AWARD NUMBER: W81XWH-19-1-0558

TITLE: Using Early Time-Restricted Feeding and Timed Light Therapy to Improve Glycemic Control in Adults with Type 2 Diabetes

PRINCIPAL INVESTIGATOR: Courtney M. Peterson, Ph.D.

CONTRACTING ORGANIZATION: University of Alabama, Birmingham, AL

REPORT DATE: October 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2022	Annual	01Sep2021 – 31Aug2022

4. TITLE AND SUBTITLE

Using Early Time-Restricted Feeding and Timed Light Therapy to Improve Glycemic Control in Adults with Type 2 Diabetes

5a. CONTRACT NUMBER
W81XWH-19-1-0558

5b. GRANT NUMBER
GRANT12715627

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Courtney Peterson, Ph.D.; Lynn Dill, Lynn B. S. N., R.N.

E-Mail: cpeterso@uab.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Alabama at Birmingham
UAB
701 S 20TH ST
BIRMINGHAM, AL 35294-0001

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

In this clinical trial, we will test whether two circadian-based therapies--a form of meal timing called early time-restricted eating (eTRE) and timed light therapy--can improve blood sugar control in adults with type 2 diabetes. Approximately 344 adults with type 2 diabetes will be randomized to the following 2 x 2 study design: (1) control group, (2) eTRF, (3) timed light therapy, and (4) eTRF and timed light therapy. Participants will follow their assigned lifestyle intervention for 16 weeks and be followed for a total of one year. In addition, we will determine whether the two circadian therapies can improve circadian rhythms, sleep quality, weight loss, cardiovascular health, quality of life, and psychological health. We are currently enrolling participants and collecting data. The delivery of the intervention is going well, and adherence is high. We experimented with several different approaches to recruitment and advertising. In the past three months, we experienced a major improvement in recruitment, and we are now confident that we can recruit participants at our target rate.

15. SUBJECT TERMS
Early Time-Restricted Feeding, Bright Light Therapy, Circadian Rhythms, Intermittent Fasting

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	17	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

- **INTRODUCTION**

  This clinical trial will investigate whether two circadian-based therapies can improve blood sugar control, reduce diabetes complications, explain some of the heterogeneity of type 2 diabetes, and improve several other aspects of health. In this clinical trial, we will test for the first time whether a form of meal timing called early time-restricted feeding (eTRF) and/or timed light therapy can improve blood sugar control in adults with type 2 diabetes. Approximately 344 adults with type 2 diabetes will be randomized to the following 2 x 2 study design: (1) control group, (2) eTRF, (3) timed light therapy, and (4) eTRF and timed light therapy. Participants will follow their assigned lifestyle intervention for 16 weeks and be followed for a total of one year. In addition, we will determine whether the two circadian therapies can improve circadian rhythms, sleep quality, weight loss, cardiovascular health, quality of life, and psychological health. We will also determine which patients benefit the most from these therapies.

- **KEYWORDS**

  Type 2 Diabetes, Early Time-Restricted Eating, Bright Light Therapy, Circadian Rhythms, Chronobiology, Intermittent Fasting, Veterans

- **ACCOMPLISHMENTS:**

  - **What were the major goals of the project?**

TASKS	MONTHS	PROGRESS
TASK 1: SET-UP CLINICAL TRIAL		
Advertise, interview, and hire a research coordinator with prior experience in managing clinical trials at UAB	*2 months prior to start date*	*Complete*
Refine the protocol and informed consent	1-2	Complete
Develop recruiting materials and screening forms, and refine the screening process	1-3	Complete
Set-up recruiting processes at the Birmingham VA Medical Center and UAB Hospital	1-4	Complete
Order supplies and equipment	1-4	Complete
Review the recent literature on bright light exposure protocols, finalize the bright light exposure protocol, and write a review article	1-4	Complete
Develop procedure manuals for the lifestyle interventions and for behavioral counseling	2-3	Complete
Set-up a material transfer agreement with Brigham and Women's Hospital (BWH) to analyze sleep data (Aim 3)	2-3	Complete
Finalize the study protocol and informed consent	2-3	Complete
Set-up the study database and questionnaires in REDCap	2-4	Complete
Develop procedure manuals for all study procedures	2-4	Complete
Train nursing staff in the operation of PSG equipment	2-4	Complete
Set-up the rooms for inpatient testing	2-5	Complete
Develop data collection forms for nurses to use during the 38-hour inpatient testing	3-5	Complete
Train behavioral counselor	4-5	Complete
Train nurses to perform 38-hour inpatient tests and study procedures	4-5	Complete
Rehearse screening process and procedures	5	Complete
Milestone achieved: IRB & HRPO approval	5	Complete
Milestone achieved: All project-related staff trained	5	Complete

