Use (post-use)
- ( ) Unsure if this proposal requires IRB review (Not Human Subject Research)

Note: The Type of Submission cannot be changed after this application has been submitted for review.

4 Original Version #:
25MAR2022

ID: VIEW4DF8709A33C00
Name: v2_Introduction Page

HP-00099067 Research Team Information_V2

Research Team Information

1 * Principal Investigator - Who is the PI for this study (person must have faculty status)? ***Faculty status is defined as being a full-time (>51% effort) faculty member holding one of the following titles at UM: Professor; Associate Professor; Assistant Professor.***
Amber Kleckner

CITI Training:ID00012414

1.1 * Does the Principal Investigator have a potential conflict of interest, financial or otherwise, related to this research?
◯ Yes ● **No**

2 Point of Contact - Who is the alternative point of contact for the PI? This person can be a study coordinator or any other study team member. In case the IRB cannot contact the PI, this person is a secondary person to contact:
Carin Clingan

CITI Training:ID00013429

2.1 Does the Point of Contact have a potential conflict of interest, financial or otherwise, related to this research?
◯ Yes ● **No**

3 Other Team Members - list all additional members of the research team for this study. DO NOT include the PI or POC in this list:

Name	Edit Submission	cc on Email	Research Role	Has SFI?	CITI Training
View Shari Youngblood	no	no	Study Coordinator	no	ID00013331
View IKMAT ADESANYA	no	no	Study Coordinator	no	ID00016576
View Ahleah Gavin	no	no	Study Coordinator	no	ID00009862
View Shijun Zhu	no	no	Statistician	no	ID00004186
View Alice Ryan	no	no	Research Team Member	no	ID00012869
View Ashkan Emadi	no	no	Research Team Member	no	ID00006806
View Alexie Oppermann	no	no	Other	no	ID00015502
View Javier Rosales	yes	no	Study Coordinator	no	ID00014393

IMPORTANT NOTE: All research team members (including PI) must have current CITI and HIPAA training completed.

ID: VIEW4DF85C16F2800
Name: v2_Research Team Information

HP-00099067 Resources_V2

Resources

If this study is a collaborative UM/VA study, please clarify which resources are being used at each institution.

1 * Describe the time that the Principal Investigator will devote to conducting and completing the research:
The principal investigator will devote 20% effort (equivalent to 8 hours per week) to this project for the duration of the study to conduct and complete the research.

2 * Describe the facilities where research procedures are conducted:
This study will be conducted out of University of Maryland School of Nursing (SON) and recruitment will occur mainly from University of Maryland Greenebaum Comprehensive Cancer Center (UMGCCC) in Baltimore, MD. Dr. Kleckner has sufficient office space, computers, locked cabinets, and other resources to conduct this study. Dr. Kleckner has access to a dedicated clinical testing room on the 7th floor of the School of Nursing to conduct consents and perform study activities.

3 * Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:
We do not anticipate the need for additional medical or psychological resources as a result of participation in this study. However, in case the need arises, participants will have access to all of the medical and/or psychological resources available at the University of Maryland Greenebaum Comprehensive Cancer Center (UMGCCC) and the University of Maryland Medical Center (UMMC) more broadly. Any participants who experience emotional distress while completing study procedures will be referred to their healthcare provider. In the case of a medical or psychiatric emergency (e.g., verbalization of suicidal thoughts), we will call 911 and ensure safe transport of the participant to a hospital.

4 * Describe the process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions:
Dr. Kleckner will oversee all training of the study team members to ensure proper execution of the research procedures. All members of the study team will have working knowledge of the protocol and expert knowledge in the areas in which they are directly involved. Dr. Kleckner will meet with the study coordinator(s) at least biweekly and more frequently as needed to discuss the progress and logistics of the study. Dr. Kleckner will meet with the other members of the study team at a frequency that is decided upon initiation of their involvement, based on their individual role.

ID: VIEW4DF83CB976400
Name: v2_Resources

HP-00099067 Sites Where Research Will Be Conducted_V2

Sites Where Research Activities Will Be Conducted

1 * Is this study a:

- ○ Multi-Site
- ● **Single Site**

2 * Are you relying on an external IRB (not UM) to be the IRB of Record for this study?

○ Yes ● **No**

3 * Are any other institutions/organizations relying on UM to be the IRB of Record for this study?

○ Yes ● **No**

3.1 Attach the applicable regulatory documents here (i.e., IRB Authorization Agreement (IAA), FWA, local ethics approval, other IRB approvals, etc.). Final UM approval will be contingent upon final execution of all required regulatory approvals:

Name	Created	Modified Date

There are no items to display

4 * Is UM the Coordinating Center for this study? (Applicable for multi-site studies. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project.)

○ Yes ● **No**

5 Is VA the Coordinating Center for this study? (Applicable for Collaborative studies between the VA, UM and other sites. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project)

○ Yes ● **No**

6 * Institution(s) where the research activities will be performed:

- ☑ **University of Maryland, Baltimore**
- ☐ University of Maryland, Upper Chesapeake Kaufman Cancer Center
- ☐ VAMHCS
- ☐ UMB School of Medicine
- ☑ **Marlene and Stewart Greenebaum Cancer Center**
- ☐ University Physicians Inc.
- ☐ Shock Trauma Center
- ☐ General Clinical Research Center (GCRC)
- ☐ Maryland Psychiatric Research Center (MPRC)
- ☐ Johns Hopkins
- ☐ International Sites
- ☐ UMB Dental Clinics
- ☐ Center for Vaccine Development
- ☐ Community Mental Health Centers
- ☐ Private Practice in the State of Maryland
- ☐ Institute of Human Virology (IHV) Clinical Research Unit
- ☐ Joslin Center
- ☐ UMB Student Classrooms
- ☐ National Institute of Drug Abuse (NIDA)
- ☐ National Study Center for Trauma and EMS
- ☐ Univ of MD Cardiology Physicians at Westminster
- ☐ Nursing Homes in Maryland
- ☐ University of Maryland Biotechnology Institute
- ☐ Maryland Department of Health
- ☐ Maryland Proton Treatment Center
- ☐ Mount Washington Pediatric Hospital
- ☐ Institute of Marine and Environmental Technology (IMET)
- ☐ Other Sites
- ☑ **University of Maryland Medical System (Select below)**

* UMMS Sites:

- ☐ University of Maryland Medical Center
- ☐ UMMC Midtown Campus (formerly Maryland General Hospital)
- ☑ **UM St. Joseph Medical Center**

- [x] **UM Baltimore Washington Medical Center**
- [ ] UM Capitol Region Health
- [ ] UM Charles Regional Medical Center
- [ ] UM Shore Medical Center at Easton
- [ ] UM Shore Medical Center at Chestertown
- [ ] UM Shore Medical Center at Dorchester
- [ ] UM Shore Emergency Center at Queenstown
- [ ] UM Shore Regional Health
- [ ] University of Maryland Rehabilitation & Orthopaedic Institute (formerly Kernan Hospital)
- [ ] UM Upper Chesapeake Health
- [x] **UM Upper Chesapeake Medical Center**
- [ ] UM Harford Memorial Hospital
- [ ] University of Maryland Community Medical Group

ID: VIEW4DF870DF2C000
Name: v2_Sites Where Research Activities Will Be Conducted

Funding Information

1 * Indicate who is funding the study:

- [x] **Federal**
- [ ] Industry
- [x] **Department / Division / Internal**
- [ ] Foundation
- [ ] Private
- [ ] State Agency

2 * What portion of the research is being funded? (Choose all that apply)

- [ ] Drug
- [ ] Device
- [x] **Staff**
- [x] **Participant Compensation**
- [x] **Procedures**
- [x] **Other**

3 Please discuss any additional information regarding funding below:

This study is being supported by the Institute of Clinical and Translational Research (ICTR) Accelerated Translational Incubator Pilot (ATIP) grant, funded by the National Center for Advancing Translational Science (NCATS), and start-up funds to Dr. Amber Kleckner.

ID: VIEW4DF85DF452400
Name: v2_Funding Information

HP-00099067 DHHS Funded Study_V2

DHHS Funded Study

You indicated that this is a Federally funded study.

1 * Is this study sponsored by a Department of Health and Human Services (DHHS) agency?

● **Yes** ○ No

2 You may upload any grant documents here:

Name	Created	Modified Date
1UMB_Amber Kleckner_ATIP_NOA_2022_NCATS.pdf(0.01)	3/24/2022 2:50 PM	3/24/2022 2:50 PM

ID: VIEW4DF87B9560800
Name: v2_DHHS Funded Study

Federal Agency Sponsor Contact Information

You indicated that this is a Federally funded study.

1

* Agency Name:
National Center for Advancing Translational Science (NCATS)

* Address 1:
31 Center Drive, Suite 3B11

Address 2:

* City:
Bethesda

* State:
MD

* Zip Code:
20892

* Contact Person:
Stephen Davis

* Phone Number:
410-328-2488

* Federal Agency Email:
info@ncats.nih.gov

Grant Number 1 (if applicable):
1UL1TR003098- OR - Check here if Grant 1 is not assigned a number. ☐

If Grant 1 has no number, please provide the following information:
Title of Grant 1:

PI of Grant 1:

Grant Number 2 (if applicable):
- OR - Check here if Grant 2 is not assigned a number. ☐

If Grant 2 has no number, please provide the following information:
Title of Grant 2:

PI of Grant 2:

Grant Number 3 (if applicable):
- OR - Check here if Grant 3 is not assigned a number ☐

If Grant 3 has no number, please provide the following information:
Title of Grant 3:

PI of Grant 3:

Grant Number 4 (if applicable):
- OR - Check here if Grant 4 is not assigned a number. ☐

If Grant 4 has no number, please provide the following information:
Title of Grant 4:

PI of Grant 4:

ID: VIEW4DF8584874400
Name: v2_Federal Agency Sponsor Information

Research Protocol

1 * Do you have a research protocol to upload?

- ○ Yes
- ● **No, I do not have a research protocol and will use the CICERO application to enter my study information**

2 If Yes, upload the research protocol:

Name	Created	Modified Date
There are no items to display		

ID: VIEW4E00563F8D000
Name: v2_Research Protocol

HP-00099067

Risk Level_V2

Risk Level

What is the risk level of your study? (Ultimately, the IRB will determine the appropriate risk level and your designation is subject to change.)

* Choose One:

- (●) **Minimal - The probability & magnitude of harm/discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations/tests.**
- ( ) Greater Than Minimal - Does not meet the definition of Minimal Risk.

ID: VIEW4E02805225800
Name: v2_Risk Level

HP-00099067 Exempt Categories_Fed

Exempt Categories

You indicated on the "Risk Level" page that this study is Minimal Risk.

1 * Please review the following categories to determine if your research may be Exempt from IRB oversight. If you believe that your study qualifies as Exempt, select the Category under which it qualifies. If your research does not qualify as Exempt, select **"The research does not qualify as Exempt".**

☐ **Category 1**: Research, conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Category 2: Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

☐
i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.
ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.
iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by .111(a)(7).

Category 3: Research involving benign behavioral interventions (brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and not offensive or embarrassing) in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

☐
i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.
ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.
iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by .111(a)(7).

Category 4: Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

☐
i. The identifiable private information or identifiable biospecimens are publicly available.
ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects.
iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E [HIPAA], for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b).
iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

☐ **Category 5**: Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

Category 6: Taste and food quality evaluation and consumer acceptance studies:

☐
i. If wholesome foods without additives are consumed, or
ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the U.S.D.A.

☑ **The research does not qualify as Exempt.**

ID: VIEW8D50FF499486A05
Name: v2_Exempt Categories

HP-00099067 Type of Research_V2

Type of Research

1 * Indicate **ALL** of the types of research procedures involved in this study (Choose all that apply):

- [ ] Use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol.
- [ ] Evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.
- [x] **Use of device(s) whose use is specified in the protocol**
- [x] **Psychological/Behavioral/Educational Method or Procedure (i.e., survey, questionnaires, interviews, focus groups, educational tests).**
- [ ] Sample (Specimen) Collection and/or Analysis (including genetic analysis).
- [x] **Data Collection or Record Review (i.e., chart review, datasets, secondary data analysis).**
- [ ] None of the above.

2 * Is this study a clinical trial OR will this study be registered at ClinicalTrials.gov?
A clinical trial is 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.

(●) **Yes** ( ) No

ID: VIEW4E0280569E000
Name: v2_Type of Research

HP-00099067 Lay Summary_V2

Lay Summary

1 * Provide a summary of the background and purpose of the study in language that can be understood by a person without a medical degree.

Cancer-related fatigue affects at least 30-90% of patients with cancer, depending on the type of cancer and their treatment(s) (e.g., chemotherapy, radiation). It is not relieved by sleep or rest, and it sometimes can persist for years after a person's cancer was treated. The fatigue can be so bad that people cannot return to work, hobbies, family roles, or other daily activities, thereby greatly reducing quality of life. The causes of this fatigue are unknown, and we currently do not have anything that can reliably prevent or cure the fatigue. However, there are recent data suggesting that circadian rhythm, or a person's internal body clock, may be disrupted by the cancer experience and contribute to fatigue. Food intake is an external cue that can entrain circadian rhythm. We recently showed that cancer survivors are willing and able to eat all their food within a 10-hour eating window—a practice called time-restricted eating. Herein, we are testing time-restricted eating against a control group to see if time-restricted eating can indeed alleviate cancer-related fatigue.

All participants will be asked to use the myCircadianClock smartphone app to log their food intake and weekly body weight measurements. The app can also be used to log sleep (recommended), exercise (optional), and other health measures (optional). The participants assigned to the time-restricted eating group will be asked to eat all their food in a 10-hour window during the day. People can choose their start time based on their schedule and preferences, but we ask that the window is the same for the whole study (e.g., 7am-5pm, 9:30am-7:30pm). Black coffee and unsweetened tea are allowed before the eating window, and water and medicines are allowed at all times. The participants in the control group will not be restricted to when they can eat. Participants in both groups will give us valuable information regarding how daily behaviors (e.g., diet, physical activity, sleep patterns) are related to the experience of fatigue.

The first aim of our project is to test whether we are able to deliver a 12-week time-restricted eating program. The second aim is see if participants in the time-restricted eating group have less fatigue at week 12 compared to those in the control group, taking into account their fatigue at the beginning of the study. To look more closely at the biology and physiology underlying fatigue, we will measure circadian rhythm at the beginning, the middle (week 6), and the end of the study (week 12) using a wrist-worn actigraph (like a Fitbit or Apple Watch), as well as sugar metabolism using a continuous glucose monitor (nonintrusive device that sticks to the back of the upper arm). We hypothesize that time-restricted eating will lead to less fatigue, a stronger circadian rhythm, and healthier sugar metabolism.

ID: VIEW4E02805CF7000
Name: v2_Lay Summary

Justification, Objective, & Research Design

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the purpose, specific aims, or objectives of this research. State the hypothesis to be tested:

This pilot randomized controlled trial will test the effects of time-restricted eating vs. an unrestricted eating pattern (i.e., control) on persistent cancer-related fatigue, circadian rhythm, and metabolism. These data build upon a study conducted by Dr. Amber Kleckner (PI) that established the feasibility and safety of time-restricted eating among cancer survivors—cancer survivors were willing and able to eat within a 10-hour window for 14 days. The specific aims are as follows:

Aim 1: To assess the feasibility of time-restricted eating for 12 weeks, utilization of the myCircadianClock app, continuous interstitial glucose monitoring, and the wrist-worn actigraph. We hypothesize that 80% of participants will provide evaluable data regarding their eating window via the app at baseline and 12 weeks. We also hypothesize that at least 80% of participants who are in the time-restricted eating arm and provide evaluable data will eat within a daily average window that is ≤10 hours.

Aim 2: To estimate the preliminary efficacy of a 12-week time-restricted eating intervention vs. an unrestricted eating pattern on patient-reported fatigue among fatigued cancer survivors, as measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire. We hypothesize that FACIT-F fatigue subscale scores will be lower for those in the time-restricted eating group compared to the control group at week 12, controlling for baseline levels.

Mechanistic (exploratory) aims: To assess the effects of a 12-week time-restricted eating intervention vs. an unrestricted eating pattern on circadian rhythm (mesor, amplitude, and acrophase from actigraphy), sleep parameters (e.g., sleep efficiency), and biomarkers of metabolism (fasting blood glucose, glucose excursions).
1. To assess cross-sectional associations between circadian rhythms, metabolism, and fatigue at baseline.
2. To explore associations between changes in circadian rhythms, metabolism, and fatigue from baseline to 6 weeks and baseline to 12 weeks.
3. To explore associations between adherence to the intervention and changes in the same measures.

2 * Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.:

This is a pilot randomized controlled trial. Participants will be randomized 1:1, intervention: control. Therefore, there is a 50% chance of any given participant to be in the control group, and a 50% chance of any given participant to be in the intervention group.

3 * Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data:

Cancer-related fatigue is a prevalent symptom of cancer and side effect of treatment that can be severe and persistent for years into survivorship. The etiology and pathophysiology of cancer-related fatigue are not well understood [1], though metabolic and circadian processes have been suggested to contribute to its severity. Cancer and cancer treatment, specifically chemotherapy [2-4], disrupts circadian rhythm. Environmental signals that regulate circadian rhythm, or 'zeitgebers' include physical activity, light, and food intake. Several studies have used bright light therapy to entrain circadian processes and have shown positive effects on fatigue among cancer survivors [5, 6]. Also, there is emerging evidence that time-restricted eating can entrain circadian rhythm, but not yet in the cancer population [7]. However, there have been no studies, to our knowledge, that test the ability of time-restricted eating to address cancer-related fatigue.

We recently completed a single-arm feasibility trial in which we investigated whether cancer survivors with persistent fatigue were willing and able to eat within a 10-hour window every day for two weeks. In total, 36/39 (92%) completed all questionnaires and daily diaries. Our preliminary data show that 80% had an average eating window ≤10 h and the average eating window was 9 hours, 14 minutes. There were no severe adverse events or rapid weight loss (mean±SD change in weight: -1.3±2.5 lbs). Patients reported meaningful improvements in fatigue for both the FACIT-F fatigue subscale (mean change±SD= 5.3±8.1 points, p<0.001, effect size=0.55) and the FACIT-F total score (change 9.3±13.3, p<0.001, effect size=0.50). We concluded that cancer survivors were willing and able to adhere to a 10-h TRE intervention. The program was feasible and safe, and fatigue improved with moderate effect sizes after two weeks.

4 * Provide the scientific or scholarly background, rationale, and significance of the research and how it will add to existing knowledge:

Cancer-related fatigue affects at least 30-90% of patients undergoing chemotherapy, depending on the type of cancer and treatment as well as the method used to diagnose cancer-related fatigue [8, 9]. It is not relieved by sleep or rest, and its severity can greatly hinder the ability to perform activities of daily living and decrease quality of life. The mechanisms behind the etiology and pathophysiology of cancer-related fatigue seem to be related in part to inflammation, hypothalamic–pituitary–adrenal (HPA) activation dysfunction, metabolic and/or endocrine dysregulation, or other mechanisms, but are largely not understood, thereby thwarting the development of effective preventative strategies and treatments [1].