Milestone achieved: Study is set-up and ready to recruit participants	5	Complete
Milestone achieved: Submit review article on recent bright light therapy protocols and their effects on the circadian system and cardiometabolic health	5	Mostly drafted. Revised target is December 2022.
TASK 2: CONDUCT CLINICAL TRIAL		
Recruit, consent, screen, and enroll potential participants	6-38	Ongoing
Milestone achieved: First participant enrolled	6	Complete
Participants follow their assigned intervention for 16 weeks	6-42	Ongoing
Perform behavioral counseling every 2 weeks	6-42	Ongoing
Aim 1: Perform procedures related to glycemic control	6-42	Ongoing
・Three 3-hour meal tolerance tests		
・24-hour measurement of glucose, insulin, and C-peptide		
・HbA1c		
Aim 2: Perform procedures related to the circadian system	6-42	Ongoing
・24-hour measurement of melatonin and cortisol		
・Constant glucose infusion procedure		
Aim 3 (Sleep): Perform polysomnography (PSG) and administer sleep questionnaires	6-42	Ongoing
Aim 3 (Body Weight): Measure weight and body fat (DXA)	6-42	Ongoing
Aim 3 (Cardiovascular): Measure blood pressure and heart rate and draw blood to measure lipids and inflammatory markers	6-42	Ongoing
Aim 3 (Quality of Life and Psychological Health): Administer questionnaires and perform semi-structured interview	6-42	Ongoing
Aims 1, 2, and 3: Perform assays of glucose, insulin, C-peptide, HbA1c, cortisol, melatonin, lipids, and inflammatory markers	6-42	Ongoing
Collect other outcome data: daily survey, Actiwatch data, food records, accelerometry, physical activity questionnaire, appetite questionnaire, and resting metabolic rate	6-42	Ongoing
Monitor intervention adherence and daily surveys	6-42	Ongoing
Monitor participant safety	6-end	Ongoing
Follow-up with participants to recollect any missing data	6-end	Ongoing
Monitor data validity and integrity	6-end	Ongoing
・Glycemic data (Aim 1 and glucose infusion data from Aim 2)		
・24-hour measurement of melatonin and cortisol (rest of Aim 2)		
・Sleep data (part of Aim 3)		
・Cardiovascular data (part of Aim 3)		
・Semi-structured interview (part of Aim 3)		
・Electronic questionnaires and study database in REDCap		
・All other outcomes		
Collect 8-month and 12-month follow-up data	14-end	Ongoing
Write and submit a manuscript on the study protocol	20-24	Will complete this coming fiscal year.
Accrual and adherence meetings	Twice a month	Ongoing
Monthly progress meetings	Monthly	Ongoing
Data and safety monitoring meetings	Quarterly	Ongoing
Submit quarterly reports to the DoD	Quarterly	Ongoing
Submit protocol amendments, adverse events, and protocol deviations to IRB and HRPO	As needed	Complete and ongoing

Submit annual reports for continuing review to IRB and HRPO	Annually	Complete and ongoing
Milestone achieved: Last participant enrolled	38	Not started
Milestone achieved: Last participant completes the intervention	42	Not started
TASK 3. ANALYZE DATA AND REPORT STUDY OUTCOMES		
Aim 3: Analyze sleep (PSG) data	6-42	Ongoing
Analyze food intake and Actiwatch data	6-42	Ongoing
Analyze physical activity data from accelerometers	6-42	Ongoing
Final quality check of entire study database and study closeout	36-43	Not started
Analyze, write, and submit a manuscript on the baseline data	35-40	Not started
Aims 1-3: Perform statistical analyses on all data	38-46	Not started
Aim 1: Mathematically model data from meal tolerance tests to calculate insulin sensitivity and secretion	40-43	Not started
Aim 1: Mathematically model 24-hour glucose, insulin, and C-peptide data to extract key glycemic endpoints	40-43	Not started
Aim 2: Mathematically model the 24-hour melatonin and cortisol data to determine rhythms of the central clock	40-43	Not started
Aim 2: Mathematically model data from the constant glucose infusion procedure to determine rhythms of the peripheral clocks	40-43	Not started
Aim 3: Analyze quality of life and psychological health data	40-45	Not started
Aim 3: Mathematically model the 24-hour blood pressure data to extract blood pressure endpoints	44-45	Not started
Write and submit manuscripts on the study results and disseminate findings	42-48	Not started
Milestone achieved: All manuscripts submitted	48	Not started

- **What was accomplished under these goals?**

Recruitment

Recruiting has dramatically improved over the past year, with the greatest improvements starting this summer. In July 2022, we met our target recruitment rate for the first time—a major milestone.

In the **first quarter** of Year 3 (September 2021 - November 2021), we sent ~1,000 postcards per week to patients with type 2 diabetes identified through medical records at the UAB Hospital and Birmingham VA Medical Center. This constituted the majority of our recruitment efforts this quarter and was our largest source of applicants as well. In total, we sent out more than 10,000 postcards. The response rate was about 1%, which was lower than expected. We also appeared on the local TV station WBRC on September 23rd and ran ads on a popular radio station via "I Heart Radio" starting in October and ending in December. We also put up dozens of laminated flyers in the UAB Hospital, including in plastic mounts in high-traffic areas such as the pharmacy and waiting rooms, and in other clinics and campus buildings.

In the **second quarter** of Year 3 (December 2021 - February 2022), we continued to send postcards in early December and early January to patients with type 2 diabetes identified through medical records at the UAB Hospital and Birmingham VA Medical Center. In total, we sent out about 3,000 postcards. On January 17th, we began digital recruiting via social media platforms, such as Facebook, Instagram, and Google. We retained a clinical trial advertising company called Trialfacts (www.trialfacts.com) to run the ads. We had signed a contract to run the ads until 27 qualified applicants were referred, which was projected to take about 3 months. We ended up achieving this target much faster than expected and within less a month's time. From February 7th until the end of February, the campaign was paused while we waited for the company to draw up a new contract to continue the campaign. Also, in late January, we received IRB approval to start our new recruiting partnership with three divisions/departments within the UAB Hospital: Primary Care; Endocrinology, Diabetes, and Metabolism; and Family and Community Medicine. In mid-February, we began sending PDF letters by email to patients of these clinics. The response rate was lower than we expected (~1%), so we began experimenting with calling these patients by phone starting in late February/early March.

In the **third quarter** of Year 3 (March 2022 - May 2022), Dr. Peterson (PI) was able to negotiate a month-to-month contract with the social media advertising company Trialfacts. On March 4th, our social media advertising campaign relaunched. We also experimented with cold-calling the clinic patients after they received the PDF letters. While we received a decent response to the cold calling, it was not necessarily easy to reach patients by phone, and the ratio of effort to enrollment was less than ideal. So instead, we tested a new strategy to recruit patients via the electronic medical records. We worked with the hospital to create a weekly report of all individuals who meet our study criteria and had an appointment with either a primary care physician, endocrinologist, or family and community medicine physician in the past week. We receive the report on a weekly basis, and each week, we mail those patients a postcard. This strategy allows us (1) to target people while their health was forefront on their minds and while they were more likely to want to improve their health, (2) to target people who we knew were more likely to show up for appointments, and (3) to target patients whose contact information was also likely to be up-to-date. We found this approach to be more successful on a per postcard basis than other strategies we have tried. During March and part of April, we sent out postcards at a rate of about 300-600 per week. Due to staff turnover and hiring new staff in May 2022, we temporarily had to halt all advertising for 3 weeks in May (last month of the quarter).

In the **fourth quarter** of Year 4 (June 2022 - August 2022), we finished training new research staff and resumed recruiting. We relaunched our social media advertising campaign and reinitiated sending postcards. We also continued to advertise around the university and the hospital. In June, recruitment started picking up again. In July, we met our target recruitment goal of finding 2 eligible participants per week for the first time since the study started—a major victory. Although we were able to *recruit* 2 eligible patients per week in July, we were not able to *randomize* 2 patients per week due to 2 of 4 full-time research nurses deciding to step down from their positions in late June/mid-July. This caused our research unit to operate at less than 50% capacity this quarter. Therefore, we had to slow down recruitment again starting in August. Nonetheless, we achieve a major milestone of finally being able to recruit 2 patients per week.

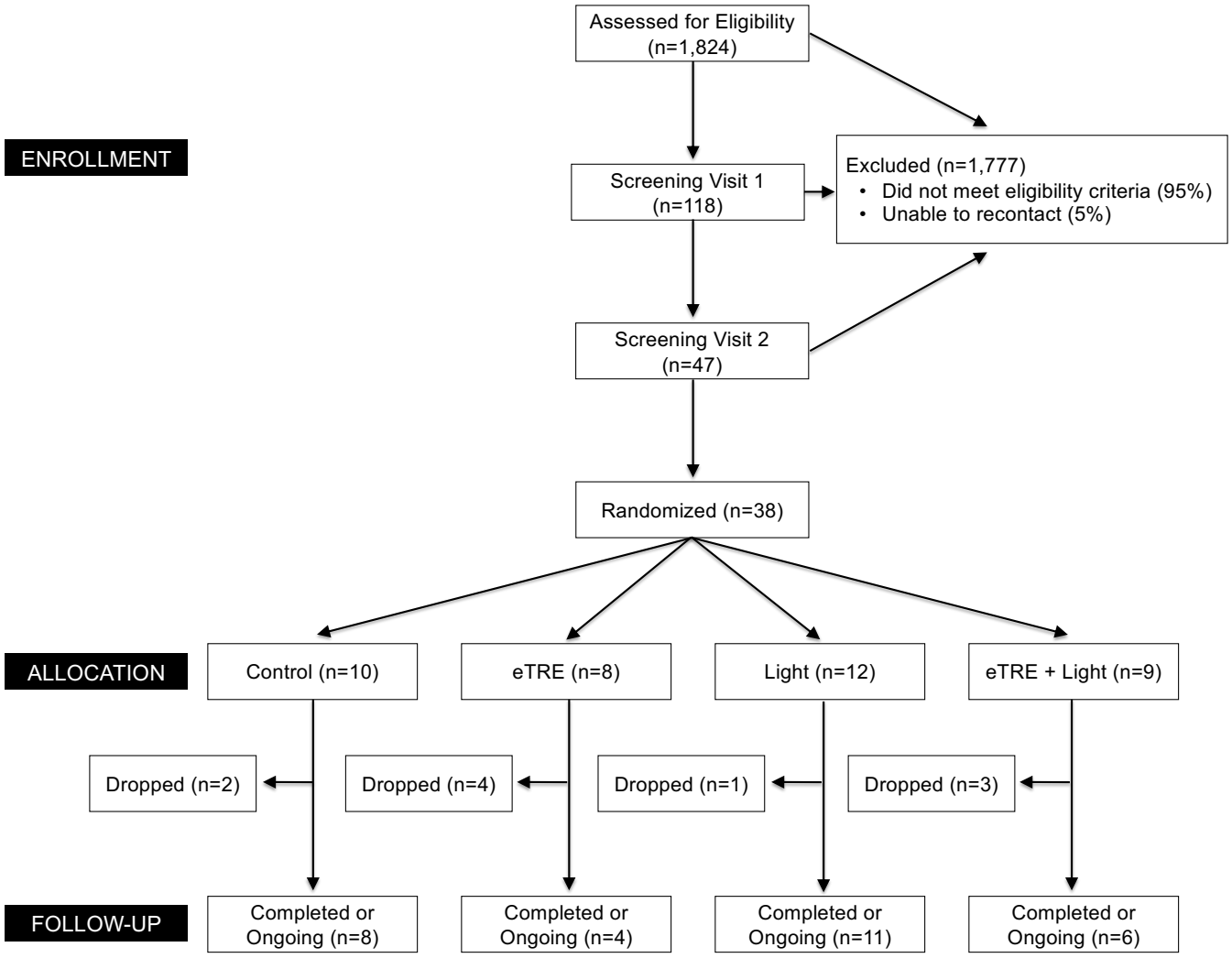
Overall, to summarize, recruitment has been slower than expected for most of the year, and we did experience a high no-show rate for appointments, largely due to the COVID-19 pandemic. We experimented with several different recruitment methods, shifting our approach each quarter, to determine which recruitment methods are most effective. In the fourth quarter of this year, we finally started recruiting at 100% of our target rate of 2 participants per week. We attribute this major achievement to a combination of three factors: (1) finally figuring out the most effective recruiting methods for our study population (which, for us, has been social media advertising and strategic mailing of postcards to hospital patients); (2) the pandemic waning and people returning to their normal lives; and (3) having excellent staff who worked tirelessly. Importantly, we demonstrated for the first time that we can meet our target recruitment rate, even during the pandemic, as a single clinical trial site.