Circadian rhythms are biological diurnal cycles that work in synchrony to regulate hormone secretion, the sleep/wake cycle, core body temperature, and other processes. Circadian rhythm and human health have a bidirectional relationship, and circadian disruption is associated with a broad range of pathologies including, purportedly, cancer-related fatigue [2, 10, 11]. Circadian regulation occurs via genetic and physiological processes, and is important to maintain homeostasis of the endocrine system, autonomic nervous system, and nutrient metabolism [12, 13]. The importance of maintaining circadian rhythm is clear when traveling across time zones, and "jet lag" is a common experience of fatigue when the circadian clock is disrupted [13]. Chemotherapy treatment disrupts circadian rhythm, and changes in circadian rhythm are associated with fatigue [2].

Regulation of circadian rhythm relies heavily on regular sleep habits, and interventions to regulate circadian clock currently include light therapy, exercise, melatonin supplementation, and more recently, nutrient timing [13]. Indeed, there are consistent animal and human data demonstrating that aberrant feeding/eating patterns dysregulate objective circadian clock measures (i.e., expression of genes that show strong diurnal oscillations) [14]. In an observational study among 156 healthy American adults in California, Gill and Panda [15] showed that approximately 50% of people eat within a window greater than 14.75 hours per day; only 10% eat within a window 12 hours or less [12]. Similar results were observed in our pilot feasibility trial—out of 60 people expressing interest in the trial, only 5 (8%) already ate within a 10-h window). A consistent, shorter window of eating, for example 10 hours or shorter, may aid in the regulation of the circadian clock and improve metabolic homeostasis with broad health outcomes [12, 16, 17]. Restricting eating to a certain time window is called "time-restricted eating" (TRE).

TRE as a therapeutic approach has garnered a large appreciation in the literature and in the public in the last decade for its ability to mediate the circadian clock and prevent and treat various pathologies [7, 16, 17]. TRE involves restricting the consumption of calories to a short window (4-12 hours) during normal waking hours, for example 8am-6pm; water is never restricted. Human (time-restricted eating) and rodent (time-restricted feeding) studies have shown that TRE helps to maintain metabolic homeostasis and, as a result, prevents excess body weight, improves sleep, and attenuates age- and diet-induced heart disease (review [17]). One study clearly demonstrated the effects of nutrient timing on metabolic regulation: time-restricted feeding vs. time-unrestricted feeding of mice led to weight loss despite equal energy intake [18]. In humans, Gabel et al. performed an 8-h TRE study among obese adults for 12 weeks (n=23) [19]. Despite the diet being ad libitum, caloric intake decreased 341±53 kcal/day. Body weight decreased 2.6±0.5%, and systolic blood pressure decreased 7±2 mmHg. However, there were no significant changes in body composition, circulated lipids, fasting blood glucose, or fasting insulin. Also, Wilkinson et al. performed a 10-h time restricted eating study among patients with metabolic syndrome for 12 weeks (n=19) [12]. They observed improvements in sleep efficiency and quality, a safe rate of decrease in body weight and body fat percentage, a reduction in total and low density lipoprotein (LDL) cholesterol, and reductions in systolic and diastolic blood pressure [12]. While these studies were implemented for 12 weeks, benefits have been seen in glucose and lipid metabolism and circadian clock gene expression in as short as 4 days [20].

To date, aside from our own single-arm feasibility trial, TRE has only been studied in healthy participants or those who are overweight, obese, or with metabolic disorders (Lowe et al. [21] and references within the review by Wilkinson et al. [12], but not yet the cancer population [7]). These studies have collectively shown that a 10-h TRE window is feasible, safe, and effective at improving metabolic markers among their respective populations. Thus, the next logical step is to evaluate TRE vs. a control arm in a randomized controlled trial with the ultimate goal of evaluating its effectiveness to treat cancer-related fatigue.

This study will fill a large gap in the literature by being the first study, to our knowledge, to test the effects of time-restricted eating vs. a control arm on cancer-related fatigue.

ID: VIEW4E02805EA0C00
Name: v2_Justification, Objective, & Research Design

Supporting Literature

1 * Provide a summary of current literature related to the research: ***If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.***

1. Saligan, L.N., et al., The biology of cancer-related fatigue: a review of the literature. Support Care Cancer, 2015. 23(8): p. 2461-78.
2. Roscoe, J.A., et al., Temporal interrelationships among fatigue, circadian rhythm and depression in breast cancer patients undergoing chemotherapy treatment. Support Care Cancer, 2002. 10(4): p. 329-36.
3. Savard, J., et al., Breast cancer patients have progressively impaired sleep-wake activity rhythms during chemotherapy. SLEEP, 2009. 32(9): p. 1155-1160.
4. Sultan, A., V. Choudhary, and A. Parganiha, Worsening of rest-activity circadian rhythm and quality of life in female breast cancer patients along progression of chemotherapy cycles. Chronobiol Int, 2017. 34(5): p. 609-623.
5. Johnson, J.A., et al., Bright light therapy improves cancer-related fatigue in cancer survivors: a randomized controlled trial. J Cancer Surviv, 2018. 12(2): p. 206-215.
6. Redd, W.H., et al., Systematic light exposure in the treatment of cancer-related fatigue: a preliminary study. Psychooncology, 2014. 23(12): p. 1431-4.
7. Christensen, R.A.G. and A.A. Kirkham, Time-Restricted Eating: A Novel and Simple Dietary Intervention for Primary and Secondary Prevention of Breast Cancer and Cardiovascular Disease. Nutrients, 2021. 13(10).
8. Berger, A.M., et al., Cancer-Related Fatigue, Version 2.2015, Clinical Practice Guidelines in Oncology. Nat Comp Cancer Netw, 2015. 13(8): p. 1012-1039.
9. Servaes, P., C. Verhagen, and G. Bleijenberg, Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. European Journal of Cancer, 2002. 38: p. 27-43.
10. Abbott, S.M., R.G. Malkani, and P.C. Zee, Circadian disruption and human health: A bidirectional relationship. Eur J Neurosci, 2018.
11. Payne, J.K., Altered circadian rhythms and cancer-related fatigue outcomes. Integr Cancer Ther, 2011. 10(3): p. 221-33.
12. Wilkinson, M.J., et al., Ten-Hour Time-Restricted Eating Reduces Weight, Blood Pressure, and Atherogenic Lipids in Patients with Metabolic Syndrome. Cell Metab, 2019.
13. Forbes-Robertson, S., et al., Circadian disruption and remedial interventions. Sports Med, 2012. 42(3): p. 185-208.
14. Zarrinpar, A., A. Chaix, and S. Panda, Daily Eating Patterns and Their Impact on Health and Disease. Trends Endocrinol Metab, 2016. 27(2): p. 69-83.
15. Gill, S. and S. Panda, A Smartphone App Reveals Erratic Diurnal Eating Patterns in Humans that Can Be Modulated for Health Benefits. Cell Metab, 2015. 22(5): p. 789-98.
16. Chaix, A., et al., Time-Restricted Eating to Prevent and Manage Chronic Metabolic Diseases. Annu Rev Nutr, 2019. 39: p. 291-315.
17. Melkani, G.C. and S. Panda, Time-restricted feeding for prevention and treatment of cardiometabolic disorders. J Physiol, 2017. 595(12): p. 3691-3700.
18. Hatori, M., et al., Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. Cell Metab, 2012. 15(6): p. 848-60.
19. Gabel, K., et al., Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: A pilot study. Nutr Healthy Aging, 2018. 4(4): p. 345-353.
20. Jamshed, H., et al., Early Time-Restricted Feeding Improves 24-Hour Glucose Levels and Affects Markers of the Circadian Clock, Aging, and Autophagy in Humans. Nutrients, 2019. 11(6).
21. Lowe, D.A., et al., Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men With Overweight and Obesity: The TREAT Randomized Clinical Trial. JAMA Intern Med, 2020.

2 If available, upload your applicable literature search:

Name	Created	Modified Date

There are no items to display

ID: VIEW4E02805A7E400
Name: v2_Supporting Literature

Study Procedures

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below. (If this study is a collaborative UM/VA study please list each procedure that is being conducted and the locations where it is being conducted.)

1 * Describe all procedures being performed for research purposes only (these procedures would not be done if individuals were not in the study) and when they are performed, including procedures being performed to monitor subjects for safety or to minimize risks:

This is a pilot randomized controlled trial that works within the framework of the Obesity-Related Behavioral Intervention Trials (ORBIT) model for behavioral treatment development. This trial will assess the feasibility of our methods to conduct a 12-week randomized controlled trial that implements TRE as well as the preliminary efficacy of TRE vs. a control group on cancer-related fatigue. We will recruit 50 patients who are 2 months-2 years post-treatment for cancer (e.g., surgery, radiation, chemotherapy) and are suffering from moderate-severe cancer-related fatigue. They will be randomized 1:1 intervention:control (approximately 15 in each arm). This will be an open label study because, due to the nature of the intervention, it is not possible to blind participants and, due to the active involvement of the PI in data acquisition, it is not feasible to blind the PI. Participants will be told that we are using a new smartphone app that helps us explore how behaviors such as diet, exercise, and sleep are related to fatigue; some people will be asked to also engage in TRE while some will be asked to follow their normal eating patterns.

Participants will be recruited from the University of Maryland Medical System, including the Greenebaum Comprehensive Cancer Center, St. Joseph Medical Center, Upper Chesapeake Medical Center, and Baltimore Washington Medical Center. The whole study can be conducted remotely, but if the participant would prefer an in-person visit for consenting or any other study activity, we will meet them at either Greenebaum Cancer Center or the School of Nursing.

Potential participants will be identified using four methods: (i) screening medical records, (ii) direct referral from providers (e.g., nurses, nurse navigators, physicians), (iii) flyers, and (iv) advertising via standard UMB- and ICTR-networks. The study staff will screen for potential participants using EPIC or, alternatively, patients may be referred to the study team by a provider or acquaintance. Initial contact will occur via the following methods: i) the treating oncologist or a member of the medical team (e.g., nurse practitioner) will introduce the study to the participant via a clinic appointment (in person or telehealth) and inquire if it would be okay for our study team to talk with them after their visit or contact them, ii) with approval of the treating oncologist or a designee, a recruitment letter will be sent to the potential participant briefly describing the study and asking them to contact us if they would like more information, and iii) with approval of the treating oncologist or a designee, a message will be sent to the potential participant via MyPortfolio briefly describing the study and asking them to contact us if they would like more information. If a potential participant is interested, the study team will provide more information about the study in-person or via phone.

The study activities are briefly described here; the study schema is illustrated in Figure 1 (see Additional Documents, "schema-data-collection.pdf," page 1).

At baseline, participants will complete an on-study form that includes demographics and clinical characteristics as well as questionnaires (see below). We will obtain a baseline body weight measurement. For one week (week 0), participants will wear an actigraph (i.e., activity tracker) and a continuous glucose monitor and complete a food log using the myCircadianClock app.

After the baseline period, they will be randomized 1:1, TRE:control. Those in the time-restricted eating group will be asked to eat all food and beverages in a self-selected 10-hour window during the day. The start time of the window can be chosen based on the participant's schedule and preferences, but it should be the same for the duration of the study. We will not restrict what people eat. Black coffee and unsweetened tea will be allowed before the window, and water and medications are allowable any time. Those in the control group will be asked to not make any changes to their current dietary patterns.

For the duration of the 12-week study, all participants may engage with the myCircadianClock app (see below) as much or as little as they like—with user input the app monitors eating, exercise, sleep patterns, and other measures. Also, the app will deliver weekly health tips and provide reminders about study activities (e.g., "Remember to weigh yourself today!"). To ensure that weight loss does not occur at an unhealthy rate, we will be providing participants with a bathroom scale for weekly measurements. Approximately every two weeks, the participant will receive a call from a study team member to check in; ask about symptoms and gauge use of the myCircadianClock app; ask about eating, sleeping, and exercise patterns; and for those in the TRE group, discuss adherence to the TRE pattern including barriers and how to overcome any barriers (See Engagement Script). During week 6 (midpoint), participants will be asked to complete questionnaires, log their sleep and eating habits using the app, wear the actigraph, and wear a continuous glucose monitor. During the last week of the study, week 12, participants will again be asked to complete questionnaires, log sleep and eating habits using the app, wear the actigraph, and wear a continuous glucose monitor. After completion of the study, participants will be asked to participate in a semi-structured interview during which we will solicit feedback on the study—what they liked about it, what they did not like about it, if they would recommend it to friends, etc. This will last approximately 15-30 minutes and will be audio-recorded with specific permission. Participants will receive $25 at each time point if they complete at least 3/4 of the baseline, week 6, and week 12 study activities (5+ days of logging food intake, questionnaires, actigraphy, and continuous glucose monitoring) for a total of $75; we will emphasize the importance of the food logs and questionnaires to answer our primary research questions. After completion of the study, those in both groups will have continued use of the myCircadianClock app.

myCircadianClock application ("app").
The myCircadianClock app is designed to run on both Android and iOS devices that account for more than 90% of all smartphones and uses HIPAA-compliant Amazon Web Server (AWS) for server-side operations. A dedicated team of developers make periodic updates to the app and to the backend server to comply with updates released by Apple, Google, and Amazon. The server side is designed to run multiple independent studies and the app is designed for individual customization. This allows study-specific customization by the investigator and user-specific customizations by participants. For those in the intervention group, participants can set their daily eating periods and receive alerts and reminders specific to their eating window. For example, participants can receive an automated alert 15 or 30 minutes prior to the end of the eating interval to finish their last meal of the day. All subjects can log their food, sleep, and activity via the app. The research team can visualize real-time data from individual participants and will receive a daily summary of data logs. For food entries, the user can annotate the food picture with food name and any other descriptor (portion size, left over etc.). The app will be customized to add push notifications, reminders, and educational materials that are structured to guide the participants throughout the study, enable self-monitoring, and improve compliance. This app is user-friendly and has been used in several circadian rhythm clinical trials. Data collected from the app will include all user inputs (i.e., photos or names of food/beverages, activity/exercise, sleep, and health entries) as well as language, timestamp of entries, and geographic location data from entries (to obtain country and time zone information). Entering food and sleep behaviors will total approximately 5 minutes/day during weeks 0-12.

Food Record:
Participants will be asked to record all foods and beverages consumed during all seven days of Week 0, Week 6, and Week 12 using the myCircadianClock app (the "Food Record"). It will take the participants about 30 seconds per meal to enter the data. The default mode of collecting food data is to take a picture and add a short description (e.g., bagel with cream cheese). The app stores previously entered food, so it is fast and easy to record habitual meals. Participants can also scan a barcode or QR code of a food/beverage to obtain manufacturer's nutritional information. With each entry, the app asks whether the event is current or in the past and, if in the past, what time. The Food Record will be analyzed for total calories, macronutrients, micronutrients, and bioactive compounds using Nutrition Data System for Research (NDSR; Regents of the University of Minnesota, Minneapolis, MN) or a similar program. The Food Record will also be analyzed for eating window (time between first and last calorie) and other aspects of eating patterns.

Questionnaires:
Questionnaires will be administered at baseline (Week 0), Week 6, and Week 12. Questionnaires will be administered via REDCap or on paper and then manually entered into REDCap. There are a total of 9 questionnaires. The On Study form will be completed at baseline only, and the 8 others will be completed at Week 0, Week 6, and Week 12. The battery of questionnaires will include the following:
1. Functional Assessment of Chronic Illness-Fatigue (FACIT-F) questionnaire: The FACIT-F is a 40-item, validated, commonly used measure of fatigue that is comprised of five subscales: physical well-being, social well-being, emotional well-being, functional well-being, and fatigue. It captures symptoms in these categories over the last 7 days.
2. Brief Fatigue Inventory (BFI): The BFI is a 10-item fatigue questionnaire that is also validated and commonly used. It captures fatigue now and the usual and worst in the last 24 h. It also includes 6 single-item questions regarding how fatigue has interfered with general activity, mood, work, etc.
3. Symptom Inventory (SI): The symptom inventory (modified from the MD Anderson Symptom Inventory) includes 19 items that are common in the cancer experience (e.g., pain, distress, lack of appetite, numbness and tingling), as well as 8 items related to how much these symptoms interfere with activities of daily living and quality of life. Many symptoms often correlate with each other including fatigue (i.e., symptom clustering), so it is important to capture the change in many symptoms from baseline to post-intervention.
4. Positive and Negative Affect Schedule (PANAS)-SF: The PANAS-SF is a 20-item measure of mood. It asks the extent to which a person has felt certain emotions (e.g., enthusiastic, proud, irritable) over the last week. There are 5 response choices ranging from 1 (very slightly or not at all) to 5 (extremely). It has been deemed reliable and valid in the non-clinical population and is routinely used in the cancer survivorship population.
5. Brief Pain Inventory-Short Form (BPI-SF): The BPI-SF assesses severity of pain and its impact on functioning. If a person reports feeling pain, it asks what area(s) hurt the most; a pain rating from 0-10 for pain at its least, worst, and average in the last 24 hours; pain right now; medications taken for pain; and how the pain has interfered with general activity, mood, walking, work, relations with other people, sleep, and enjoyment of life. The BPI-SF has been validated and has been deemed reliable in the cancer population.
6. Insomnia Sleep Index (ISI): The ISI is a 7-item questionnaire that assesses sleep quality. It assesses difficulties falling asleep, staying asleep, waking up too early, satisfaction with sleep pattern, how noticeable any sleep problem is to others, worry about sleep problems, and interference of sleep problems with daily functioning. It has been deemed reliable and valid in the cancer population.
7. Global Physical Activity Questionnaire (GPAQ): The GPAQ is a 16-item questionnaire designed to estimate an individual's level of physical activity in three domains: work, transportation, and leisure time, as well as time spent in sedentary behavior. It has been deemed valid and reliable to survey and measure changes in physical activity among many diverse populations. It is commonly used in the cancer literature.
8. Multidimensional Assessment of Interoceptive Awareness (MAIA)-2: The MAIA is a 37-item questionnaire that evaluates interoception, or how much a person is in-tune with sensations from their body. It includes questions such as 'I trust my body sensations' and 'I notice how my body changes when I feel angry.' There is no objective measurement that can be used to validate the MAIA scales and, because interoception is a relatively new concept in the field of oncology, it has been only seldom used in the cancer population.
The 8 questionnaires that will be completed at Week 0, Week 6, and Week 12 should take approximately 30-60 min in total to complete.

Circadian rhythm via actigraphy

With a wrist-worn actigraph (e.g., MotionWatch-8) at baseline, week 6, and week 12, we can assess activity in three axes, recorded as “counts.” Counts are used to calculate the strength of circadian rhythms as well as deduce active periods and sleep measures (i.e., sleep latency, efficiency, duration; wake after sleep onset; daytime napping). By combining these measures with sleep logs via myCircadianClock, we can infer whether any improvements in fatigue are derived from improved sleep and/or increased daytime activity. These actigraphs also have a light sensor.

The actigraph and glucose monitor (see below) will be mailed to participants approximately one week before they are supposed to wear them. Included in the package will be a prepaid shipping label to return the actigraph, glucose sensor, and sensor reader in the box in which they were sent.