Screening and Enrollment

This year, we pre-screened 1,382 applicants by phone or online, which is more than 100 per month on average. In total, since we began enrolling patients in May 2021, we have pre-screened 1,824 applicants. The six most common reasons for ineligibility are shown below. The most common reason is an HbA1c level that is too low.

Most Common Exclusion Reasons	Percent
HbA1c outside of 7 - 10%	27%
Spends an average of more than 1.5 hrs/day outdoors	19%
Exclusionary disease, condition, or medical procedure (e.g., cancer, GI surgery, pregnancy, sleep disorder)	16%
On insulin	8%
Unable or unwilling to follow the study protocol	5%
Unable to recontact	5%

As mentioned previously, due to the COVID-19 pandemic, we had a much higher than expected no-show rate for in-person screening appointments. In total, we have screened 118 applicants in person (does not include no-shows). Of these, 47 were eligible to enroll in the study, and 38 participants have been randomized. (Most of the remaining participants are scheduled to be enrolled in the future.) Shown below is an abbreviated CONSORT diagram for the study.



Retention

Retention has been good and slightly better than expected. Currently, retention is 74%, which is better than our project rate of 70%. To date, 10 participants have dropped out of the study. The most common reasons for dropping out of the study include venous access issues or other issues preventing the successful completion of the inpatient stay (50%, n=5), loss to follow-up (20%, n=2), and lack of sufficient time to participate in the study (20%, n=2). In addition, one person was administratively withdrawn after an unrelated medical event, which was reported in the first quarter's report.

Adherence

Most participants have been very dedicated and committed, so adherence has been excellent and on track with what we hoped. Nearly all participants have adhered >80% of the time, with a majority adhering >90% of the time.

Data Collection

Data collection has gone well overall, with only a couple of minor issues that we are further refining. Venous access issues are the most frequent cause of incomplete. In those cases, we attempted to regain access, discontinued the infusion and discharged the participant, and/or attempted to repeat the testing later. Minor issues include the ambulatory blood pressure monitor occasionally missing some time points (known issue; part of Aim 3) and the YSI machine missing some time points (part of Aim 2). These issues are minor. Calibration issues with the YSI have caused it to not be used for several participants. The company has been contacted, and the YSI will be sent in for re-calibration. In lieu of using the YSI to measure glucose in real-time, we are pilot-testing whether continuous glucose monitors (CGMs) can be used instead of the YSI machine. Finally, due to a national shortage of 10% dextrose in an IV bag, we

could not perform the constant glucose infusion in two participants. All other aspects of data collection have gone very well, particularly the measurements involving polysomnography (PSG).

Adverse Events & Safety

There have been no serious or unexpected adverse events over the past year. Adverse events definitely related to the study include IV infiltration (n=1), hyperglycemia (n=1), vein rupture (n=1), and extravasation of an IV (n=1), all of which occurred during the inpatient testing. The one instance of extravasation of IV from the dextrose infusion was accompanied by immediate swelling and blisters, which all resolved within 1-3 days. Further, one of the glucose (CGM) sensors accidentally broke off under one participant's skin. This is a known issue with the product (not an unexpected adverse event). After removing the sensor, no further medical attention was needed.

Adverse events possibility related to the study include malaise (n=1), orthostatic dizziness (n=1), chest pain (n=1), and headache (n=1). Adverse events unrelated to the study include nausea or fatigue from the COVID-19 booster (n=2), dry eyes (n=1), bladder infection (n=1), nausea due to a GI virus (n=3), foot cramping (n=1), atrial flutter (n=1), and intermittent eye pain likely attributed to a neurologic issue (n=1). In addition, one participant complained of chest pain, headache, and fainting with slight convulsions at home. Hospital doctors believed it was a panic attack. Out of an abundance of caution, we administratively withdrew the participant. We previously reported this AE via one of our quarterly technical reports. None of the AE's needed to be reported immediately to the IRB and have been or will be reported at the time of the continuing review. We have continued to meet with our independent safety monitors once a quarter (Drs. Holly Wyatt and Stewart Frank) to evaluate patient safety. In addition, we continue to collect safety data by having participants self-report their fasting glucose and blood pressure every other week.

Regulatory & Subcontracts

We submitted continuing reviews to all regulatory bodies and have received approval from the UAB IRB and BVAMC IRB. We are currently awaiting approval from the HRPO. Additionally, our co-investigator Dr. Sarah-Jeanne Salvy received IRB approval at Cedars-Sinai Medical Center. Subawards were also completed for the past year.

Staffing and Training

- **Nurses**. In late June and July of 2022, our university's clinical research unit lost two of its four full-time research nurses that work day- or nightshifts for research studies that involve inpatient testing. One nurse left for a higher-paying job to support herself while completing schooling, and a second nurse left due to not wanting to work so many weekends and to spend more time with her family. So, for the last 3 months, our research nurse unit has been understaffed, and we have been quite limited in how many participants we can randomize per month. This is why we can recruit 2 eligible patients per week but cannot randomize 2 per week. This has been our largest bottleneck this past quarter. During the first week of June, we posted ads to hire two new nurses to replace the ones who left. In August, after more than two months of searching, we finally found two full-time nurses to replace the two nurses who left. Unfortunately, one of the newly hired nurses (who was supposed to be moving to the area) backed out of her contract the week that she was supposed to start. The other newly hired nurse will complete training in October 2022. At present, we are still looking to fill one full-time nightshift position, as well as a one part-time dayshift position to accommodate the recently increased influx of participants).
- **Research Nurse Manager.** Our former nurse manager, Ms. Rachel Benz, left her position in January 2022. Ms. Lynn Dill replaced Ms. Benz in this position and received a few weeks of training prior to Ms. Benz's departure. Thereafter, we continued Ms. Dill's intensive training with support from other staff in the lab. Ms. Dill began working mostly independently in the middle of the second quarter. (As a result, we were not able to devote as much time to recruiting that quarter.) Ms. Dill has an extensive research background and has been a major asset to the team.
- **Research Coordinators**. We have also experienced turnover among our own research staff. Ms. Errin Jessie (who worked full-time on this trial) and Ms. Kim Armstead (who worked part-time on this trial) left their positions in the spring of 2022 for higher-paying jobs. The same month they announced their departures, the university—sensing the rapidly-changing job market and a significant exodus of workers from the labor market—finally announced large pay increases for research staff across the entire university in order to better retain research staff and compete in the post-pandemic job market. The university as a whole, as well as our lab, is now in a much better position to retain research staff.

Thereafter, we hired two coordinators. Ms. Rachel Hart, Coordinator I, joined the team in May 2022, and Mr. Isaac Martinez, Coordinator III, joined the team in July 2022. In the long-term, they will devote a combined total of 1.5 FTE to the study. Our team spent time training both new coordinators.

- **Student Workers.** We hired and trained a couple new student workers to assist with mailing postcards and processing biospecimens this summer.
- **Behavioral Counselor**. Ms. Sara Hannum has continued to serve as a behavioral counselor with the study, managing all visits with all participants. The participants enjoy their visits with Ms. Hannum and express this frequently.
- **All study staff** were retrained in all relevant BVAMC privacy and security measures, and WOC appointments are still active.

Other Activities

- Monthly meetings continue with co-investigators, including the following people:
  - The study statistician Dr. Joshua Richman
  - Co-investigator and circadian expert Dr. Karen Gamble
  - Co-study physicians Drs. Tim Garvey and Dr. T. Brooks Vaughan
  - Co-investigator Dr. Sarah-Jeanne Salvy
  - Paid independent consultant Dr. Frank Scheer (BWH)
- We also continue to have our quarterly safety and progress meetings with our independent safety monitors.
- Finally, we are nearly finished with writing the review article on light therapy. We have brought on an expert in light therapy and circadian rhythms, Dr. Parisa Vidafar, to ensure the completeness of our literature search.

- **What opportunities for training and professional development has the project provided?**
  Nothing to Report

- **How were the results disseminated to communities of interest?**
  Nothing to Report

- **What do you plan to do during the next reporting period to accomplish the goals?**

  Despite several challenges due to the pandemic, the situation has turned around dramatically these past three months, and we are now able to recruit eligible participants at our target rate of 2 per week. Currently, our only bottleneck is the national shortage of nurses, which has led to our clinical research unit being temporarily short-staffed. We anticipate that enrollment will be limited for the next quarter (September – November) due to insufficient nurses to conduct the inpatient testing. We are optimistic that our clinical research unit will be able to return to full staffing capacity by the end of November, as the unit has already found one excellent new nurse. Once the clinical research unit is fully staffed, we expect to be able to randomize patients at our target rate of 2 per week. We will continue recruiting at a lower rate in the interim. Starting in October or November, we anticipate relaunching all our recruitment campaigns and recruiting at full capacity.

  1. **Social Media Advertising**. We will re-launch our digital advertising campaign on Facebook, Google, Instagram, and Twitter. When active, these ads typically bring in about 40-45 applicants per week.