Continuous glucose monitoring
At baseline, week 6, and week 12, we will assess interstitial glucose concentrations using a FreeStyle Libre continuous glucose monitor (Abbott Labs). From these data we will extract fasting glucose, average daily glucose, average waking and nocturnal glucose, maximum glucose, and area under the curve. This device is placed on the back of the participant’s upper arm for up to two weeks. It is unobtrusive and does not interfere with normal bathing, exercising, or swimming. Data are saved automatically every 15 min. Interstitial glucose reflects blood glucose concentrations, though measures are delayed by 4-15 minutes. The benefit of continuous interstitial glucose monitoring over blood glucose is that it avoids frequent, painful finger pricks or venipunctures.
- These data will be used for research purposes only and not diagnostic purposes. The monitor itself does not have a screen, and it will not be required for the participant to view or interpret their blood glucose data at any time. The researchers will not have access to the data in real-time. The monitors are disposable and will be mailed back to us after they wear them. We will be able to upload the data from the monitor and provide the data to the participant upon request at the end of the study, and the participant will be able to share their results with their provider if they are concerned with their glucose regulation.
-If any individual happens to observe a hyperglycemic event of greater than about 200 mg/dl (11.1 mM) and told us, we will discuss the circumstances surrounding the event with the participant and any symptoms that might have cooccurred, and we will discuss the event with the study doctor. We will decide what course of action to take, including encouraging the participant to talk to their primary care physician. It is very unlikely that time-restricted eating will cause hyperglycemia, so it is unlikely but possible that we will withdraw them from the study if they are in the intervention arm.
-If an individual happens to observe a hypoglycemic event less than about 70 mg/ml (3.9 mM) and told us, we will similarly discuss the circumstances and symptoms surrounding the event and discuss the event with the study doctor, Dr. Emadi. We will decide on the best course of action, which might include lengthening the eating window or withdrawing the person from the study if they are in the intervention arm.
-Data from the continuous glucose monitors will be compiled and analyzed at the end of the study. Therefore, neither the study coordinators nor the participants need directed training to monitor or interpret glucose levels during the study.

Body weight
We will provide participants with a bathroom scale. Participants will be asked to place the scale on a level, hard surface (e.g., tile, wood), and weigh themselves in the morning shortly after waking with minimal clothing. Weekly body weight will be recorded in the myCircadianClock app.

Exit interview
After completion of the study (or earlier if a participant withdraws early from the study), a member of the study team will conduct an exit interview to understand the participants’ experience being in the study. We will ask them what they liked about the study, did not like about it, what features they liked/did not like about the myCircadianClock app, if they would recommend the study to others, etc. This interview will be audio-recorded with explicit permission at the time of the interview, then transcribed for mixed methods data analysis.

2 * Describe all procedures already being performed for diagnostic or treatment purposes (if not applicable to the study, enter "N/A"):
N/A

3 * Describe the duration of an individual participant's participation in the study:
Participants will participate in the study for approximately 14 weeks, including consent, baseline assessments, a 12-week intervention, and an exit interview.

4 * Describe the amount of time it will take to complete the entire study:
Upon opening of the study, we expect that approximately 3-5 participants will be recruited per month for approximately 9 months. Data originating from questionnaires, actigraphs, glucose monitors, and exit interviews will be entered, processed, and/or cleaned (as applicable) as they come in. We will perform an interim analysis of feasibility of the study after the 10th participant is enrolled and make any logistical adjustments to the protocol as necessary. Data analysis will take place soon after all data are collected.

These data will be used to inform a follow-on randomized clinical trial, for example a phase II or multisite clinical trial. It is anticipated that at least two manuscripts will emerge from this study, the first of which will be submitted for publication within one year of the study closing (the primary aims paper).

5 * Describe any additional participant requirements:
None

ID: VIEW4E0280585B400
Name: v2_Study Procedures

Sample Size and Data Analysis

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Provide the rationale and sample size calculations for the proposed target population:

This is a two-arm pilot randomized controlled trial that will assess the feasibility of recruitment and retention to a 12-week TRE trial facilitated by the myCircadianClock app as well as the preliminary efficacy of TRE vs. a control arm on the treatment of cancer-related fatigue.

It is common that single-arm pilot studies implementing dietary interventions recruit 10-40 participants (e.g., TRE study among overweight older adults, n=10; ketogenic diet among patients with recurrent glioblastoma, n=20; lifestyle intervention including diet among overweight breast cancer survivors, n=14). In total, 30 participants will be recruited, and approximately 10-20% attrition is anticipated, providing evaluable data from approximately 25 participants. We had more dropouts than anticipated and are upping our sample size to 50 participants so that we can have about 25 participants with evaluable data.

2 * Provide the plan for data analysis. Include in the description the types of comparisons that are planned (e.g., comparison of means, comparison of proportions, regressions, analysis of variance, etc.), which is the primary comparison/analysis, and how the analyses proposed will relate to the primary purposes of the study:

We will conduct an interim analysis of feasibility after 10 participants have been enrolled. If any unanticipated barriers arise in regard to feasibility of recruitment, data collection, and/or retention, logistical changes will be made to the protocol as appropriate.

Aim 1 assesses the feasibility of time-restricted eating over 12 weeks. We will note how many people we can screen; how many we can approach; how many are eligible; how many consent; and what percentage provide evaluable data at baseline and 12 weeks. Using data from myCircadianClock, we will extract how many days the participants ate within a 10-h window and the average length of the eating window at baseline, week 6, and week 12. We will consider a participant "adherent" if they ate within the 10-h window at least 80% of days. This goal is based on prior TRE studies. In regard to retention, it is hypothesized that at least 80% (24 out of 30) of those who provide baseline data also provide data at 12 weeks; this goal is based on colleagues' prior behavioral intervention studies with supportive care outcomes.

Aim 2 aims to provide estimates of efficacy comparing time-restricted eating vs. control on fatigue. Linear mixed models (LMMs) for longitudinal data will be used to assess the intervention effect on continuous outcomes (e.g., fatigue) accounting for correlations between the repeated measures. Generalized Linear Mixed Model (GLMM) analyses will be conducted to assess the effect of the intervention on count outcomes. The fixed effects included in the models will be treatment group (TRE versus control), time (baseline, 6 and 12 weeks), group-by-time interaction term and relevant covariates. Random effects will include individual patients. The hypotheses will be tested by evaluating the interaction term of group and time (i.e.,12 weeks). The results of the analyses together with the mean and SD of FACIT-F values as well as change scores will be used in planning future RCTs. All hypothesis testing will be at the two-sided level of 0.05. Following the intent-to-treat principle, all participants will be analyzed as randomized, regardless of their adherence with the intervention.

Mechanistic exploratory aims will be evaluated using the same analytical approach as for the primary aim. For circadian rhythm, we will use actigraphy and patient-reported myCircadianClock app data to measure objective symptoms of sleep quality. We can use the actigraph to assess activity in three axes, recorded as "counts." Counts are used to calculate the strength of circadian rhythms as well as deduce active periods and sleep measures (i.e., sleep latency, sleep efficiency, sleep duration, wake after sleep onset, daytime napping). To evaluate circadian activity, we will use a two-oscillator (12 and 24 hours) cosinor model to estimate key circadian rhythm parameters. Also at baseline and week 12, we will assess interstitial glucose concentrations using a continuous glucose monitor. From these data we will extract fasting glucose, average daily glucose, average waking and nocturnal glucose, maximum glucose, and area under the curve. We will explore associations between objective and subjective measures at baseline, adjusting for confounding factors (e.g., age, depression), in addition to changes over time and effects of the intervention on these parameters.

Quality control
Electronic forms will be used and our database will be checked for appropriateness by the study team. All data will be visually inspected. For exploratory measures, if distributional assumptions are not met (e.g., normality of residuals), transformations or nonparametric methods will be used. Outliers will be closely examined to determine if they are erroneous; if they are valid, sensitivity analyses (with and without outliers) will be used. Hypothesis testing will use α=0.10 (two-tailed). The study team will work closely with Dr. Shijun Zhu and his biostatistics team at ICTR.

Missing data
Every effort will be made to facilitate participants' completion of questionnaires and provision of data from wearable devices. However, some missing data are inevitable. The magnitude and the reasons for missing data will be recorded and tabulated according to treatment group. If a large proportion of data is missing we will conduct sensitivity analyses using appropriate statistical methods (e.g., maximum likelihood, multiple imputations). If the estimates are similar to the ones obtained from the simpler analysis of only complete cases, we will report the complete-case analysis results.

REDCap allows data entry forms to facilitate completion of all measures. The reasons for missing data will be tabulated. Under the missing at random (MAR) assumption, multiple imputation will be used to obtain unbiased estimates of key statistics. If data are suspected to be missing not at random (MNAR), we will perform a sensitivity analysis such as pattern mixture models. Should these procedures impact the hypothesis tests, we will report all study outcomes both with and without sensitivity analysis.

Note on adherence/non-compliance
This will be an intent-to-treat analysis, and participants will be analyzed in the group to which they were assigned. It is very possible (even likely) that a few participants in the time-restricted eating group will not change their eating habits (non-compliance), and a few people in the control group will be eager to start time-restricted eating (contamination). We will collect data on eating times from the myCircadianClock app during weeks 0, 6, and 12 for both groups, and emphasize the importance of honesty in data collection. Thus, we will be able to assess associations between the length of the eating window and fatigue in exploratory analyses.
It is possible that participants will make drastic changes to their behaviors of the course of the study that are independent to their eating window. People might want to initiate a vegetarian diet, weight loss program, exercise program, etc. While we will ask people to continue their normal behaviors, we cannot control people's behaviors and we will not withdraw participants from the study for implementing health behaviors. Any changes in habits will likely occur regardless of what group they are in; therefore there will be noise in the data but we will still be able to estimate the effects of time-restricted eating vs. an unrestricted eating pattern on our outcomes.

ID: VIEW4E02806052800
Name: v2_Sample Size and Data Analysis

HP-00099067 Sharing of Results_V2

Sharing of Results

1 * Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared:

Participants may see their complete individual glucose and/or activity data upon request after they complete the study. We will not share data collected for this study with the participant's clinical care team, but the participant is welcome to share it. We will post the final results of the study on clinicaltrials.gov at the completion of the study and share de-identified aggregate results as part of abstracts and manuscripts.

ID: VIEW4E02808CBD800
Name: v2_Sharing of Results

HP-00099067 Research with Medical Devices_V2

Research with Medical Devices

You indicated on the "Type of Research" page that your study involves the evaluation of device(s) for safety or effectiveness or use of a HUD.

1 * List all devices to be used in this study:

	Device Name	FDA Approved?	Labeled	IDE Number	IDE Holder
View	Actigraph	yes	yes		no
View	Continuous glucose monitor	yes	no		no
View	Bathroom scale	yes	yes		no

2 * Attach the device labeling or device manual for the devices being used in this study:

Name	Created	Modified Date
Scale-description.pdf(0.01)	3/16/2022 3:05 PM	3/16/2022 3:05 PM
The MotionWatch User Guide.pdf(0.01)	3/16/2022 3:04 PM	3/16/2022 3:04 PM
CGM-User-manual.pdf(0.01)	3/16/2022 3:04 PM	3/16/2022 3:04 PM

3 * Are you requesting a nonsignificant device risk determination by the IRB? (*Applicable if the FDA has not issued an IDE and the device does not qualify to be IDE exempt.)*

◯ Yes ● **No**

4 If yes, please provide the rationale for how the device(s) used in the study meet the following criteria:

- Is NOT intended as an implant, is NOT purported or represented to be for use supporting or sustaining human life, and is NOT for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health.
- DOES NOT present a potential for serious risk to the health, safety, or welfare of a subject.

5 * Do you have a plan regarding access controls for essential and appropriate research personnel?

● **Yes** ◯ No

6 * Will you have procedures for verifying physical access of the device?

● **Yes** ◯ No

7 * Will the storage of the study device be in a secure environment and include locks on doors and controlled access?

● **Yes** ◯ No

8 * Will there be an establishment of equipment control both in to and out of the research site?

● **Yes** ◯ No

9 * Will there be a development of Security Incident Procedures to report any privacy breaches?

● **Yes** ◯ No

10 If applicable, do you have data backup, storage, and emergency mode procedures?

◯ Yes ◯ No

11 If applicable, will the storage of the device be at the appropriate temperature, with a storage and temperature log?

◯ Yes ◯ No

ID: VIEW4E0514D4C8C00
Name: v2_Research with Medical Devices

Psychological/Behavioral/Educational Methods & Procedures

You indicated on the "Type of Research" page that your study involves a psychological/behavioral/educational method or procedure such as a survey, questionnaire, interview, or focus group.

1 * Select all behavioral methods and procedures which apply to this study:

- [x] **Surveys/questionnaires**
- [x] **Key informant or semi-structured individual interviews**
- [ ] Focus groups or semi-structured group discussions
- [x] **Audio or video recording/photographing**
- [ ] Educational tests or normal educational practices (education instructional strategies, techniques, curricula, or classroom management methods)
- [ ] Individual or group behavioral observations
- [x] **Psychosocial or behavioral interventions**
- [ ] Neuropsychological or psychophysiological testing
- [ ] Deception
- [x] **Other psychosocial or behavioral procedures**

ID: VIEW4E09416F57800
Name: v2_Psychological/Behavioral/Educational Methods and Procedures

Surveys/Questionnaires

You indicated that this study involves surveys and/or questionnaires.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all questionnaires/surveys to be used in the study, including both standardized and non-standardized assessments:

On Study
Functional Assessment of Chronic Illness-Fatigue (FACIT-F)
Brief Fatigue Inventory (BFI)
Symptom Inventory (SI)
Positive and Negative Affect Schedule (PANAS)-SF
Brief Pain Inventory (BPI)
Insomnia Severity Index (ISI)
Global Physical Activity Questionnaire (GPAQ)
Multidimensional Assessment of Interoceptive Awareness (MAIA)-2

2 * Upload a copy of all questionnaires/surveys:

Name	Created	Modified Date
BPI.pdf(0.02)	12/21/2021 5:13 PM	4/29/2022 12:39 PM
Symptom-Inventory.pdf(0.01)	2/22/2022 11:41 AM	2/22/2022 11:41 AM
GPAQ.pdf(0.01)	2/22/2022 11:40 AM	2/22/2022 11:40 AM
ISI.pdf(0.01)	2/17/2022 2:44 PM	2/17/2022 2:44 PM
OnStudy.pdf(0.01)	2/17/2022 2:40 PM	2/17/2022 2:40 PM
PANAS.pdf(0.01)	2/17/2022 2:39 PM	2/17/2022 2:39 PM
FACIT-F.pdf(0.01)	12/21/2021 5:14 PM	12/21/2021 5:14 PM
MAIA.pdf(0.01)	12/21/2021 5:14 PM	12/21/2021 5:14 PM
BFI.pdf(0.01)	12/21/2021 5:13 PM	12/21/2021 5:13 PM

3 * What is the total length of time that each survey is expected to take?

On Study: 3-8 min
Functional Assessment of Chronic Illness-Fatigue (FACIT-F): 5-10 min
Brief Fatigue Inventory (BFI): 2-4 min
Symptom Inventory (SI): 2-4 min
Positive and Negative Affect Schedule (PANAS)-SF: 5-10 min
Brief Pain Inventory (BPI): 2-5 min
Insomnia Severity Index (ISI): 2-5 min
Global Physical Activity Questionnaire (GPAQ): 2-8 min
Multidimensional Assessment of Interoceptive Awareness (MAIA)-2: 3-10 min

4 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

● **Yes** ○ No

5 * Do any questions elicit information related to the potential for harm to self or others?

○ Yes ● **No**

5.1 If Yes, what procedures are in place to assure safety?

These questionnaires contain information that might be distressing or private (e.g., "I am satisfied with family communication about my illness" from the FACIT-F). Participants are able to skip any questions they are not comfortable answering, and they can take a break or stop answering the questionnaires at any time.

We do not ask about illegal activities.

ID: VIEW4E09460F5EC00
Name: v2_Surveys/Questionnaires

HP-00099067 Interviews_V2

Interviews

You indicated that this study involves key informant or semi-structured individual interviews.

1 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

◯ Yes ● **No**

2 * Upload a copy of the interview script or guide that will be used to guide the interviews:

Name	Created	Modified Date
Exit-interview-questions.pdf(0.02)	2/22/2022 11:29 AM	3/10/2022 2:08 PM

3 * What is the individual duration of each interview and what is the entire duration of the interviews?

15-30 minutes for the single interview

4 * How will the interview responses be recorded and by whom?

A member of the study team will conduct the interview in-person, by phone, or by videoconference. He or she will take notes during the interview, as well as record the interview with an audio-recorder (Only the audio will be recorded, even for interviews conducted via video conference). The recording will later be transcribed into a de-identified file for qualitative and mixed methods data analysis.

5 * Do any questions elicit information related to the potential for harm to self or others?

◯ Yes ● **No**

5.1 If Yes, what procedures are in place to assure safety?

ID: VIEW4E0947A633C00
Name: v2_Interviews

HP-00099067 Audio or Video Recording_V2

Audio or Video Recording/Photographs

You indicated that this study involves audio or video recording/photographing.

1

* Indicate the type of recording (check all that apply):

- [ ] Video
- [x] **Audio**
- [ ] Still Photo
- [ ] Other

1.1

If Other, specify:

2

* What is the purpose of the recording? (i.e., for therapeutic purposes, to establish treatment fidelity, or to establish reliability of assessments)

We will garner feedback on the intervention and the study. Using transcriptions, we will identify themes related to responses in order to optimize the study and the intervention.

3

* Could the recording be likely to cause discomfort in participants or cause harm if their confidentiality were breached?

○ Yes ● **No**

4

* How will individuals' identities be protected?

Files with interview questions + notes taken during the interview will only be identified with a participant ID (e.g., FRE01). Audio files will be transferred from the recorder to a UMB-issued (password-protected, HIPAA-compliant) computer within two business days of acquisition, and then will be promptly deleted from the device. Audio files will be transcribed, resulting in de-identified transcriptions of conversations for use in data analysis. Because voices can be identifiable, no audio clips will ever be played in public or in presentations.

ID: VIEW4E094C128C800
Name: v2_Audio or Video Recording / Photographs

Behavioral Intervention

You indicated that this study involves psychosocial or behavioral interventions.

1 * Describe the intervention (duration, number of sessions, focus, etc.):

Participants will be randomized to one of two arms: TRE or control.

TRE arm: Participants in the TRE arm will be asked to engage in time-restricted eating for 12 weeks. The TRE window is 10 hours long and will be selected by the participant based on their normal meal patterns and preferences. For example, the window could be 7am-5pm, 8:30am-6:30pm, or 12:00pm-10:00pm. However, the window should not change during the intervention period. Every day for the 12 weeks, participants will be encouraged to consume all food and beverages only within the 10-h window; water and medications will be allowable any time and only black coffee and unsweetened tea will be allowable in the mornings before the eating window, as has been done in previous TRE studies to facilitate adherence. Other than black coffee and unsweetened tea in the morning, because of the potential of caffeine and artificial sweeteners to affect circadian rhythm, coffee, tea, chewing gum, and diet beverages will be discouraged during the fasting window.

Control arm: The control arm will be asked to not make drastic changes to their daily routines or lifestyle behaviors. We will emphasize the importance of their participation because we do not know a lot about the relationships between lifestyle behaviors (e.g., nutrition, physical activity, sleep) and cancer-related fatigue in survivorship. We will ask them to provide feedback on the usability and usefulness of the app for logging these behaviors.