  2. **Mailing Postcards**. We will continue mailing roughly 300 postcards per week to patients with type 2 diabetes identified via electronic medical records at the UAB Hospital and the BVAMC. We will continue to target patients who have recently seen their healthcare provider in the last two weeks, as we have found this strategy to be more effective for recruiting participants.

  3. **UAB Clinical Trials Webpage.** We will continue to recruit patients through UAB's Clinical Trials Webpage (called the Clinical Trials Reporter), which brings in a steady flow of participants.

  4. **Flyers at UAB Hospital**. We will continue to refresh our laminated flyers in the UAB Hospital, including in plastic mounts in high-traffic areas such as the pharmacy and waiting rooms.

Also in the next year, we will continue screening and enrolling applicants, delivering the intervention, and collecting study data. Finally, we will finish our light therapy review article and the study protocol manuscript, and we will resolve the issue of whether to use the YSI machine vs. CGM to measure glucose levels in real-time during the dextrose infusion.

- **IMPACT:**

  - **What was the impact on the development of the principal discipline(s) of the project?**
    Nothing to Report

  - **What was the impact on other disciplines?**
    Nothing to Report

  - **What was the impact on technology transfer?**
    Nothing to Report

  - **What was the impact on society beyond science and technology?**
    Nothing to Report

- **CHANGES/PROBLEMS:**

  - **Changes in approach and reasons for change**
    We modified our eligibility criteria to allow individuals taking sulfonylureas to enroll if they have an HbA1c between 7.5-10%. Previously, the range was 8-10%. The rationale for this change is that the stricter criteria excluded some people who would otherwise qualify, and to date, we have had no reports of hypoglycemia.

  - **Actual or anticipated problems or delays and actions or plans to resolve them**

    Previously, we previously experienced a one-year delay due to the COVID-19 pandemic temporarily shutting down our research facilities and affecting research operations. We also experienced a few-month slowdown in the number of patients we could enroll due to renovations within our hospital's research facility that were delayed by the pandemic.

    This year, we experienced the following delays and problems, all related to the COVID-19 pandemic:

    1. **Slower Recruitment and More No-Shows Than Typical**. For the first three quarters of this year, we experienced slow recruitment and a larger number of no-shows than experience. For instance, during a two-week period in mid-August, we had a ~65% no-show rate across two of our studies. (For reference, our hospital was also similarly seeing a large increase in their no-show rate.) As a result, recruitment was much slower than expected. Over the course of several months, we were able to resolve these issues as follows:
        i. We launched several major advertising campaigns and experimented with different advertising methods. We found the combination of social media advertising and targeting postcards to patients at UAB hospital who had recently seen their physician.
        ii. We hired and trained a part-time coordinator in order to screen more patients and schedule more screening visits. This brought our total research coordinator support on this study up to 2.5 FTE.

       Through a combination of hard work, hiring extra recruiting support, and change in attitudes toward the pandemic, we successfully overcame all recruiting challenges in July 2022.

    2. **Staffing Issues**. As described above, our Clinical Research Unit is currently short-staffed and does not have sufficient nurses to conduct inpatient research testing; they are currently at less than 50% capacity. We recently hired one full-time nurse, who is currently undergoing training, and we are looking for one more full-time nurse to work the nightshift and a part-time nurse. This is our biggest and only remaining challenge at the moment. We are optimistic that we can resolve this issue by the end of the first quarter of the new year. We also had turnover among

research staff in our own lab. This reduced recruitment intermittently for a few months. This issue has been resolved by the university implementing large increases in salaries among research staff across the university and by us hiring new staff.

3. **Supply Shortages**. We occasionally experience shortages of medical supplies and equipment, such as dextrose solution. In most cases, we have been able to mitigate these delays by reordering supplies earlier than needed and/or borrowing supplies.

- **Changes that had a significant impact on expenditures**
  Nothing to Report (similar status as last year)

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
  Nothing to Report

- **Significant changes in use or care of human subjects**
  Nothing to Report

- **Significant changes in use or care of vertebrate animals.**
  Not Applicable

- **Significant changes in use of biohazards and/or select agents**
  Not Applicable

- **PRODUCTS**

  - **Publications, conference papers, and presentations**

    - **Journal publications**
      Nothing to Report. Two publications are planned for the coming fiscal year, to catch up with the original timeline.

    - **Books or other non-periodical, one-time publications**
      Nothing to Report

    - **Other publications, conference papers, and presentations**
      Nothing to Report

  - **Website(s) or other Internet site(s)**
    Nothing to Report

  - **Technologies or techniques**
    Nothing to Report

  - **Inventions, patent applications, and/or licenses**
    Nothing to Report

  - **Other Products**
    Nothing to Report (same products as last year)