Both arms will be provided with the myCircadianClock app, which allows users to log food intake, exercise patterns, sleep behaviors, and body weight. Through the app, both arms will receive weekly tips for healthy lifestyle behaviors (i.e., diet and nutrition, exercise, sleeping habits, not smoking, see "Additional documents"). For weeks 0, 6, and 12, participants are expected to log food (required) at every eating session, though entries can be made later. For these same weeks, participants are expected to log sleep (recommended, hit “Start Sleep” before bed and then “End Sleep” upon waking). Also, participants can enter whether or not they felt rested (binary). There are other features of the app that participants can use but are not required or even recommended, including logging exercise (“Start” and “End Exercise,” type of exercise, intensity) and other health parameters (e.g., vitals, labs). We expect that using the app will take about 5-8 minutes each day.

For weeks that are not data collection weeks, participants have the choice to use the app or not.

ID: VIEW4E0BC12A9F800
Name: v2_Behavioral Interventions

HP-00099067 Other_V2

Other Psychosocial or Behavioral Procedures

You indicated that this study involves other psychosocial or behavioral procedures.

1 * Describe the other psychosocial or behavioral procedures that will be involved in the research:
Physical activity measurement via actigraphy and measurement of interstitial glucose via continuous glucose monitoring

2 Upload any relevant materials:

Name	Created	Modified Date

There are no items to display

3 * What is the individual duration of each procedure and what is the entire duration of all procedures?
Both the actigraph and the glucose monitor will be donned at the beginning of the week and can be worn for 7 days straight without charging or actively syncing with a mobile device. Actigraphy and glucose monitoring will occur for 7 days at baseline (week 0), week 6, and week 12 and not weeks 1-5 or 7-11. Actigraphs will be set up in the lab prior to mailing and the participant will not need to do anything except wear it and return it for us to retrieve the data. Continuous glucose monitors will be put on by the participant (or another person of their choice) using instructions provided by the manufacturer. They will hold the reader to the sensor to start collecting data, then do not have to do anything else for the rest of the week. We will ask that they return the reader and sensor with the actigraph the next week, after data collection.

4 * Are any of the procedures (or do any of the procedures elicit information) likely to cause discomfort in participants or cause harm?
● **Yes** ○ No

4.1 If Yes, what procedures are in place to assure safety?
The actigraph is a non-invasive device that is worn like a wrist watch. There is a very low potential for causing discomfort (more like annoyance once in a while).

The continuous glucose monitor (CGM) is applied to the back of the arm using an applicator that comes with the device. The CGM includes a filament that inserts about 5 mm into the skin. There is a water-proof adhesive that keeps the monitor in place. There is potential for causing minor, brief discomfort when device is applied and removed. If a participant desires, the back of the arm can be cooled with an ice pack before the glucose monitor is applied. The participant has the option to come on site for help applying and/or removing the device. To reduce discomfort, we will tell participants to avoid hitting it directly or pulling on it (see Study Packet). They can still do all typical activities of daily living, including working out and showering as normal.

ID: VIEW4E0BC6EF1E800
Name: v2_Other Psychosocial or Behavioral Procedures

Data Collection/Record Review

You indicated on the "Type of Research" page that your study involves data collection or record review (i.e., chart review, not self-report).

1 * What type of data will be collected/analyzed in this study? (Check all that apply)

- ☐ Retrospective/Secondary Analysis (data has already been collected at the time of initial IRB submission)
- ☑ **Prospective (data is not yet in existence and/or collected)**

2 * Will this study involve adding data to a registry or database for future use?

○ Yes ● **No**

3 * Will the data be released to anyone not listed as an investigator on the protocol?

○ Yes ● **No**

3.1 If Yes, give name(s) & affiliation(s):

ID: VIEW4E0E25A8CA400
Name: v2_Data Collection / Record Review

HP-00099067 Prospective Data_V2

Prospective Data

You indicated that the study involves the collection of prospective data.

1 * Where is the data being collected from? (Check all that apply)

- [x] **Medical records**
- [ ] Medical images
- [ ] Commercial (for profit) entity
- [ ] Publicly available records
- [ ] Schools
- [x] **Other**

1.1 If Other, please specify:
myCircadianClock app, questionnaires, researcher-provided glucose monitor and actigraph, interview, adverse events

2 * What data fields will you have access to/collect for the study? For example, name, initials, date of birth, Social Security number, income, demographic information, family units, housing, etc.
The Clinical Record form will be completed by study staff from the medical record. The Clinical Record form contains demographics, height, weight, current menopausal status, Karnofsky Performance Status or Eastern Cooperative Oncology Group (ECOG) Performance Status, comorbidities, cancer stage, surgical procedures, types and doses of treatments (e.g., chemotherapy type and dosing, hormone therapy), most recent blood work (e.g., hemoglobin, hematocrit, lymphocytes, etc.), and medical history (e.g., prior myocardial infarction).

myCircadianClock app: diet, sleep, exercise, and health data (We will have access to all that the participant inputs.)

Questionnaires: Please see section 5, Surveys/Questionnaires

Glucose monitor: Interstitial glucose data

Actigraph: Movement data (counts in three axes) and data from the light sensor

Adverse events: patient-reported worsening of symptoms, with special attention to weight loss and severe adverse events (e.g., hospitalization) as defined by the CTCAE v 5.0. Please see section 12, Study Monitoring.

You can also upload a copy of the data fields/variables to be collected for the study:

Name	Created	Modified Date
Clinical-record.docx(0.01)	2/22/2022 11:32 AM	2/22/2022 11:32 AM

ID: VIEW4E0E25B643800
Name: v2_Prospective Data

Clinical Trial Registration

You indicated on the "Type of Research" page that your study is a clinical trial.

1 * Does the UM Clinical Trials Registry policy require registration of this trial?

(●) **Yes** ( ) No

2 * Has this trial been registered?

(●) **Yes** ( ) No

ID: VIEW4E093BF078C00
Name: v2_Clinical Trial Registration

HP-00099067 Clinical Trial Registration Info_V2

Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

1 * Was this trial registered at www.clinicaltrials.gov?
(●) **Yes** ( ) No

2 If no, was this trial registered on a site other than clinicaltrials.gov?
( ) Yes ( ) No

2.1 If Yes, specify the name of the other site:

2.2 Provide justification for registering this trial on this site:

3 * Registration Number
NCT05256888

ID: VIEW4E093BF1D0800
Name: v2_Clinical Trial Registration Information

HP-00099067 Participant Selection_V2

Participant Selection

1 * How many local potential participants (or specimens/charts) do you anticipate will be screened for this study? ***Screening includes determining potential participants' initial eligibility for and/or interest in a study.***
300

2 * How many participants (or specimens, or charts) will be enrolled/used for this study? ***A local prospective participant is considered enrolled in the study when a UM-approved Informed Consent Document (not including separate screening consent forms) is signed.***

Local - the number being enrolled at this site:
50

Worldwide - the number being enrolled total at all sites (including local enrollment):
50

3 * Gender:
- [x] **Male**
- [x] **Female**

4 * Age(s):
- [ ] 0 to 27 days (newborn infants)
- [ ] 28 days to 12 months (Infant)
- [ ] 13 months to 23 months (Toddler)
- [ ] 2 to 5 years (Preschool)
- [ ] 6 to 11 years (Child)
- [ ] 12 to 17 (Adolescents)
- [x] **18 to 88 years (Adult)**
- [x] **89 years and older**

5 * Race/Ethnicity:
- [x] **All Races Included**
- [ ] American Indian or Alaskan Native
- [ ] Asian/Other Asian
- [ ] Asian/Vietnamese
- [ ] Black or African American
- [ ] Hispanic or Latino
- [ ] Mixed Race or Ethnicity
- [ ] Native Hawaiian or Pacific Islander
- [ ] White or Caucasian

6

* Language(s):
- [x] **English**
- [ ] Chinese
- [ ] French
- [ ] Italian
- [ ] Japanese
- [ ] Korean
- [ ] Local Dialect
- [ ] Spanish
- [ ] Vietnamese
- [ ] Other

6.1 Specify Other:

7

* Are you excluding a specific population, sub-group, or class?
○ Yes ● **No**

7.1

If Yes, indicate your justification for excluding a specific population, sub-group, class, etc.:

ID: VIEW4E0E519C1D000
Name: v2_Participant Selection

Vulnerable Populations

1 * Will you be targeting ANY of the following Vulnerable Populations for enrollment? (Select all that apply)

- [ ] Employees or Lab Personnel
- [ ] Children (Minors)
- [ ] Cognitively Impaired/ Impaired Decision Making Capacity
- [ ] Pregnant Women/Fetuses
- [ ] Wards of the State
- [ ] Students
- [ ] Prisoners
- [ ] Nonviable Neonates or Neonates of Uncertain Viability
- [ ] Economically/Educationally Disadvantaged
- [x] **None of the above**

Only select populations which you will be targeting for enrollment. Do not include populations that may be enrolled incidentally. Enrollment of a vulnerable population is considered to be "targeted" if the study team will be aware that a subject is from a vulnerable group as a result of interaction with the subject or collection of specific information about the subject, and the research team does not wish to exclude them. "Incidental" enrollment is limited to situations where a study team is unaware that a subject is from a vulnerable group.

ID: VIEW4E0E519917800
Name: v2_Vulnerable Populations

HP-00099067 Eligibility_V2

Eligibility

1 * Do you have an existing Eligibility checklist(s) for this study?

◯ Yes ● No

1.1 If Yes, upload here. If you need a template, you can download it by clicking **HERE**. The checklists you upload will also be available under the Documents tab of this application.

Name	Created	Modified Date

There are no items to display

1.2 If No, create an eligibility checklist below:

List inclusion criteria (List each Inclusion Criteria individually, using the ADD button):

	Number	Criteria
View	1	Have completed adjuvant chemotherapy, surgery, and/or radiation for cancer, including chemotherapy for hematological neoplasms, at least 2 months and not more than 2 years prior to enrolling. Participants are eligible if they are on maintenance therapy with non-conventional chemotherapy (e.g. targeted therapy)
View	2	Have a baseline level of fatigue, as determined by reporting a score of 4 or higher for the question, “In the last week, how bad was your worst fatigue on a scale from 0-10?”
View	3	Be able to speak and/or read and write in English
View	4	Be at least 18 years old
View	5	Own a smartphone
View	6	Be willing and able to adhere to study procedures, including use of a smartphone app
View	7	Be able to provide informed consent

List exclusion criteria (List each Exclusion Criteria individually, using the ADD button):

	Number	Criteria
View	1	Already eat all their food within a window that is 10 h or shorter most (6/7) days of the week
View	2	Be underweight, as defined as a body mass index ≤18.5 kg/m2
View	3	Have surgery planned during the study duration
View	4	Have any contraindications to the proposed nutrition intervention as identified by their medical provider, their designee, or the study team (e.g., type 1 diabetes, risk for hypoglycemia, medication requirements, pregnancy, breastfeeding, recent history of an eating disorder)
View	5	Be taking insulin
View	6	Be on enteral or parenteral nutrition

After entering the inclusion and exclusion criteria above, click the Save link. CICERO will automatically generate a printable Eligibility Checklist for you to use in your research. To review the checklist, click on the resulting link below. This checklist is also available under the Documents tab of this application.

Eligibility Checklist for HP-00099067_2 v1-23-2023-1674502822585(0.01)

ID: VIEW4E0E5185F9000
Name: v2_Eligibility

HP-00099067 Recruitment_V2

Recruitment

1 * Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them: (If this study involves the VA please list all sites at which recruitment will take place.):

1) Identification
Before recruitment, approval will be obtained by UMGCCC Clinical Research Center (CRC), the University of Maryland School of Nursing (UMSON), and the UMB Institutional Review Board (IRB). The study team will recruit participants using UMSON Department of Pain and Translational Symptom Science established procedures. Potential participants will be identified using three methods: a) screening medical records, b) direct referral from providers (e.g., nurses, nurse navigators, physicians), c) flyers, and (d) advertising via standard UMB- and ICTR-networks (e.g., the Elm).

a) Identification via medical records
Potentially eligible participants receiving care at UMGCCC will be identified in a HIPAA-compliant manner by study personnel via review of scheduled outpatient appointments (via EPIC) with Dr. Emadi, an oncologists on the study team. If other clinician(s) would like to participate in our study, we will add them to the study team and obtain permission to access their clinic schedule(s). Medical records typically show time since completion of adjuvant therapy (e.g., surgery, chemotherapy). If an individual appears to be eligible, the study team will contact the oncologist (or a designee) to notify them of a potential candidate and obtain approval to speak with/contact the patient.

b) Identification via direct referral from clinicians (e.g., physicians, physician assistants, nurses)
The study team is working with several oncologists (including, but not limited to Dr. Emadi) and their medical teams (e.g., nurses, physician assistants) to identify potential patients at UMGCCC who are likely eligible for our study. If the patient is eligible based on information in the medical records, the provider will be asked to refer the person to the study team, tell the person about the study at their appointment (in person or telehealth), or give them a flyer. The medical team is not expected to field detailed questions related to the study.

c) Flyers
Flyers advertising our study will be placed in locations designated for such use. Potential participants can contact a member of the study team directly via phone or email for more information. Their medical provider will be contacted to ensure that the study is appropriate for the potential participant before consenting them.

d) Email advertising
We will advertise our trial via email through the UMB Office of Communications and Public Affairs's Elm Weekly and ICTR's relationship with ResearchMatch. As with flyers, potential participants can contact a member of the study team directly for more information. Their medical provider will be contacted to ensure that the intervention is appropriate for the potential participant before consenting them.

2) Recruitment
a) If the provider gives the study team permission to contact the participant, we will mail them a recruitment letter and/or send them a message via myPortfolio briefly introducing the study and asking them to contact us for more information.
b) If the provider introduced the study to the participant and has gotten permission for us to contact them, we will either meet them at/after their oncology appointment, send them an email, or call them.

After a potential participant has shown an initial interest in the study, we will review eligibility and discuss the study activities. If the person volunteers to participate, study personnel can obtain informed consent then or at a later date. After consent is provided, the participant will be provided with study materials.

3) Screening
For convenience to the potential participant, the person's clinic appointment might be combined with their screening and/or consent, or participants can undergo the screening and/or consent process remotely via phone and eConsent. To protect the privacy of potential participants, face-to-face recruitment discussions will be conducted in a private location.

A member of the study team will meet the potential participant in person or talk to them over the phone to explain the project and invite them to participate. It is expected that some patients will decline to participate, and some will not be eligible; approaching the same individual twice will be avoided by keeping a screening log containing the following information:
• Screening ID (1, 2, 3,…)
• Name
• Date of contact
• Medical record number
• How the participant learned of the study (e.g., our team, provider, flyer)
• Where/how we talked to the potential participant (e.g., clinic location, phone)
• Whether the patient was eligible or not
• If ineligible, the reason they are ineligible
• Whether the patient ultimately consented or declined
• If declined consent, the reason for declining consent
• If consented, the participant ID in the study (e.g., FRE01, FRE02, FRE03, …)
Patients will need medical clearance from their provider to participate in the study.

Attached files:
Recruitment-letter.docx: For people whom we have gotten permission to contact from the oncology care team
telephone-script.docx: For people who have provided permission for us to contact them
telephone-script-2.docx: For people who call us for more information

2 * Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):
To minimize coercion, the study team will emphasize that participation is completely voluntary and their cancer care will not be affected by their participation in the study.

3 * Who will recruit participants (or acquire charts/records/samples) for this study? (Check all that apply)

- [x] **PI**
- [x] **Study Staff**
- [ ] Third Party

3.1 If you are using a third party, specify Third Party Recruiters:

4 Upload any recruitment tools such as screening/telephone scripts and introductory letters (do not upload advertisements here):

Name	Created	Modified Date
Recruitment-letter.docx(0.03)	2/22/2022 11:24 AM	3/11/2022 11:42 AM
telephone-script-2.docx(0.01)	3/10/2022 5:07 PM	3/10/2022 5:07 PM
telephone-script.docx(0.02)	2/22/2022 11:24 AM	3/10/2022 5:07 PM

ID: VIEW4E0BCAA0A6C00
Name: v2_Recruitment

HP-00099067

Advertising_V2

Advertising

1 * Will you be using advertisements to recruit potential participants?
Yes ○ No

ID: VIEW4E0BCCF811000
Name: v2_Advertising

HP-00099067 Advertising Detail_V2

Advertising Detail

You indicated that you will be using advertisements to recruit potential participants.

1.1 * Select the mode(s) of advertising (check all that apply):

- [ ] Radio
- [ ] Internet
- [x] **Print**
- [ ] Television
- [x] **Other**

1.1.1 If Other, specify:
Email: Elm Weekly, ResearchMatch
MyPortfolio

1.2 * Provide exact text of all proposed advertisement(s):
Cancer survivors: Did your treatment-related fatigue just never go away? Join a research study at University of Maryland, Baltimore, that aims to understand how diet, physical activity, and sleep patterns contribute to persistent fatigue

Who is eligible?
-Cancer survivors who finished chemotherapy, radiation, and/or surgery 2 months-2 years ago
-People who are experiencing at least moderate fatigue on a regular basis
-People who tend to eat in a window greater than 10 hours on most days (e.g., breakfast at 8 a.m. and dinner at 7 p.m., a window of 11 hours)

What do I have to do?
- Participate in a 12-week study that collects data on food intake, physical activity, sleep patterns, sugar metabolism, and your symptoms, with a focus on fatigue.
- Provide feedback on a smartphone app that monitors food intake, physical activity, and sleep patterns for one week at the beginning, middle, and end of the study.
- Fill out questionnaires related to your eating patterns, fatigue, and other symptoms at the beginning, middle, and end of the study.
- Wear a physical activity monitor (e.g., FitBit) and glucose monitor for one week at the beginning, middle, and end of the study.
- Some participants will be asked to eat all their food within a self-selected 10-hour window during the day (e.g., 9am-7pm).

Do I get paid to participate?
Yes, Up to $75.

Can I participate remotely?
Yes, all research activities can be done at home.

Please contact the study chair, Amber Kleckner, PhD, for more information.
amber.kleckner@umaryland.edu

1.3 * Upload advertisement(s) here:

Name	Created	Modified Date
SON-FREDA-Study-PC-v5.pdf(0.02)	2/22/2022 11:28 AM	3/11/2022 11:44 AM

ID: VIEW4E0BCE82B8C00
Name: v2_Advertising Detail

Research Related Risks

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1 * Individually list each research-related risk, using a separate line for each. Next to each risk, delineate the likelihood/seriousness of the risk, and the provisions for minimizing the risk:

a) Weight loss due to the intervention
Some studies have documented weight loss upon adoption of a TRE dietary pattern (10 hours of feeding/14 hours of fasting) despite consuming calories ad libitum. This intervention diet will be ad libitum and participants will be encouraged to satisfy thirst and hunger. However, due to the time-restrictive nature of the TRE diet compared to the typical American eating patterns, there is a chance that patients could enter a calorie deficit and lose weight during the course of the intervention. Minor weight loss will not be considered an adverse event (less than 3% in one week or 5% body weight every two weeks). However, if a patient experiences rapid, unintentional weight loss, the participant will be encouraged to contact the study team, medical monitor, and/or their treating oncology team. The CTCAE, version 5, will be used to report weight loss as an adverse event:
- Weight loss of 5% to less than 10% from baseline with no intervention indicated will be considered a Grade 1 adverse event.
- Weight loss of 10% to less than 20% from baseline and indicated nutritional support will be considered a Grade 2 adverse event.
- Weight loss greater than or equal to 20% from baseline with indicated tube feeding or total parental nutrition (TPN) will be considered a Grade 3 adverse event.