- **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

  - **What individuals have worked on the project?**

Name	Courtney Peterson, Ph.D.
Project Role	Principal Investigator

Researcher Identification (ORCID #)	0000-0002-4845-6782
Nearest Person Month Worked	5
Contribution to the Project	Dr. Peterson is serving as the study PI. She oversees all aspects and operations of the clinical trial (except where noted below). She also is reviewing study data on an ongoing basis to ensure data validity.
Funding Support	
Name	T. Brooks Vaughan, M.D.
Project Role	Co-Investigator and Study Physician
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	1
Contribution to the Project	Dr. Vaughan oversees patient safety and medical eligibility for the clinical trial.
Funding Support	
Name	Sarah-Jeanne Salvy, Ph.D.
Project Role	Co-Investigator and Clinical Psychologist
Researcher Identification (ORCID #)	0000-0002-8202182X
Nearest Person Month Worked	1
Contribution to the Project	Dr. Salvy designed the behavioral aspects of the intervention and crafted behavioral SOPs. She currently oversees the behavioral counseling and participant adherence and is responsible for ensuring quality control.
Funding Support	
Name	Joshua Richman, M.D., Ph.D.
Project Role	Co-Investigator and Statistician
Researcher Identification (ORCID #)	0000-0002-6166-7488
Nearest Person Month Worked	1
Contribution to the Project	Dr. Richman assisted with designing the study database in REDCap and created the statistical and data validity protocols for the trial, using software programming. He also created the randomization code. He is overseeing data management and the study database on an ongoing basis.
Funding Support	
Name	Karen Gamble, Ph.D.
Project Role	Co-Investigator and Circadian Biologist
Researcher Identification (ORCID #)	0000-0003-3813-8577
Nearest Person Month Worked	1
Contribution to the Project	Dr. Gamble has provided important guidance on the light therapy intervention, protocol, and circadian rhythms measurements. She also helped negotiate for and set up the inpatient testing rooms. Dr. Gamble is currently overseeing the collection of circadian data.
Funding Support	
Name	Rachel Benz, M.S.N., R.N.
Project Role	Research Nurse Manager
Researcher Identification (ORCID #)	0000-0001-6211-7771
Nearest Person Month Worked	5
Contribution to the Project	Lead research coordinator and nurse manager
Funding Support	
Name	Kimberly Armstead, B.S.
Project Role	Research Coordinator

Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	7
Contribution to the Project	Research coordinator, with a focus on recruiting, screening, and consenting participants.
Funding Support	
Name	Shelby Leverett, B.S.N.
Project Role	Research Nurse
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	8
Contribution to the Project	Perform nursing and collect research data during the 38-hour inpatient tests. Also assist with phlebotomy and screening visits.
Funding Support	
Name	Haley Hulsey, B.S.N.
Project Role	Research Nurse
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	7
Contribution to the Project	Perform nursing and collect research data during the 38-hour inpatient tests. Also assist with phlebotomy and screening visits.
Funding Support	
Name	Cynthia Venton, B.S.N.
Project Role	Research Nurse
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	8
Contribution to the Project	Perform nursing and collect research data during the 38-hour inpatient tests. Also assist with phlebotomy and screening visits.
Funding Support	
Name	Elizabeth Cochran, B.S.N., R.N.
Project Role	Research Nurse
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	7
Contribution to the Project	Perform nursing and collect research data during the 38-hour inpatient tests. Also assist with phlebotomy and screening visits.
Funding Support	
Name	Lynn Dill, B.S.N., R.N.
Project Role	Research Nurse Manger
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	8
Contribution to the Project	Lead research coordinator and nurse manager
Funding Support	
Name	Rachel Hart, B.S.
Project Role	Research Coordinator
Researcher Identification (ORCID #)	N/A
Nearest Person Month Worked	4
Contribution to the Project	Research coordinator, with a focus on recruiting, screening, and consenting participants.
Funding Support	
Name	Isaac Martinez, B.S.
Project Role	Research Coordinator
Researcher Identification (ORCID #)	N/A

Nearest Person Month Worked	2
Contribution to the Project	Research coordinator, with a focus on recruiting, screening, and consenting participants.
Funding Support	

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Dr. Salvy (co-investigator) has three new sources of support and is no longer supported by one grant:

New Support
No Number (Salvy) 9/1/21 – 9/31/23 0.12 Calendar
Cedars-Sinai Medical Center
Hope Warshaw Center for Integrated Research in Cancer and Lifestyle
The primary objective of the proposed study is to evaluate the preliminary efficacy of gamified inhibitory control training with or without leisure-time physical activity on cognitive functioning among healthy cancer survivors.
Role: PI

P50 MD017344 (Goran & Baezconde-Garbanati) 10/1/21 – 9/31/26 0.0 Calendar
NIH/NIMHD
Southern California Center for Chronic Health Disparities in Latino Children and Families
This coalition of academic, clinical, government, and community stakeholders aims to: (i) understand the complex inter-play between multi-level factors that contribute to multiple chronic disease disparities in Latinos across the life course, and (ii) develop and evaluate family-based, culturally sensitive solutions.
Role: Mentor and investigator

CIHR464007 (Barnett) 10/1/21 – 9/30/26 0.0 Calendar
Canadian Institutes of Health Research (CIHR)
Personal Social Networks, Built Environment and Cardiometabolic Risk Factors: Prospective Investigation with Young Adults
The primary objective of the proposed study is to evaluate the preliminary efficacy of gamified inhibitory control training with or without leisure-time physical activity on cognitive functioning among healthy cancer survivors.
Role: Consultant

Moved to Past Support
U54MD000502 (Salvy and Dutton) 9/1/17 – 8/31/22 1.2 Calendar
NIH/NIMHD
Obesity Health Disparities Research Center (Project #2)
This two-arm, parallel, randomized controlled trial tests the effectiveness of an obesity intervention based on habit formation and manipulation of the home environment to address obesity and health-related disparities among socioeconomically disadvantaged mothers and their young children enrolled in federally funded maternal-child health services.
Role: MPI