Weight loss can cause anxiety in cancer survivors who might think that their cancer is recurring. However, knowing that this dietary intervention often results in weight loss, particularly in people who are overweight, can be reassuring in that weight loss is due to dietary change and not a manifestation of progressive cancer, particularly if there are no other concerning symptoms.
As always, the patient has the right to eat or drink outside of the 10-h window, and to withdraw from the study at any time.

Likelihood: Moderate probability that some weight loss will be experienced, especially in patients with excess body fat; very low probability that a dangerous amount of weight will be lost

Seriousness: Low

Provisions for minimizing risk: In order to closely monitor weight change, each participant will be provided with a scale to use at home. It is likely that some participants will have personal goals to lose excess body fat—we will explain that this is not a weight loss study. In the event that rapid, unintentional weight loss occurs, the treatment team's recommendations for nutritional interventions due to any weight loss will be followed.

b) Hunger and hunger-related symptoms due to the intervention
Eating within a 10-h window will mean re-adjusting participants' typical eating patterns. Many participants will need to rearrange their meal times—either delay breakfast, eat dinner earlier, and/or forgo after-dinner snacks. If they delay breakfast, they might feel hungry in the few hours leading up to their eating window, especially in the first few days of the study. Similarly, they might crave something before bed if they are in the habit of eating before bed. With hunger can come lack of concentration, fatigue, dizziness, irritability, and other symptoms.

Likelihood: Moderate-high

Severity: Low to moderate

Provisions for minimizing risk: All participants will be encouraged to stay hydrated and to consume a snack outside of the window if symptoms become debilitating.

c) Emotional distress due to the intervention or the outcome measures
There is a chance that participants could become emotionally distressed by the expectation to consume food only in the 10-h window.

Likelihood: Low

Severity: Low

Provisions for minimizing risk: Each participant will be reassured that deviations from the plan are permitted, especially if they are feeling sluggish, dizzy, or sick, or if they are on a short trip/vacation.

d) Breach of confidentiality
There is always a risk of a breach of confidentiality in which sensitive medical information (e.g., medical history, AIDS status) could become known to persons outside the research team.

Likelihood: Very low

Severity: Low to high

Provisions for minimizing risk: To avoid leakage of sensitive information, only Dr. Kleckner (the study chair), coordinator(s), and any individual designees will have access to the screening log and the file that links participant name with participant number (both will be encrypted); these files will be stored on password-protected computers in the Department of Pain and Translational Symptom Science in the School of Nursing. All data files will reference participants by a non-identifiable Participant ID and will be stored on secure servers at UMB. All paper consent forms will be stored in a locked cabinet in Dr. Kleckner's or the coordinator's office. If Dr. Kleckner shares data with any other researcher for analyses, all data will be deidentified (i.e., void of name, birthdate, and contact information). Presentation of data in the form of posters, presentations, grant applications, and manuscripts, either in private or public settings, will not have any identifiable information. Dr. Kleckner and all members of the study team participate in ethical training in accordance with University of Maryland policies (e.g., online coursework via the CITI collaborative).

e) Hypoglycemia due to fasting
The pancreas, via secretion of insulin and glucagon, maintains a constant blood sugar concentration of about 4-6 mM. After a meal, the pancreas will secrete insulin to promote the uptake of glucose into cells and, in response to falling glucose concentration a few hours later, the pancreas will secrete glucagon to promote gluconeogensis, or the production/release of glucose in/from the liver and other tissues. This is a normal metabolic routine that occurs daily, especially during sleep (typically about 8 hours with no food). Fasting for prolonged periods of time to can lead to hypoglycemia for a small percentage of individuals who have metabolic disorders and glucose dysregulation.

Likelihood: Low

Severity: Low to high

Provisions for minimizing risk: We are excluding participants who have type 1 diabetes, risk for hypoglycemia, or any other contraindications as determined by their provider. People who have type 1 diabetes or are at risk for hypoglycemia tend to know, and know that they should not fast for 14 hours overnight. In the consent form, we describe symptoms that are associated with hypoglycemia. We underlined that we encourage them to eat outside their eating window if they feel sluggish, dizzy, or sick. We will emphasize this while we go over the consent form with them and before they sign it. In the event that hypoglycemia occurs or is expected based on the participant's symptoms, the PI will meet with the participant to discuss the events surrounding the hypoglycemic episode and then meet with Dr. Emadi, the study doctor, to determine the course of action, which might include extending the eating window or having the participant stop the study.

ID: VIEW4E1B52509F000
Name: v2_Research Related Risks

Potential Benefits and Alternatives

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the potential direct benefit(s) to participants:
Participants may or may not directly benefit from this study. Participants in the intervention arm will be encouraged to consume a new dietary pattern that has been shown to improve health. Participants in both arms will likely become more aware of the composition of their diet as well as their eating and sleeping habits from logging them. It is hypothesized that time-restricted eating will have a positive effect on their symptoms, though it may not.

2 * Describe the importance of the knowledge expected to result from the study:
Cancer-related fatigue is a common, persistent, and debilitating condition with no known treatments. This study will shed light on underlying metabolic and circadian processes that might underlie fatigue. If our hypothesis is correct, it will be one of the first nutrition-based intervention to address persistent cancer-related fatigue.

3 * Describe how the potential risks to participants are reasonable in relationship to the potential benefits:
The physical and emotional risks to the participants are low. Many people take pride in contributing to research and knowing that their time and effort in a study might help patients in the future.

4 * Describe the alternatives to participation in this study. If there are no alternatives, state that participation is voluntary and the alternative is not to participate. For intervention studies, describe appropriate alternative clinical procedures or courses of treatment available to subjects.
Participation in this study is voluntary and the alternative is not to participate. Survivors can seek other nutritional services at UMMC and in their communities. The participant may choose to not participate in the study without penalty or effects on their medical care.

ID: VIEW4E1B5251B0400
Name: v2_Potential Benefits and Alternatives

Withdrawal of Participants

If the questions below are not applicable to the research (i.e., chart review), enter "N/A".

1 * Describe anticipated circumstances under which subjects will be withdrawn from the research without their agreement:

The participant can be removed from the study by the investigator or the sponsor. A participant may be withdrawn from the study if their disease becomes worse or if their doctor feels that staying in the study is harmful to the participant's health. The study team also holds the discretion to withdraw a participant from the study if their participation becomes harmful to a study team member. It is unlikely but possible that the entire study may be stopped by the sponsor, the investigator, the Institutional Review Board, the facility where the study is being carried out, or the University. In that case, participants' participation will end.

2 * Describe procedures for orderly termination:

Upon completion of data collection and return of the actigraph, each participant will be thanked for their participation in the study and compensated for their time.

If a participant withdraws (or is withdrawn) before the end of the study, they will be paid for the time they spent providing data and the study team will not contact the person anymore. A 10-20% withdraw rate is built into the study design and recruitment goal, so there should not be a need to replace participants who withdraw before completing the study.

3 * Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection:

If a participant wishes to withdraw from the study, we will ask if the participant would like to continue participation in some but not all of the research activities. If they would like to participate in only some of the research activities, we will note which ones and the participant will not be formally withdrawn from the study. If they wish to withdraw completely, a written withdrawal request is required and should be sent to the PI (email preferred). The written request for withdrawal will be included in the participant's study record as documentation of the reason for removing a participant from the study. If a participant makes a verbal request and does not provide a written request, the verbal request will be documented by the study team member who receives the request and added to the participant's study record. Data that have been collected thus far will be analyzed.

ID: VIEW4E1B52531F800
Name: v2_Withdrawal of Participants

Privacy of Participants

If the study does not involve interaction with participants, answer "N/A" to the questions below.

1 * Describe how you will ensure the privacy of potential participants throughout the study ***(privacy refers to persons and their interest in controlling access to themselves):***

Potential participants who are approached in-person will be led to a private location for to discuss the study (e.g., consult or examination room in the UMGCCC, clinical testing room in the School of Nursing; see below). For phone calls, appointments will always be made ahead of time so that the participant can ensure they are in a desired environment.

2 * Describe the location where potential participants will receive research information and detail the specific actions the study team will take to ensure adequate privacy areas:

We will discuss the study with potential participants in a private consult or examination room in the UMGCCC, other private room in the hospital, or a clinical testing room in the Department of Pain and Translational Symptom Science (School of Nursing). Alternatively, participants may learn about the study via a letter in the mail, myPortfolio message, or a flyer, in which case they will call us for more information. After baseline assessments, the participant will be randomized and instructions will be given regarding the study activities for the next 13 weeks. This information will similarly be provided in a private room in UMGCCC or the School of Nursing or via the telephone or video conference. For in-person meetings, we will close the door and only the study staff and participant (and person(s) accompanying the participant, if desired) will be present; no members of the clinical care team or hospital staff will be present unless specifically invited by the potential participant.

3 * Describe potential environmental stressors that may be associated with the research:

There will be no more environmental stressors than typically experienced at a doctor's appointment. We will do what we can so that the room is comfortable to facilitate conversation regarding the study and its components (good lighting, comfortable temperature). We will make accommodations (as able and reasonable) for people with disabilities (e.g., comfortable place to sit, space to maneuver wheelchair, etc.)

4 * Will this study have a site based in the European Union?

○ Yes ● **No**

5 * Will the study have planned recruitment or data collection from participants while they are located in the European Union?

○ Yes ● **No**

Access link below for information about the EU General Data Protection Regulations to assist in answering these questions.
https://www.umaryland.edu/oac/general-data-protection-regulation/

ID: VIEW4E1B525B87C00
Name: v2_Privacy of Participants

HP-00099067 Confidentiality of Data_V2

Confidentiality of Data

1 * Will stored research data contain identifiers or be able to be linked to and identify individual participants (either directly or through a code/research ID)?

- (●) **Yes**
- ( ) No, the data will be stored de-identified/anonymous (stripped of all identifiers, no way to identify individual participants)

2 * Where will research data be kept (address electronic and paper data as applicable)? (If this is a VA study please list specific sites that data will be kept.)

Data will be stored both at UMB and the myCircadianClock server associated with the Salk Institute.

3 * How will such data be secured?

Both the UMB study team and myCircadianClock app designers are taking extensive measures to ensure privacy of participants.

The UMB study team will assign a numerical Participant ID to each participant once they have signed the consent form (e.g., FRE01, FRE02, etc.). Notes and databases will use this number and the participant's first and last initials as identifiers to ensure data integrity (e.g., FRE25 JB). Other identifying information will not exist on these forms. A complete list of study participants with Participant ID, name, and contact information will be maintained separately for the purpose of contacting participants if necessary; this database will be maintained for at least six years after the study is complete. This linkage information will be maintained and only accessible to Dr. Kleckner (PI) who will provide individuals with private access only if necessary. Data are stored on Dr. Kleckner and/or the study team's university-owned computers and backed up on the HIPAA-compliant Microsoft OneDrive, as recommended by UMB Information Technology (IT).

Paper-based data will be stored in a locked cabinet in Dr. Kleckner's office in the Department of Pain and Translational Symptom Science in the School of Nursing. Electronic data will be stored on a UMB-issued computer as part of Dr. Kleckner's lab in the School of Nursing. The School of Nursing is secured by electronic key cards and a security guard at the front desk; Dr. Kleckner and her coordinator's personal office is secured by traditional keys; Dr. Kleckner's file cabinet is secured by a unique traditional key; and computers in Dr. Kleckner's lab are password-protected. Electronic research records are stored on UMB's password-secured and firewall-protected networks. These are the same methods of security used for patient medical records. myCircadianClock data will be stored in a HIPAA-compliant server associated with the Salk Institute for Biological Sciences in La Jolla, CA. All study data will be kept for at least six years after the study and all reports and publications are complete.

Privacy measures by the myCircadianClock team to protect the privacy of the individual and the participant's app data:
○ The following personal health information will be collected by the app: country, language, photos or names of food/beverages the participant takes, activity/exercise, sleep, and health entries, timestamp of entries, and geographic location data from entries.
○ The first time the app is launched it creates and stores a 20 character alphanumeric identifier for the device, e.g. Bw2iAm67juEglgN1qK8t. This identifier is unique and permanent for the duration of the study, stored on the device as well as the server and serves the purpose of uniquely but anonymously keeping track of multiple users.
○ Whenever app data is transferred to a research study computer, it will be encrypted so that others cannot interpret the data or associate it back to the participant.
○ Encrypted app data (stripped of personal identifiers, and associated only with a random code) will be sent to secure data servers used for the research study, where it will be stored with a unique identifier.
○ Encrypted data will also be sent to a secure database where it will be stored with a unique identifier. The identifier does not contain any personal information. The participant will receive their encrypted data back from the server for visualization on their phone.
○ App-generated data is associated only with a random participant code, and this code is used in all future analyses, separating it from any personally identifiable information.
○ Study investigators chose Amazon Web Services for this important responsibility because they are a world leader in the secure storage and protection of sensitive data. They have a proven track record of safeguarding and managing potentially sensitive biomedical data in accordance with regulations that govern human research and medical information (e.g., regulations mandated by Institutional Review Boards [IRB] and the Health Information Portability and Accountability Act [HIPAA]).
○ While the established procedures de-identify data and use secure computers, we cannot ensure complete privacy.
○ One potential loss of privacy would be if someone sees a participant's data from myCircadianClock on their smartphone. For security, myCircadianClock suggests that the participant's smartphone be protected either by a passcode or fingerprint sensor. This ensures that only the participant can enter and use the app.
○ These steps ensure that researchers analyzing the coded study data will not be able to connect it to any individual user.
○ myCircadianClock data are backed up on a HIPAA-compliant server. By design, the filenames include a randomly generated string, date and time in the filename making it virtually impossible to guess a particular filename.

4 * Who will have access to research data?

Only members of the study team will have access to the stored data. All individuals who have access to the data will need to complete human participant training as required by UMB.

The myCircadianClock team will have access to the raw data from the myCircadianClock app.

Any investigator who would like access to deidentified data must submit a request to the study chair (i.e., Dr. Amber Kleckner) via a written request (e.g., email). If Dr. Kleckner considers the project appropriate, she will approve a release of the data and transfer it in a safe, HIPAA-compliant manner according to UMB rules. We will obtain a data use agreement if outside UMB, approval from the IRB, and/or Not Human Subjects Research (NHSR) determination, as appropriate.

5 * Will study data or test results be recorded in the participant's medical records?

- ( ) Yes
- (●) **No**

6 * Will any data be destroyed? ***(Please note that data for FDA regulated research cannot be deleted however, VA data must be destroyed according to the VHA Records Control Schedule (RCS) 10-1)***

- (●) **Yes**
- ( ) No

6.1 If Yes, what data (e.g., all data, some recordings, interview notes), when and how?

Audio-recordings of exit interviews will be transferred to the computer and then deleted off the recording device.

7 Do you plan to obtain a Certificate of Confidentiality?

- ( ) Yes
- (●) **No**

7.1 If Yes, upload your Certificate of Confidentiality. If you have not yet obtained the Certificate, please note that once it is obtained, you will need to submit an amendment to attach the document, make any needed changes to the submission and make needed changes to the Informed Consent Document.

Name	Created	Modified Date

There are no items to display

8 * Discuss any other potential confidentiality issues related to this study:

We are working with the myCircadianClock team to customize the app specifically for this study. We will only collect the data we need to answer the research question and no superfluous data.

Presentation of data in the form of posters, presentations, grant applications, and manuscripts, either in private or public settings, will not have any identifiable information.

ID: VIEW4E1B5265E0400
Name: v2_Confidentiality of Data

HP-00099067 Monitoring Plan Selection_V2

Monitoring Plan Selection

1 * Type of data safety monitoring plan for the study:

- ○ Will use/defer to the external sponsor's Data Safety Monitoring Plan
- ● **Data Safety Monitoring by a Committee**
- ○ Data Safety Monitoring by an Individual
- ○ There is no data safety monitoring plan in place

ID: VIEW4E1B00E30D400
Name: v2_Monitoring Plan Selection

HP-00099067 Monitoring Plan - Committee_V2

Monitoring Plan - Committee

You indicated that the monitoring will be done by a Committee.

1 * Will the Committee be Internal or External?

- (●) **Internal DSMB**
- ( ) External DSMB

2 * What data will be reviewed?

- [x] **Adverse Events**
- [x] **Enrollment Numbers**
- [ ] Patient Charts/Clinical Summaries
- [ ] Laboratory Tests
- [ ] Medical Compliance
- [ ] Procedure Reports
- [ ] Raw Data
- [ ] Outcomes (Primary, Secondary)
- [ ] Preliminary Analyses
- [ ] Other

2.1 If Other, specify:

3 * What will be the frequency of the review?

- ( ) Annually
- (●) **Bi-Annually**
- ( ) Other

3.1 If Other, specify:

4 * Safety monitoring results will be reported to:

- [x] **IRB**
- [ ] GCRC
- [ ] Sponsor
- [ ] Other

4.1 If Other, specify:

ID: VIEW4E1B025761800
Name: v2_Monitoring Plan - Committee

Monitoring Plan - Internal DSMB

You indicated that the monitoring committee will be an internal DSMB.

1 * List Internal DSMB Members:

Name
View Michael Kleinberg, MD, PhD
View John Baddley, MD
View Amin Benyounes, MD
View Jacqueline Bork, MD
View Susan Dorsey, PhD, RN
View Caitlin Eggelston, BS
View Olga Goloubeva, PhD, MS
View Petr Hausner, MD
View Laura Hearson, RN, OCN
View Yixing Jiang, MD, PhD
View Myounghee Lee, PharmD, PhD
View Heather Mannuel, MD, MBA
View Gautam Rao, MD
View David Reidel, MD
View Katherine Tkaczuk, MD

2 * Confirm that no financial or other conflicts of interest exists for the above individuals.

● **Yes** ○ No

3 * Will there be an interim efficacy analysis?

○ Yes ● **No**

3.1 If Yes, when?

4 * Briefly describe the DSM review process itself. Will it be an open or closed review to the investigator? Blinded/unblinded data? How will confidentiality of individual participant data be maintained?

the UMGCCC DSM/QAC will provide independent monitoring. The below items are considered in DSM/QAC annual review. The semi-annual review will include only those items below related to safety.

• A cover form (Annual Renewal DSM/QAC) completed by the study team summarizing the activities of the prior reporting period.
• All severe adverse events (SAEs) and protocol-designated expeditiously reportable adverse events (AEs), internal and external, including those that have previously been reported to the DSM/QAC. The DSM/QAC will have a full report on all internal SAEs concerning that clinical trial, including the nature of the SAE, grade, therapeutic agents involved, whether they were reported to all appropriate agencies within the mandated timeframes, and the investigator's assessment of whether the toxicity was study-related. The DSM/QAC may recommend to the CRC to close studies with adverse event profiles that deviate in a substantial way from expected patterns of events.
• The consent form to determine if modifications are needed based on the accumulated AEs and SAE information.
• A summary of protocol deviations that have not yet been reviewed by the DSM/QAC.
• If available, interim outcomes and other results are assessed to see if response rates conform to estimates used to develop the statistical analysis. The DSM/QAC may recommend study closure to the CRC for studies with poorer than expected response rates that cannot meet stated outcomes targets even if the trial accrued fully. Conversely, response rates significantly greater than expected may lead to early termination of trials to prevent further assignment of patients to the inferior treatment arms in comparative trials.
• Periodic audit results, if available. The DSM/QAC may recommend study closure to the CRC for studies when the PI or research team show a pattern of persistent non-compliance with Good Clinical Practices policies.

Upon conclusion of review, the DSM/QAC decides one of the following:
• Award final DSM/QAC approval to the protocol
• Find that minor revisions are needed for final DSMB approval
• Find that major corrections are needed to the protocol
• Suspend immediately to prevent harm to subjects or others
• Recommend closure of the protocol to the CRC due to GCP non-compliance or low accrual.
• Refer the protocol back to the CRC for scientific re-review if new information has called into question the original study hypothesis.

DSM/QAC actions are approved by majority committee member vote. Members with conflicts of interest will not serve as reviewers for protocols for which they are conflicted and will recuse themselves from discussions and voting on such studies.

The record of DSM/QAC actions for a protocol consist of:
• Chair notes, consisting of findings of the DSM/QAC reviewer, discussions and decisions by the DSM/QAC and specific issues requiring remediation
• DSM/QAC correspondence with the PI, specifying the actions to be taken (if applicable) and the acceptable turnaround time for response
• PI responses to DSM/QAC inquiries are reviewed at the next DSM/QAC meeting
• Final DSM/QAC review outcome provided to the PI

Records of these reviews are made available to the IRB for consideration in their deliberations.

5 * What are the criteria defined in the protocol to be used for decision making regarding continuation, modification, or termination of study?

A possible modification may be made to the protocol if we are recruiting fewer than one participant per month for 3 consecutive months.

ID: VIEW4E1B0261D9400
Name: v2_Monitoring Plan - Internal DSMB

HP-00099067 Research Related Costs_V2

Research-Related Costs

1 * Is the study's financial supporter (e.g., commercial sponsor, federal or state grant or contract, private foundation, physician-sponsor) covering any research-related costs?

- ○ No
- ● **Yes**

1.1 If Yes, check all that apply:

- ☑ **Research-Related Services (personnel costs, tests, supplies, exams, x-rays, or consultations required in the study)**
- ☐ Investigational or Study Device
- ☐ Investigational or Study Drug
- ☐ Investigational Procedure(s)

1.2 If No, who is responsible for payment?

2 * Who is responsible for the uncovered research-related costs?

- ☐ Participant
- ☐ Sponsor
- ☐ UM
- ☐ Other
- ☑ **There will be no uncovered research-related costs**

2.1 If Other, specify:

3 If the participant is responsible for any research-related costs, identify and estimate the dollar amount:

ID: VIEW4E1B5D9641800
Name: v2_Research Related Costs

Compensation for Research-Related Injury

1 * Is this study under a master agreement that includes a provision requiring the sponsor to provide compensation to participants for research-related injury?

◯ Yes ● **No**

1.1 If Yes, please provide the date and title of the agreement and upload the portion of the contract language relevant to compensation for research-related injury:

Name	Created	Modified Date

There are no items to display

1.2 If No (the study is not under a master agreement), is there proposed contract language concerning payment to participants for treatment in the event of a research-related injury?

◯ Yes ● **No**

1.2.1 If Yes, indicate the status of the contract review/approval with the ORD and upload the proposed language relevant to compensation for research-related injury:

1.2.2

Name	Created	Modified Date

There are no items to display

ID: VIEW4E1B629EEC000
Name: v2_Compensation for Research-Related Injury

HP-00099067 Payment to Participants_V2

Payment/Reimbursement to Participants

1 * Will participants receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research?

(●) Yes ( ) No

ID: VIEW4E1C52A5D7800
Name: v2_Payment to Participants

HP-00099067 Payment Detail_V2

Payment/Reimbursement Detail

You indicated that participants will receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research.

1 * Payment/reimbursement to participants will be for: (check all that apply)

- [ ] Travel
- [x] **Parking**
- [ ] Meals
- [ ] Lodging
- [x] **Time and effort**
- [ ] Other

1.1 If Other, specify:

2 * What is the total dollar value of the payments/reimbursements over the duration of the study? ***Total payment(s) for participation in research of $600 or more in a calendar year is required to be reported on an IRS Form 1099.***

$75

3 * Describe the timing and distribution plan for the payment/reimbursement (schedule, means, etc.)?

Participants will receive payments of $25 to complete baseline measures (3 of the 4 including questionnaires, logging food and sleep in the app, actigraphy, and continuous glucose monitoring), week 6 measures, and week 12 measures for a total of $75. They will also be able to keep the portable scale. We will provide a parking voucher for in-person visits if the person drove specifically for the study visit. Payments will be made after each study time point.

4 * Method(s) of payment/reimbursement to be Used:

- [ ] Cash
- [ ] Check
- [ ] Money Order
- [x] **Gift Certificate/Gift Card**
- [x] **Other**

4.1 If Other, specify:

electronic gift card, parking voucher

ID: VIEW4E1C54A6ACC00
Name: v2_Payment Detail

HP-00099067 HIPAA_V2

HIPAA (Health Insurance Portability and Accountability Act)

1 * Are you affiliated with, or will you be accessing data from a HIPAA-covered entity? A covered entity might be a hospital, a physician practice, or any other provider who transmits health information in electronic form.

• At UMB, this includes UMB schools designated as covered entities (School of Medicine and School of Dentistry) and entities under the University of Maryland Medical System (UMMS). The Baltimore VA Medical Center is also a covered entity.

• If you are a researcher from any school that is not a covered entity but is accessing electronic medical records from a covered entity (such as UMMC), HIPAA would be applicable. Please see a list of covered entities included under UMMS here: *executed-ace-designation-042018.pdf*

● **Yes** ○ No

2 * If Yes, will the study view, access, share, collect, use, or analyze health information that is individually identifiable under HIPAA?

● **Yes** ○ No

ID: VIEW4E1B0A2114400
Name: v2_HIPAA

Protected Health Information (PHI)

You indicated that HIPAA applies and the study will view, access, share, collect, use, or analyze health information that is individually identifiable.

1 * Which PHI elements will be used or disclosed in this study? (Check all that apply)

- [x] **Name**
- [x] **Address (if more specific than Zip Code)**
- [x] **Dates**
- [x] **Ages over age 89**
- [x] **Telephone numbers**
- [ ] Fax numbers
- [x] **Email addresses**
- [ ] Social Security numbers
- [x] **Medical record numbers**
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate/license numbers
- [ ] Vehicle identifiers and serial numbers, including license plate numbers
- [ ] Device identifiers and serial numbers
- [ ] Web universal resource locators (URLs)
- [ ] Internet protocol (IP) address numbers
- [x] **Biometric identifiers, including fingerprints and voiceprints**
- [ ] Full-face photographic images and any comparable images
- [ ] Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification
- [ ] None

2 * Why is the PHI necessary for this research?

If SSNs are going to be used, describe the specific use and type of SSN to be used (real, scrambled, last 4 digits).

Name- to identify, recruit, and communicate with the participant
Address- to mail actigraphs, continuous glucose monitors, and gift cards if the participant chooses not to come in
Dates- dates of cancer treatment are necessary for eligibility determination
Age- while the study team will know the person's birthdate, including year, we will not report any specific ages in our presentations or manuscripts. Only averages or categories will be presented.
Telephone number- we will check in with each participant approximately every two weeks via phone
Email- we will email questionnaire links to participants
Medical record number- we will access participants' medical records as part of the study
Biometric identifiers- we will have audio-recorded interviews and, in some cases, paper-based forms with handwriting. All these data will be transferred to electronic forms so that they are not identifiable during analysis.

3 * What is the source(s) of the PHI?

Name- medical record
Address- on study form (patient-report)
Dates- medical record
Age- medical record
Telephone number- on study form (patient-report)
Email- on study form (patient-report)
Medical record number- EPIC
Biometric identifiers- audio-recordings from interviews, paper-based data collection forms (handwriting)

4 * Provide written assurance that Protected Health Information will not be reused. (Note: this refers to re-use on another study or for a purpose which has not been approved, not to the re-use of screening data during the current study).

Protected Health Information that is collected for this study will be used only for this study and not for any ongoing or future studies.

5 * How will permission to allow the use/disclosure of the individual's protected health information (PHI) be obtained? (Choose all that apply:)

- [x] **Obtain written authorization *(upload authorization form at the end of the application under "Consent and HIPAA Authorization Forms")***
- [x] **Requesting waiver/alteration of authorization (includes waiver of authorization for recruitment only)**
- [ ] Qualifies as a limited data set (LDS)

5.1 If you are using a limited data set (LDS), please attach the Data Use Agreement (DUA):

Name	Created	Modified Date

There are no items to display

ID: VIEW4E1B0A24AA400
Name: v2_Protected Health Information

Waiver/Alteration of Authorization

You indicated that a waiver/alteration of authorization is requested.

1 * Provide rationale for how the research presents no more than minimal risk to the privacy of individuals:

A waiver of authorization will be requested for screening purposes only. Our screening log contains the following information:
- Screening ID (1, 2, 3,…)
- Name
- Date of contact
- Medical record number
- How the participant learned of the study (e.g., our team, provider, flyer)
- Where/how we talked to the potential participant (e.g., clinic location, phone)
- Whether the patient was eligible or not
- If ineligible, the reason they are ineligible
- Whether the patient ultimately consented or declined
- If declined consent, the reason for declining consent
- If consented, the participant ID in the study (e.g., FRE01, FRE02, FRE03, …)

The log will not contain any other details, including any data from the medical record.

2 * Describe the plan to ensure the protection of PHI collected during this study from improper use and disclosure:

The screening log will be doubly password-protected. It will be a password-protected Excel spreadsheet on a password-protected UMB computer (two different passwords).

3 * Describe the plan to destroy the PHI collected during this study at the earliest opportunity consistent with the conduct of the research. If there is a need to retain PHI, provide a justification:

With regard to the conduct of the research, the screening log may destroyed after publication of the CONSORT diagram, which will likely be published as part of the primary aims manuscript. We will retain the data longer if deemed necessary by the sponsor or university.

4 * Why could the research not practicably be done without access to and use of this PHI?

It is necessary to have a member of the study team screen and identify potential participants, or else the rate of recruitment will be greater hindered.

5 * Why could the research not practicably be done without the waiver or alteration?

Recruitment will occur much slower if we rely on participants to contact us in response to advertising or if we have to rely on clinicians, who are very busy, to identify potential participants.

6 * Will the subjects' PHI be disclosed to (or shared with) any individuals or entities outside of UM?

◯ Yes ● **No**

6.1 If Yes, describe the individuals or entities outside of UM to whom PHI will be disclosed.

ID: VIEW4E1B0A2896400
Name: v2_Waiver/Alteration of Authorization

Informed Consent Process

If the study does not involve interaction with participants or a waiver of consent is being requested , answer "N/A" to the questions below.

1 * Indicate the type(s) of consent that will be involved in this study: (check all that apply)

- [ ] Not applicable (study may qualify as exempt)
- [ ] Request to Waive Consent/Parental Permission (Consent is not being obtained)
- [ ] Request to Alter Consent (Some Elements of Consent Waived)
- [ ] Request to Waive Documentation of Consent (Verbal/Oral Consent)
- [x] **Written Consent Form**
- [x] **Electronic Consent**

2 * Describe the Informed Consent process in detail:

1) Leading up to consent
If a member of the study team sees a potential participant after a doctor's appointment, consent can be done at that time or at a later date (either in person or eConsent).

If a member of the study team and a potential participant talk on the phone, regardless of who called whom, the participant will have the option of completing eConsent or in-person consent. After explaining the details of the study, if the person is interested, we will send a pdf copy of the consent and make a future appointment (in-person or phone/videoconference) to conduct the consent.

2) Obtaining consent
a) Written consent
For people who are interested in participating, a member of the study team will meet with the potential participant in a private room. She or he will go through the consent form with the patient face-to-face to ensure comprehension. They will then be given the option to sign the consent form. Members of the study team including Dr. Kleckner (PI) will be available to answer any questions the potential participant may have about any aspect of the study prior to consenting and throughout the entire study period. The participants will also have access to the dietitians at UMMC if they have other diet-related questions. Potential participants will be allowed to take the consent form home to think about and discuss with family or friends; each potential participant will have sufficient time to consider participation.

b) eConsent
In lieu of the paper-based consent document, consent may occur using the IRB-approved eConsent document provided via REDCap. The study staff will screen for potential participants using the above screening procedures and initiate initial contact via the following methods: i) the treating oncologist or a member of the medical team (e.g., nurse practitioner) will introduce the study to the participant via a clinic appointment (in person or telehealth) and inquire if it would be okay for our study team to contact them, ii) with approval of the treating oncologist or a designee, a recruitment letter will be sent to the potential participant briefly describing the study and asking them to contact us if they would like more information, and iii) with approval of the treating oncologist or a designee, a message will be sent to the potential participant via MyPortfolio briefly describing the study and asking them to contact us if they would like more information. If a potential participant is interested, the study team will talk to the person on the phone and obtain verbal permission from the patient to send a copy of the eConsent via email stating, "Because UMB can't control the security of email once we send them, we need your permission to text or email you. Do you want to receive a copy of the consent document and a link to the eConsent via email?" (or something to that effect). Verbal permission from the patient will be documented. We will email the eConsent in the form of a pdf document and set up a phone call or video conference (participant's choice) to formally go over the consent document. In a separate email, we will provide a link to the eConsent document as well as instructions on how to access the eConsent—we will use verification with a passcode based on known information (e.g., the patient's home zip code). No personal health information will be sent via any emails. The eConsent documents may be viewed on computers, electronic tablets, or smartphones. The pdf copy of the eConsent and the REDCap eConsent will have identical information; it will be optional for the person to review the consent before the study team discusses it with them. After a member of the study team reviews the consent document with the participant over the phone or computer, they will have the opportunity to electronically sign the eConsent via REDCap. The person obtaining consent will initiate the eConsent process from within REDCap for their name and a timestamp to appear on the study participant's signed consent form. In order to authenticate that the person signing is that person, we will again use a passcode based on known information (e.g., the participant's year of birth). Once the eConsent form is signed and submitted, the patient will be able to receive a print out of the paper copy, download a pdf, and/or receive an email with a PDF attachment of the signed consent form.

3) The consent document
Consent is a process that occurs throughout the life of the study. We will ensure that participants are aware that consent is a voluntary process and that they can withdraw at any time. Because this study includes only one "phase," we will not ask participants to re-consent during the study unless there is a change to the study procedures or other pertinent information that would change a person's decision to participate in the study. The consent form will also contain information regarding HIPAA authorization.

For individuals who are eligible and who provide informed consent, the following information will be entered into a secure electronic database (e.g., password-protected Excel file on a password-protected computer). This information is needed in case contact is required after the study and/or the participant requires payment through the mail.
• Participant ID number (used to identify the participant on all study forms and notes)
• Name
• Participant phone number
• Participant home address
• Participant email address
• Medical Record number
• Date of informed consent
• Date of registration

3 * Confirm that the consent process will explain the following:

- The activities involve research.
- The procedures to be performed.
- That participation is voluntary.
- The name and contact information for the investigator.

(●) **Yes** ( ) No

4 * Describe who will obtain Informed Consent:
PI or study coordinator

5 * If obtaining consent from a legally authorized representative (LAR), describe how you will confirm that the individual is the LAR and can provide legally effective informed consent. *(Answer "N/A" if not obtaining consent from LARs)*
N/A

6 * Describe the setting for consent:
In-person consent will take place in a private consult or examination room at the UMGCCC, another private room, or a clinical room in the Department of Pain and Translational Symptom Science in the UM School of Nursing (across the street from the cancer center).

Remote consent will take place wherever the potential participant wishes. An appointment to conduct remote consenting will be set up before consenting takes place to ensure the participant is not caught off guard and in an undesirable location.

The consenting appointment can always be rescheduled upon if the setting is not conducive to effective information transfer.

7 * Describe the provisions for assessing participant understanding:
A member of the study team will go through the consent document in real time with the participant and the participant will be encouraged to ask questions throughout the whole consenting process.

8 * Describe the consideration for ongoing consent:
Consent is an ongoing process that occurs throughout the life of the study. Because this is a single-phase study that requires approximately 14 weeks of participation, we expect that written consent will only be provided by participants at the beginning of the study. However, we may need to re-consent should a change occur to a study procedure or if new knowledge arises that may change a person's decision to participate.

ID: VIEW4E1C661D0AC00
Name: v2_Informed Consent Process

HP-00099067 Electronic Consent_V2

Electronic Consent

1 You indicated that consent will be obtained electronically. Please confirm the following:

- Electronic consent document includes all elements of informed consent disclosure.
- The date of the electronic signature will be captured (N/A if waiver of documentation of consent is requested).
- Questions or methods to gauge subject comprehension of key study elements are clearly defined in the informed consent procedures.
- Electronic consent process includes age appropriate materials to facilitate comprehension.
- Electronic consent process is suitable to the study population or procedures are outlined to accommodate subject's needs.
- Electronic consent document/process allows subjects to proceed forward or backward or pause for review later.
- Measures are present to ensure that subjects have access to all of the consent related materials, including hyperlinks or other external documents.
- Plans are adequate to maintain external hyperlinks or documents and subject access to these documents throughout the lifespan of the study until completion are detailed in the informed consent procedures.
- The informed consent process outlines in detail how any included documents will be utilized.
- Measures are present to ensure that the identity of the signer and the integrity of the data can be verified when consent is not witnessed by the study team.
- For FDA-Regulated Clinical Trials including children as research subjects, if the parent or guardian initially documents the child's assent, procedures are in place to verify the child's identity and assent when the child initially presents to the investigator (N/A if the research is not an FDA-Regulated Clinical Trial).

* ● Yes ○ No

ID: VIEW8D7A331327BE44D
Name: v2_Electronic Consent

Consent and HIPAA Authorization Forms - Draft

1 Upload all of your Consent Forms for approval. Use only Microsoft Word.

Name	Created	Modified Date
2024.05.21-Consent-clean.docx(0.02)	2/2/2023 11:32 AM	5/21/2024 12:35 PM

IMPORTANT NOTE: the above list of consent forms (if any) are DRAFT versions. Under no circumstances should copies of these be distributed to patients/study subjects. If/when this research submission is approved by the IRB, approved consent forms will be available for download and use from the "Documents" tab of the Submission's workspace (click Exit and then look for the Documents tab - approved submissions only)

1A Archived Consent Forms:

Name	Created	Modified Date
Consent-tracked(0.03)	7/15/2022 1:41 PM	5/21/2024 12:35 PM
Consent(0.11)	2/22/2022 2:25 PM	2/2/2023 11:12 AM
Consent-clean(0.01)	6/15/2022 9:38 PM	6/15/2022 9:38 PM

2 Upload any HIPAA authorization forms here:
There are no items to display

Please refer to HRPO's website for specific instructions for preparing informed consent documents and to access current templates:
http://hrpo.umaryland.edu/researchers/consents.html

ID: VIEW4E1C7712D3000
Name: v2_Consent Forms - Draft

Organization Review Requirements (other than IRB)

Answer the following questions to determine additional organizational review requirements:

1 **Department/Division Review** - All research submissions are required to undergo department/division/institutional review prior to IRB review. The following entity is listed as the required department/division/institutional review:

SON Pain & Trans Symptom Sci

If this information is incorrect, please notify the HRPO office.