Dr. Gamble (co-investigator) has one new source of support:

New Support
R01 HL160982 (Arora) 1/1/2022 – 12/31/2026 0.6 calendar
NIH/NHLBI
Natriuretic Peptide-Renin-Angiotensin-Aldosterone System Rhythm Axis and Nocturnal Blood Pressure

This study will assess an innovative physiologically-driven precision medicine approach of using chronopharmacology for resynchronizing the NP-RAAS-BP rhythm axis and restoring the normal BP rhythm in individuals with obesity and hypertension with non-dipping BP.
Role: Co-I

Dr. Richman (co-investigator and statistician) has several new sources of support and is no longer supported by two grants:

New Support

22CC08 7/1/22 – 6/30/23 0.3 calendar
Rally Foundation
Enhancing 6MP Adherence in Adolescents with ALL: Strategy for Dissemination
The major goal of this project is to develop strategies to disseminate evidence-based strategies to increase 6MP-adherence in adolescents with ALL.
Role: Co-I

No Number (Muntner) 10/1/21 – 9/30/25 0.6 calendar
American Heart Association (AHA)
RESTORE (Addressing Social Determinants to Prevent Hypertension) Network
The objective of this study is to serve as part of a network of linked studies at multiple institutions focused on social factors that could be leveraged to prevent hypertension.
Role: Co-I

No Number (Gangaraju) 7/1/22 – 6/30/25 0.01 calendar
American Society of Hematology
Predictors of Clonal Hematopoiesis of Indeterminate Potential and Clonal Evolution
The major goal of this project is to identify predictors of CHIP using the REGARDS cohort and explore associations between CHIP and clinical outcomes.
Role: Co-I

6652-23 (Bhatia) 7/1/22 – 6/30/25 0.3 calendar
Leukemia & Lymphoma Society
Prediction and Prevention of Therapy-Related Myeloid Neoplasms Following Autologous Transplantation
The goal of this project is to identify risk factors of myeloid neoplasms related to therapy after autologous bone marrow transplantation.
Role: Co-I

No Number (Broman) 7/1/22 – 6/30/24 0.3 calendar
American College of Surgeons
Quality of Care and Patient Preferences for Cancer Surgery at Hub versus Affiliate Sites Within Health Systems
The goal of this project is to identify within-system heterogeneity in quality of care between system ‘hubs’ and ‘spokes’.
Role: Co-I

No Number (Broman) 7/1/22 – 6/30/25 0.3 calendar
Conquer Cancer Foundation/ASCO
Health System Characteristics and Strategies that Contribute to Evidence-Based Surgical Care: A mixed methods study proposal
The goal of this project is to identify characteristics of health systems associated with evidence-based surgical care.
Role: Co-I

K23 AT011375 (Presley) 1/1/22 – 12/31/25 0.5 calendar
NIH/NCCIH
Mindfulness-Based Diabetes Education for Adults with Elevated Diabetes Distress

The proposed project will pilot test a Mindfulness-Based Diabetes Education intervention, specifically adapted for adults with type 2 diabetes and elevated diabetes distress, to assess feasibility and acceptability. Utilizing mixed-methods, this study will also characterize key contextual factors that influence intervention delivery and implementation, setting the stage for a future, larger study in safety-net healthcare settings.
Role: Co-I

Moved to Past Support
IIR 15-095 (Kertesz) 7/1/16 – 6/30/22 0.5 calendar
VA HSR&D
Primary Care Quality and Homeless Service Tailoring (PCQ-HoST)
This study aims to compare experience scores between patients who receive primary care at homeless tailored PACTS (H-PACTS) versus other forms of VA primary care and to clarify what elements of H-PACTS are associated with better patient experience.
Role: Co-I

UH2 HL130691 9/28/15 – 8/31/22 0.3 calendar
NIH/NHLBI
Collaboration to Improve Blood Pressure (BP) in the US Black Belt – Addressing the Triple Threat
The central objective is to rigorously compare two strategies designed to improve BP control in primary care practices serving rural Southeastern African Americans with low socioeconomic status (SES).
Role: Co-I

All three investigators still remain under the maximum effort allowed. There have been no other changes in active support among key personnel.

- **What other organizations were involved as partners?**
  Organization Name: Cedars-Sinai Medical Center
  - **Location of Organization:** Los Angeles, CA
  - **Partner's contribution to the project**
    - **Collaboration**
      Co-investigator Dr. Sarah-Jeanne Salvy assisted in the development of the behavioral aspects of the research protocol, including the design of behavioral counseling, behavioral interviews, psychological questionnaires, and the corresponding SOPs**.** She is currently overseeing all behavioral counseling and is responsible for ensuring quality control of the behavioral aspects of the intervention. She meets with the behavioral counselors every week to review adherence and trouble any issues with counseling.

  Organization Name: Brigham and Women's Hospital
  - **Location of Organization:** Boston, MA
  - **Partner's contribution to the project**
    - **Collaboration**
      The project's consultant, Dr. Frank Scheer, provided detailed feedback on the study protocol and timed light therapy intervention. He continues to attend the monthly co-investigator meetings and provide suggestions.

- **SPECIAL REPORTING REQUIREMENTS**

  - **Collaborative Awards**
    Not Applicable

  - **Quad Charts**
    See Next Page

- **APPENDICES**

  Nothing to Report.