2 **RSC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Radiation Safety Committee may be required.

* 2.1 Does the research involve the use of ionizing radiation? ○ Yes ● **No**

2.2 Does the research involve the sampling of radioactive human materials for subsequent use or analysis in a laboratory?

3 **IBC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Institutional Biosafety Committee may be required.

* 3.1 Does the research involve human gene transfer? ○ Yes ● **No**
-OR-
Does the research specifically apply to human studies in which induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected? This type of research is often referred to as recombinant vaccine trials.

3.2 Does the research involve the exposure of human subjects to pathogenic microorganisms, or the exposure of research staff to human subjects or samples known or reasonably expected to carry infectious disease(s)?

3.3 Does the research involve the sampling of materials from persons with no known infectious disease and where the only risk to study staff is occupational exposure to bloodborne pathogens as defined by the OSHA Bloodborne Pathogen Standard?

4 **Cancer Center Criteria** - Answer the following to determine if review by the Cancer Center (Hematology-Oncology) may be required.

* Does the protocol involve in any way studies related to the prevention, treatment, diagnosis, or imaging of neoplastic diseases? ● **Yes** ○ No

5 **General Clinical Research Center Review Criteria** - the GCRC offers free and/or cost shared resources for patient-oriented research. Click Here for more information.

Answer the following to determine if review by the GCRC may be required.

* Will the General Clinical Research Center (GCRC) facility or resources be used to conduct this activity? ○ Yes ● **No**

6 **VA Review Criteria** - Answer the following questions to determine if review by the VAMHCS R&D Committee may be required.

* 6.1 - Will the research be conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments)? ○ Yes ● **No**

* 6.2 - Will the research utilize VA resources (e.g., equipment, funds, medical records, databases, tissues, etc.)? ○ Yes ● **No**

* 6.3 - Will the research be conducted on VA property, including space leased to and used by VA? ○ Yes ● **No**

PLEASE NOTE that the research may be funded by VA, by other sponsors, or may be unfunded.

ID: VIEW4E1AF91AB2400
Name: v2_Organization Review Requirements (other than IRB)

Summary of Required Reviews (other than IRB)

1 **Additional Committee Reviews** - Based on your responses to the previous questions, you have identified the following additional reviews. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's webpage.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

2 **Required Department and Specialty Reviews** - Based on the PI's organization (department, division, etc.) affiliation and answers to previous questions (use of Cancer Center, etc.), the organizations listed below are required to review this application. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	Review Status
SON Pain & Trans Symptom Sci	Complete
SOM Oncology Program	Complete

ID: VIEW4E1C8D9AE4000
Name: v2_Summary of Required Reviews (other than IRB)

HP-00099067 Additional Documents_V2

Additional Documents

1

Upload all additional documents here:

Name	Created	Modified Date
Study-packet_tracked(0.01)	8/10/2023 3:07 PM	8/10/2023 3:07 PM
Study-packet(0.05)	2/22/2022 2:16 PM	8/9/2023 12:38 PM
james-gcp.pdf(0.01)	6/5/2023 6:19 PM	6/5/2023 6:19 PM
oppermann-HIPAA125.png(0.01)	6/2/2023 7:56 PM	6/2/2023 7:56 PM
oppermann-HIPAA201.png(0.01)	6/2/2023 7:56 PM	6/2/2023 7:56 PM
oppermann-citi.pdf(0.01)	6/1/2023 5:23 PM	6/1/2023 5:23 PM
james-hipaa201-25MAY2023.pdf(0.01)	6/1/2023 5:23 PM	6/1/2023 5:23 PM
james-hipaa125-25MAY2023.pdf(0.01)	6/1/2023 5:23 PM	6/1/2023 5:23 PM
james-citi-08MAY2023.pdf(0.01)	6/1/2023 5:23 PM	6/1/2023 5:23 PM
CoI-Amber-Kleckner-SGD.docx(0.01)	4/20/2022 11:22 AM	4/20/2022 11:22 AM
Intervention-delivery-script.docx(0.01)	3/22/2022 5:23 PM	3/22/2022 5:23 PM
After-consenting-script.docx(0.01)	3/22/2022 5:23 PM	3/22/2022 5:23 PM
Device-mailing.pdf(0.01)	3/16/2022 1:50 PM	3/16/2022 1:50 PM
Engagement-script.docx(0.01)	3/11/2022 4:40 PM	3/11/2022 4:40 PM
DSM roster 4.24.2020.pdf(0.01)	3/11/2022 4:00 PM	3/11/2022 4:00 PM
schema-data-collection.pdf(0.01)	3/10/2022 10:06 AM	3/10/2022 10:06 AM
2203GCCC_CRC final approval_Mishra 1.26.22.pdf(0.01)	3/3/2022 11:10 AM	3/3/2022 11:10 AM
FREDA_Blog12_Hydration.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog11_Cancer.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog10_HealthyFastFood.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog9_Immunity_TRE.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog9_Immunity_CON.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog8_Spec_Occasions.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog7_MindfulEating.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog6_Stress.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog5_SleepPart2_TRE.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog5_SleepPart2_CON.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog4_SleepPart1.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog3_Exercise.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog2_Nutrition_TRE-draft.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog2_Nutrition_CON-draft.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM
FREDA_Blog1_HealthandWellness.pdf(0.01)	2/17/2022 2:35 PM	2/17/2022 2:35 PM

ID: VIEW4E0962513A000
Name: v2_Additional Documents

Final Page of Application

You have reached the final page of this application. It is recommended that you click on the "Hide/Show Errors" link on the upper or lower breadcrumb row of this page. The "Hide/Show Errors" will do a search of your application, and highlight areas that are required or need to be completed prior to submitting.

By submitting this application, you are electronically routing the protocol for departmental scientific review and all other necessary reviews. According to information you have provided, this application will be routed to the following Departments for review prior to being forwarded to the IRB for review. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	**Review Status**
SON Pain & Trans Symptom Sci	Complete
SOM Oncology Program	Complete

Required Safety Committee Reviews - In addition to the IRB, the following committees must review this submission. Each additional committee has a separate online form that the study team will be required to fill out. All committee applications (IRB plus those listed here) must be completed properly before the 'package' of applications can be submitted. The team may complete these additional forms in any order or at any time prior to submission of the IRB Application. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's Workspace.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

You may check the progress of your application at any time by returning to the Workspace of this submission. A detailed history, including notes, dates, and times of events, is provided to you for this purpose.

If a reviewer returns the application to you, you must address their concerns and resubmit the protocol for review to all designated departments. After all departments have reviewed the application, it will automatically be sent to the IRB for review. Changes made to the submission after its approval must be submitted as modifications.

Investigator Attestation
By submitting this application, I, the Principal Investigator (PI), certify that the information provided in this application is complete and correct. Research will be conducted according to the submission as described, only by the approved principal investigator and study team members.

In addition, I agree to the responsibilities of a PI, including:

- Obtaining informed consent (if applicable) from all subjects as outlined in the submission.
- Reporting new information to the IRB per the requirements of the Investigator Manual.
- If Required, obtaining renewal of the protocol prior to the expiration of the approval period or halt all study activities upon study expiration.
- Accepting ultimate responsibility for the protection of the rights and welfare of human subjects, conduct of the study and the ethical performance of the project.
- Ensuring performance of all research activities by qualified personnel according to the IRB approved submission.
- Ensuring that research personnel have or will receive appropriate training.
- Ensuring no changes will be made in the research until approved by the IRB (except when necessary to eliminate apparent immediate hazards to subjects).

Click the "Finish" button and then click "Submit Application" in the submission Workspace.

ID: VIEW4E1B10C500000
Name: v2_Final Page of Application

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Shari Youngblood

2 Research Role:
Study Coordinator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
clinical dietitian and research coordination for >1 year

Add a Team Member

1 * Select Team Member:
IKMAT ADESANYA

2 Research Role:
Study Coordinator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
nurse and PhD student

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Ahleah Gavin

2 Research Role:
Study Coordinator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
experienced study coordinator

Add a Team Member

1 * Select Team Member:
Shijun Zhu

2 Research Role:
Statistician

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Experienced statistician

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Alice Ryan

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
experienced behavioral interventionist in the cancer population, experience recruiting from UMGCCC

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Ashkan Emadi

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
oncologist

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Alexie Oppermann

2 Research Role:
Other

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
summer intern

HP-00099067 IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Javier Rosales

2 Research Role:
Study Coordinator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
● **Yes** ○ No

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
full-time study coordinator

UNIVERSITY of MARYLAND BALTIMORE

RESEARCH CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:
Time-restricted eating to address persistent cancer-related fatigue

Study Number: HP 00099067

Principal Investigator: Amber Kleckner, PhD, 410-706-5961

This Consent document describes a research study, what you may expect if you decide to take part, and important information to help you make your decision. Please read this form carefully and ask questions before you agree to participate.

CONCISE SUMMARY:
Most patients experience tiredness during cancer treatment, referred to as "cancer-related fatigue." For many people, their tiredness does not go away after treatment. Doctors and scientists do not fully understand why the fatigue occurs, and we do not have good ways to treat it. There are new data suggesting that fatigue could arise from a person's body clock (i.e., circadian rhythm) being out of alignment. However, this has not been proven. In this study, we will collect data on daily activities that are related to circadian rhythm—sleep patterns, physical activity, and diet—to get more information on the relationships between circadian rhythm and fatigue.

The study lasts approximately 14 weeks. At the beginning of the study, you will be asked to complete online questionnaires related to your symptoms and feelings. For one week, we will ask you to log your diet and sleep using a smartphone app called myCircadianClock. For the same week, we will ask you to wear an actigraph on your wrist (like a watch or Fitbit) as well as a continuous glucose monitor on the back of your upper arm. After the first week, you will be randomly assigned to one of two groups: one group will be asked to eat all their food within a 10-hour window during the day for 12 weeks (you pick the start time, for example 9am-6pm); the other group will be asked to follow their normal eating schedule. At the middle (week 6) and end (week 12) of the study, we will ask you again to complete the same study activities as at the beginning (questionnaires, log diet and sleep, wear the actigraph and continuous glucose monitor). Study materials may be provided in-person or via mail—your choice (i.e., you do not have to come in). You will be paid a total of $75 for your time to complete the study activities.

Key risks: discomfort from the actigraph or glucose monitor; emotional distress; breach of confidentiality; weight loss, gastrointestinal upset, or hunger, from time-restricted eating

Participating in this research study is voluntary. Your decision to participate will not affect your healthcare or treatment for your cancer in any way.

PURPOSE OF STUDY

In this study, we want to get more information on the relationships between lifestyle behaviors—sleep patterns, physical activity, and diet—and fatigue. We would also like to get feedback on the use of a smartphone application ("app"), *myCircadianClock*, to log sleep, exercise, and diet in early survivorship. "Time-restricted eating" is when you eat all your food in a well-defined window during the day. We will test whether time-restricted eating (a 10-hour eating window), as compared to a longer eating window, helps to reset your body clock and/or reduce fatigue.

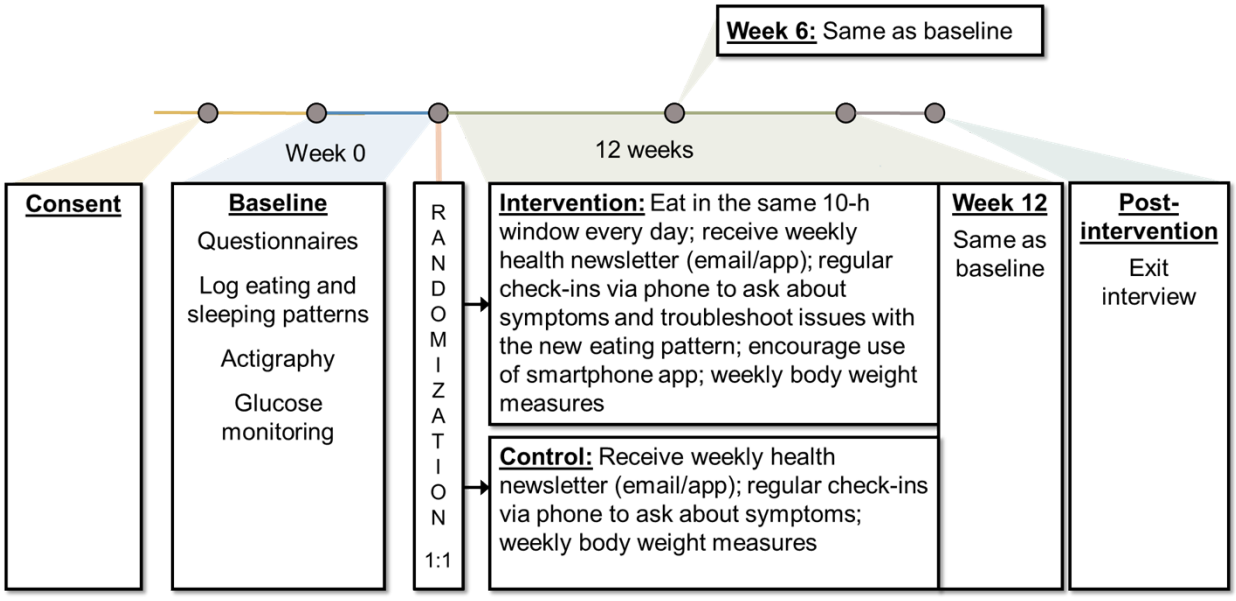
Approximately 30 participants will be recruited to take part in this study from the University of Maryland Medical System.

DISCLOSURE

The Principal Investigator's spouse, Dr. Ian Kleckner, is a member of the study team.

PROCEDURES

Here are the study activities and timeline. Each of the activities is described in more detail below.



Questionnaires: We will ask you to complete 9 online questionnaires that ask about your symptoms, feelings, and habits. These will take approximately 30-60 minutes to complete. You also have the choice to complete these on paper. We will ask you to complete questionnaires three times throughout the study—at weeks 0, 6, and 12.

Logging eating and sleeping patterns: We will ask you to log everything you eat using the myCircadianClock app every day at week 0, week 6, and week 12. In addition, we will ask you to log when you go to bed and when you get up using the app. Logging eating and sleeping patterns is optional weeks 1-5 and 7-11. This activity will take approximately 5 minutes per day.

Actigraphy: We will ask you to wear an actigraph on your wrist every day for weeks 0, 6, and 12. The actigraph monitors physical activity.

Glucose monitoring: We will ask you to wear a continuous glucose monitor every day at weeks 0, 6, and 12. This is measuring *interstitial glucose*, which is the concentration of sugar in between your cells and is highly correlated with blood sugar. The continuous glucose monitor is the size of two quarters stacked on top of one another. It is placed on the back of your upper arm. It has a thin, 5-mm-long wire that inserts under the skin and is water-resistant so that it does not bother you. It is applied once at the beginning of the week and you can keep it on for up to 14 days, but we only ask you to wear it for 7 days. We can apply it on-site at the Medical Center, or we can mail it to you to apply yourself. We will instruct you on how to apply the monitor, and we will be available if you have questions when you apply the device to yourself. It feels like a small pinch when you initially put it on.

Body weight: We will provide you with a digital bathroom scale to use at home. Please weigh yourself once per week and enter your weight via the myCircadianClock app.

Randomization and the two study groups: After the first week, you will be randomly assigned to one of two groups: the time-restricted eating group or the control group. No one on the study team knows what group you will be in until after week 0. The group you will be in is chosen by chance, like flipping a coin. There is a 50% chance you will be in the time-restricted eating group and 50% chance you will be in the control group.

- Time-restricted eating group: If you are assigned to the time-restricted eating group, you will pick a 10-hour window to eat based on your schedule and preferences. For example, this window could start at 7:00am, 9:15am, or another time. Water will be allowed any time. Unsweetened tea and black coffee are allowed in the morning before your eating window. ***All other food and beverages including artificial sweeteners (e.g., chewing gum, diet soda) will be allowed only within the 10-hour eating window.*** Within the 10-hour window, you can eat whatever you want at whatever time.
- Control group: If you are assigned to the control group, you will be asked to make no changes to your diet pattern.

Contact with the study team: We will call you about every two weeks to check in and see how you are doing. You may also call and email the study team in between these check-ins.

myCircadianClock app: In addition to using the app to log eating patterns, sleeping patterns, and body weight, everyone in the study will receive weekly tips on healthy lifestyles through the app.

Exit interview: At the completion of the study, or if you decide to withdraw early, we will "interview" you about your experience in the study. We will ask you what you liked about it, what you didn't like about it, and ask for feedback on the myCircadianClock app. If you were in the time-restricted eating group, we will ask you about your experiences with the new diet pattern. This interview will take 15-30 minutes and we will record the audio of the conversation (not video) if that is okay with you.

All of these research activities can be done remotely. However, you are welcome to come in and we will help you put on the glucose monitor, use the myCircadianClock app, complete questionnaires,

and/or complete the other study activities. We are located in the School of Nursing, across the street from Greenebaum Comprehensive Cancer Center.

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?

If you take part in this research, you will be responsible for participating in the study activities, as outlined above.

POTENTIAL RISKS/DISCOMFORTS:

As with all research studies, there are risks associated with the study activities. We have taken measures to minimize all anticipated risks. Please consider these risks while deciding if you want to participate.

1. *Discomfort from the continuous glucose monitor*
   The continuous glucose monitor is a minimally invasive device that senses sugar just under your skin. It is applied to the back of your upper arm and feels like a pinch when the small, 5-mm-long sensor is inserted. It can also cause pain if the device gets hit while you are wearing it. We selected to use this device rather than obtaining blood glucose measurements because it avoids painful finger pricks.

2. *Emotional distress*
   You could become upset or overwhelmed by the expectation to consume food only in the eating window. However, we want to emphasize that you are not "in trouble" if you do not follow the procedures exactly. We want to use what we learn from this study to improve the procedures for the next study.

   Our questionnaires contain information that might be distressing or private (e.g., "I am satisfied with family communication about my illness"). You do not have to answer any questions you are not comfortable answering, and you can take a break or stop answering the questionnaires at any time.

3. *Breach of confidentiality*
   There is always a risk of a breach of confidentiality in which sensitive medical information could become known to people outside the research team. To avoid leakage of sensitive information, only Dr. Kleckner (the study chair), Dr. Shari Youngblood (study coordinator), and any individual designees will have access to the screening log and the file that links your name with your subject number (both will be encrypted); these files will be stored on password-protected computers in their private offices. All data files will reference you by a non-identifiable Participant ID and will be stored on Dr. Kleckner's computer and secure servers at UMB. All consent forms will be stored in a locked cabinet also in her or her staff's office. All audio-recorded interviews will be transferred to Dr. Kleckner's secure computer and server at UMB within 2 business days of the interview and then immediately deleted from the recorder. All interview file names will not include your name or any identifying information. If Dr. Kleckner shares data with any other researcher for analyses, all data will be de-identified (i.e., <u>will not</u> have your name, birthdate, contact information, etc.). Presentation of study findings in the form of presentations and manuscripts, either in private or public settings, will not have any identifiable information, nor will any audio clips ever be played in public. Dr. Kleckner and all other co-investigators participate in ethical training in accordance with institutional policies.

4. *Weight loss due to time-restricted eating*
   This is not a weight loss study. Some studies have documented weight loss upon adoption of time-restricted eating despite not "cutting calories" on purpose. We encourage you to eat and drink to satisfy hunger and thirst. However, because those in the time-restricted eating group will be changing their eating patterns, there is a chance that you could lose weight during the study. Slow weight loss will not be considered dangerous (less than 3% of body weight per week), especially if you are beginning the study overweight. However, if you experience rapid, unintentional weight loss, as determined by a medical provider, your medical provider will advise you on what to do, which may involve withdrawing from the study.

5. *Gastrointestinal upset*
   With a change in diet, and especially a large change in diet, you could experience constipation, diarrhea, nausea, heartburn, etc. These effects usually go away after several days, but you will always have access to the study team to discuss how to relieve these effects.

6. *Hunger and/or hypoglycemia*
   Those in the time-restricted eating group will be eating their food in a shorter window than normal. If you are assigned to this group, you might get hungry while you are outside your eating window. With hunger can come fatigue, lack of concentration, irritability, headache, and other symptoms. These symptoms will likely go away after a few days, when your body adapts to the new pattern. However, moderate to severe symptoms can be a sign of hypoglycemia (low blood sugar) and we encourage you to eat outside the window if you are feeling sluggish, dizzy, or sick.

POTENTIAL BENEFITS
You might or might not benefit from being in this research study. You may become more aware of your diet and sleep patterns, which can contribute to overall health.

ALTERNATIVES TO PARTICIPATION
This is not a treatment study and the alternative is to not participate. Instead of participating, you may choose to log your diet and sleep patterns on your own, and/or see a clinician (e.g., dietitian, primary care physician) to explore how your diet, physical activity, and sleep patterns may be contributing to your fatigue.

COSTS TO PARTICIPANTS
There will be no fee to enroll in the study. However, you or your insurance will be billed for costs of medical care that you would have needed or received if you were not in the study.

PAYMENT TO PARTICIPANTS
You will be compensated for your time to complete the study activities. We will pay you a total of $75 to complete all study activities—$25 after week 0, $25 after week 6, and $25 after week 12. These payments

will be made in electronic gift cards (or physical gift cards if you prefer). You will be provided a parking voucher if you decide to come to campus specifically to meet about the study.

CONFIDENTIALITY AND ACCESS TO RECORDS

Using your medical record number, we will access your electronic medical record so that we can get information regarding your cancer diagnosis, cancer treatment history, medical history, and social history. We will collect your name, address, phone number, and email address in order to contact you for scheduling and reminders of upcoming study activities. Only Dr. Amber Kleckner, the principal investigator, and her trained and designated research personnel will have access to confidential information. All confidential information that includes personally identifiable information will be coded with a study ID number. The principal investigator and study coordinator(s) will be the only individuals with access to the key of the assigned ID numbers. All confidential information will be locked in a cabinet in a secured location at the University of Maryland, School of Nursing. Your personally identifiable information will not be used for this study's analyses, but it will be kept on file if federal agencies or the Institutional Review Board (IRB) are mandated to review any information.

All study records will be considered confidential, and all participants' names and personally identifiable information will not be used in reports or publications. Efforts will be made to limit access to your personal information, including research study records, to people involved with the study who have a need to review this information. We cannot promise complete secrecy. Entities that may inspect and copy your information include the IRB and other representatives of this organization. Those designated from the University of Maryland will be allowed to examine certain research records of this study; however, anyone inspecting this information is required to keep this personal information confidential. Your personal information will not be released unless mandated by law. By signing this document you are authorizing this access to the monitors, auditors, and the IRB.

The data from the study may be published. However, you will not be identified. People designated from University of Maryland and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

A description of this clinical trial is available on http://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.

We are using myCircadianClock app to collect data regarding your food intake, sleep patterns, and body weight. The myCircadianClock app was developed by researchers at The Salk Institute in La Jolla, California, and has been used in other research studies. There is detailed information regarding the app at end of this form. **We will not share any personal information (e.g., name) or medical information (e.g., details of your cancer diagnosis) with the myCircadianClock team, though they will have access to any information that you input into the app.** By consenting to this study, you are consenting to have your de-identified app data stored with the Salk Institute and combined with other myCircadianClock data in future analyses. At the end of this study, you may request to have your data removed from their database.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator, Dr. Amber Kleckner, at 410-706-5961. To discontinue your participation in the study, a written withdrawal is requested, sent to Dr. Amber Kleckner at amber.kleckner@umaryland.edu.

If you withdraw from this study, already collected data will not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, these data will be handled the same as research data.

You will be told of any significant new findings that develop during the study that may affect your willingness to continue participation.

CAN I BE REMOVED FROM THE RESEARCH?

You may be withdrawn from the study if your health becomes worse or if your doctor feels that staying in the study is harmful to your health. The study team also holds the discretion to withdraw you from the study if your participation becomes harmful to a study team member.

The sponsor can also end the research study early. The study chair will tell you about this and you will have the chance to ask questions if this were to happen.

STUDY-RELATED INJURY

If you have an injury, promptly seek medical care from any healthcare provider. If you have an emergency, call 911 or go to the nearest emergency room. You should tell the healthcare provider that you have participated in a research study.

If you believe the injury is related to the study, notify the study doctor. UMB, if requested, will assist you to get medical care or referrals.

The sponsor should not require the healthcare provider to submit claims to your health insurance, government programs like Medicare and Medicaid, or any other person or entity for costs to treat a study-related injury prior to submitting an invoice to the sponsor.

The sponsor should not require a healthcare provider to bill you or your insurance first, and then reimburse you or your insurance for costs to treat a study-related injury.

The sponsor should pay the treating healthcare provider directly.

UMB and/or its affiliated healthcare facilities or healthcare providers will not provide any financial compensation or reimbursement to you for the cost of medical care or other expenses arising from an injury.

In such cases, you or your insurance may be billed for the costs of medical care.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research studies all rights due to them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in this study. This study has been reviewed and approved by an Institutional Review Board (IRB). The IRB is a group of scientists, physicians, experts, and community representatives. The IRB's membership includes persons who are not affiliated with UMB and persons who do not conduct research studies.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland, Baltimore
Institutional Review Board
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

The myCircadianClock application

As part of this study, you will use the myCircadianClock app to log some data and you may receive information and surveys through the app. The myCircadianClock app uses encrypted methods to transmit data between the app and the database, where the data are stored. The use of the app for research studies has been reviewed and approved by the Institutional Review Board of the Salk Institute. By consenting to this study, you are also consenting to use myCircadianClock app and also allowing the Salk research team to share data from the myCircadianClock app with our team.

- **myCircadianClock smartphone application ("app")**
  - The myCircadianClock app was created by and is managed by Dr. Satchidananda Panda's laboratory at the Salk Institute for Biological Studies. It is HIPAA-compliant and double-encrypted. Consenting to use and using the myCircadianClock app is necessary and critical for participation in the study.
- **Activities**
  - The myCircadianClock app may ask you to enter data about your lifestyle, including but not limited to: survey questions about your health behaviors, your body weight, what you eat or drink, exercise, and your sleep as best as you can.
  - The app sends occasional reminders to complete study activities.
  - Educational material may be sent through the app.
- **Sensor and health data**
  - This study can gather sensor data from your phone if you allow it to upon installation.
  - The myCircadianClock app may use the built-in accelerometer in certain phones to passively keep track of physical activity (passive because this happens automatically and you do not need to enter any information). The app interprets accelerometer data as steps taken, or as different intensity levels of activity. The app can also detect when you use the phone to get an independent estimate of your rest or sleep period. You can also sync the app to Apple Health Kit or Google Fit to capture activity, heart rate, and body temperature data.
  - For these activity measures to be accurate, you should carry the smartphone on your person as much as possible (e.g., in your pocket, or clipped to your waist). For instance, if the phone is left on a desk or in your car when you go for a walk, it will not be able to detect your walking.
  - The app will also use the built in GPS sensor to tag the location only when you log your data. This will help you to track what and where you eat, which may help you adjust your diet. It helps the research to account for any unusual change in your eating or sleeping pattern due to a change in time zone when you travel. Change in time zones or moving to a different latitude within the same time zone can change the local sunrise and sunset time or local day-length, which can affect your circadian clock for a few days.
  - <u>The use of the myCircadianClock app is not intended to evaluate your health and is not a diagnostic test. If you are concerned about any aspect of your health, you should consult with your physician.</u>
- **Data gathering**
  - Our daily pattern of activity, sleep, and eating changes with season, latitude, work schedule, and travel. Collected data may reveal how daily behaviors affect your quality of life and health, and the data will advance clinical research into circadian rhythms.
  - The myCircadianClock app helps you keep track of health behaviors such as diet, activity, sleep and taking your medications or supplements.
  - Data that you share through the app as part of the research study will create an unprecedented large-scale database of daily behaviors and health provided by people just like you.

- Studying this real-world data will help researchers understand how daily behaviors influence health in real life, with a resolution never achieved before. (Traditionally, these studies are done by asking people to recall answers to very long questionnaires on paper).
- At the same time, the myCircadianClock app analyzes your data to provide personalized insights into how your daily eating, sleeping and activity patterns relate to your overall health, and can help you maintain a healthy lifestyle. Because the feedback is determined from multiple days of your routine behavior, some of these insights will be accessible in your phone after a few days of data collection.
- To improve data collection, the app may send you a reminder and push notifications. If you do not want to be bothered with these reminders, you can turn this option off.
- By combining a personal app and a research study, myCircadianClock will help explore how the smartphone may be used with new kinds of clinical research in the future.

- **Privacy**
  - The following personal health information will be collected from you by the app: country, language, photos or names of food/beverages you take, activity/exercise, sleep, and health entries, timestamp of entries, and geographic location data from entries.
  - We take several steps to protect your privacy and the privacy of your app data.
  - Whenever app data is transferred to a research study computer, it will be encrypted so that others cannot interpret the data or associate it back to you.
  - Encrypted app data (stripped of personal identifiers, and associated only with a random code) will be sent to secure data servers used for the myCircadianClock research study.
  - Your encrypted data will be sent to a secure database where it will be stored with a unique identifier. The identifier does not contain any personal information. You will also receive your encrypted data back from the server for visualization on your phone.
  - App-generated data is associated only with a random participant code, and this code is used in all future analyses separating it from any personally identifiable information.
  - Study investigators chose Amazon Web Services for this important responsibility because they are a world leader in the secure storage and protection of sensitive data. They have a proven track record of safeguarding and managing potentially sensitive biomedical data in accordance with regulations that govern human research and medical information (e.g., regulations mandated by Institutional Review Boards [IRB] and the Health Information Portability and Accountability Act [HIPAA]).
  - We will de-identify your data and use secure computers, but we cannot ensure complete privacy.
  - One potential loss of privacy would be if someone sees your data from myCircadianClock on your smartphone. For security, myCircadianClock suggests that your smartphone be protected either by a passcode or fingerprint sensor. This ensures that only you can enter and use the app.
  - These steps ensure that researchers analyzing the coded study data will not be able to connect it to any individual user.
- **Utilizing data**
  - The terms “study investigators” and “researchers” in this section refer to the research team who is conducting this study and the research team at the Salk Institute who oversee the use of the app.
  - Study investigators will analyze coded (no personal identifiers) app data from everyone who agrees to participate in myCircadianClock studies. Neither the data used for analysis nor the results will be able to be connected back to any individual user.

- The results of this research may be published in a scientific or medical research journal so that others can learn from this study. Results will never be published in a way that would allow data to be associated with individual users.
- Your coded data will be used for research and may be shared with other researchers.
- After this study is completed, other researchers may request access to the coded study data (already stripped of personal identifiers), so that it can be analyzed in a new way to benefit medical research. Those requesting data must agree to use the data for research responsibly and in accordance with applicable regulations; these data requests will be reviewed by a group of study investigators. Amazon Web Services will have no oversight over future research conducted with coded study data.
- Other researchers who are granted access to coded study data will not be able to connect the data back to you.
- Study data will never be sold to any third party.

- **Issues to consider**
  - Logging food and sleep through the app for the study will take 5-10 minutes per day on average. Entering information and responding to surveys should take on average 2-3 minutes each day. Occasionally, tasks may take a few minutes longer (e.g., a longer questionnaire).
  - Participation in this study does not require you to change anything related to your smartphone account or data plan. However, your phone must have data or Wi-Fi capability and must connect to internet in order to transmit data to our servers. The app can use either an existing mobile data plan or Wi-Fi connections: you may configure the app to use only Wi-Fi connections if you wish to limit impact on your data usage. The study team or the Salk Institute bears no responsibility for bills related to your phone or data usage for participating in this study.
- **Safety and legality**
  - As with any smartphone app, follow prevailing laws about when and where you use your smartphone. Similarly, follow local and federal regulations about the usage of a smartphone in specific areas.
  - Additionally, the app should not be used in any capacity to perform or document illegal activity.
  - The Salk Institute for Biological Studies, Dr. Satchidananda Panda and all members of his research team, including collaborators, are not liable for:
    - any illegal activity that is performed, captured, or stored by the myCircadianClock app.
    - any harm that may come from using the myCircadianClock app.
- **Study surveys**
  - For dietary information, myCircadianClock will prompt you to take pictures of every food, beverage, water, medication, and supplement(s) you take.
  - When picture taking is difficult or socially awkward as in a meeting, if you forgot to take picture or you are repeatedly eating the same item, you can also enter the information textually from a different screen.
  - In general, more data entered into the app results in more accurate and informative personalized insights.
- **Study tasks**
  - To gather additional information, including but not limited to activity (step counts/distance), heart rate, height and weight, you can sync other smartphone apps and sensory devices (such as Apple Health Kit and Google Fit) with myCircadianClock. You also have the choice to allow the myCircadianClock app to access your location in order to determine the local time. You can allow

or deny these features when you first install the myCircadianClock app, and are able to change these settings at any time.

- myCircadianClock has the option to add some information that requires a brief task away from the smartphone, such as: your weight, your height, your waist circumference, and your blood pressure. The app also has optional fields to enter relevant results from blood tests and urine samples including: blood glucose, lipid panels (total cholesterol, LDL, HDL, triglycerides), hemoglobin A1c, fibrinogen, C-reactive protein, homocysteine, and ketone bodies if you wish to monitor these parameters. Entering these data is optional.
- All data entered is used solely for tracking purposes, not diagnosis. The Salk Institute for Biological Studies, Dr. Satchidananda Panda, and his lab are not responsible for providing medical advice and are not liable for your medical care. You should contact a medical professional for medical advice.
- The myCircadianClock app may provide personalized feedback in the form of graphs and text to display your progress, and provide insights into your health behaviors.
- The app may summarize data about how food, sleep, or activity patterns in a specific time of the day are associated with your health and wellbeing. These insights may help you understand your health behaviors better, and help you manage your health. Viewing the graphs and text is optional but may be useful or interesting to you.
- For the passive sensing of your physical activity in some phone models to be accurate, it is important to carry your smartphone on your person (e.g., in your pocket, or clipped to your waist). Carrying your phone will also help you log food, beverage, water and activity data as soon as these events occur.
- In your Profile within myCircadianClock, you can set reminders for yourself to complete app activities. In general, more data entered in the app results in more accurate and informative insights.

- **Meals, activity, and sleep:** The smartphone application myCircadianClock will serve as an electronic food, activity, and sleep diary.
  - On the server side, a sub-study dashboard will be created for this specific project. Clinical coordinators from Dr. Amber Kleckner's research team will have password-protected access to the study data. In the study summary dashboard, your study code and the date of activation of the app will be shown along with your daily log. If you fail to log any food data for more than 1 day, the dashboard flags you and sends an alert to the coordinator. The coordinators will login to the dashboard at least twice weekly to monitor food intake data, and follow up with you as necessary.
  - If you are randomized to the time-restricted eating arm, you will self-select an interval of 10 hours per day within which to consume your food. You can easily track your progress of the daily eating pattern with the time-stamping feature of the app that offers a visual summary.
  - If you have any difficulty logging data, or have questions about any of the features of the app, you will be able to contact the study coordinator through the feedback feature of the app. The questions will be delivered to a HIPAA-compliant email server specifically set up for this study.

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____
Participant's Signature

Date:_____

_____
Investigator or Designee Obtaining Consent Signature

Date:_____

Health Insurance Portability and Accountability Act (HIPAA)
AUTHORIZATION TO OBTAIN, USE AND DISCLOSE
PROTECTED HEALTH INFORMATION FOR RESEARCH

Name of Study Participant:_____

Date of Birth: _____ **Medical Record Number:** _____

Name of this Research Study: *Time-restricted eating to address persistent cancer-related fatigue: A randomized controlled pilot trial among cancer survivors*

UMB IRB Approval Number: *HP 00099067*

Researcher's Name: *Amber Kleckner, PhD*

Researcher's Contact Information:
Department of Pain and Translational Symptom Science
University of Maryland School of Nursing
655 W. Lombard St.
Baltimore, MD 21201
410-706-5961

This research study will use health information that identifies you. If you agree to participate, this researcher will use just the health information listed below.

The Specific Health Information To Be Used or Shared:

- Demographics (e.g., height, weight, age, race, ethnicity, education, marital status)
- Details regarding cancer diagnosis and treatment (e.g., cancer site, cancer stage, chemotherapy type and dosing, surgical procedures, hormone therapy)
- Clinical characteristics (e.g., current menopausal status, Karnofsky Performance Status)
- Most recent blood work (e.g., hemoglobin, hematocrit, lymphocytes, etc.),
- Medical history (e.g., prior myocardial infarction, diabetes status).

Federal laws require this researcher to protect the privacy of this health information. She will share it only with the people and groups described here.

People and Organizations Who Will Use or Share This Information:

- Dr. Amber Kleckner and her research team.
- The sponsor of the study, or its agents, such as data repositories or contract research organizations
- Organization that will coordinate health care billing or compliance such as offices within University of Maryland School of Nursing; the University of Maryland, Baltimore (UMB); University Physicians, Inc. (UPI) and the faculty practices of the UMB; and the University of Maryland Medical System (UMMS).

This Authorization will not expire, but you can revoke it at any time.
To revoke this Authorization, send a letter or email to this researcher stating your decision. She will stop collecting health information about you, and she will not allow you to continue in this study. She can use or share health information already gathered.

Additional Information:

- You can refuse to sign this form. If you do not sign it, you cannot participate in this study. This will not affect the care you/your child receive at:
    - University Physicians, Inc. (UPI)
    - University of Maryland Medical System (UMMS)

  It will not cause any loss of benefits to which you/your child are otherwise entitled.
- Sometimes, government agencies such as the Food and Drug Administration or the Department of Social Services request copies of health information. The law may require this researcher, the University of Maryland School of Nursing, UPI, or UMMS to give it to them.
- This researcher will take reasonable steps to protect your health information. However, federal protection laws may not apply to people or groups outside the University of Maryland School of Nursing, UMB, UPI, or UMMS .
- Except for certain special cases, you have the right to a copy of your health information created during this research study. You may have to wait until the study ends. Ask this researcher how to get a copy of this information from her.

My signature indicates that I authorize the use and sharing of my protected health information for the purposes described above. I also permit my doctors and other health care providers to share my protected health information with this researcher for the purposes described above.

Signature: _____Date: _____

Name (printed) _____

Privacy Questions? Call the UMSOM Privacy Official (410-706-0337) with questions about your rights and protections under privacy rules.

Other Questions? Call the researcher named on this form with any other questions.