Supplemental Materials

Title: Time-Restricted Eating to Improve Cardiometabolic Health: The New York Time-Restricted Eating Randomized Clinical Trial – Protocol Overview.

Authors: Leinys S. Santos–Báez, Alison Garbarini, Delaney Shaw, Bin Cheng, Collin J. Popp, Emily N. C. Manoogian, Satchidananda Panda, Blandine Laferrère.

Supplemental Documents:

Supplemental Document 1: Instructions given to participants assigned to TRE

Supplemental Document 2: Sleep log

Supplemental Document 3: Questions asked on Visual Analog Scales (VAS)

Tables:

Supplemental Table 1: Questionnaires

Supplemental Table 2: Biomarkers

Supplemental Table 3: Primary and secondary outcomes

Figures:

Figure 1a and 1b: Food offered to participants on Day-13 of the 2-week assessment period, day preceding the OGTT.

Supplemental Document 1: Instructions for adjusting to TRE eating window.

TRE Group: Tips for Adjusting to your new 10-hour eating window

My personalized 10-hour eating window is: _____AM to _____PM

- **You are in the TRE group**: every day during the next 3-months you will follow your personalized 10 hour eating window. You can either make the switch from one day to the next, or make a gradual adjustment to the restricted eating during your first two weeks of TRE. You will receive push notifications and reminders sent through the app about when to eat or not to eat. This includes a daily reminder 1 hour before eating can begin, and 1 hour before your eating window will end.

- **Recommended:** If you're having trouble sticking to your new eating window, it may be helpful to decrease your window ***gradually*** over the next 2 weeks.

  For example, if you usually have breakfast at 10AM, but now need to start eating at 8 AM, try eating 15-30 minutes earlier each morning. That means you can have your first meal at 9:45 AM on day 1, 9:30 AM on day 2, 9:15 AM on day 3 etc.

  Similarly, if you usually eat your last meal around 8PM, but you now need to stop eating by 6 PM, try eating 15-30 minutes earlier each night. That means you can have your last meal at 7:45 PM on night 1, 7:30 PM on night 2, 7:15 PM on night 3 etc.

  Try out this gradual adjustment, and within 2 weeks, you should be well adjusted to your new eating schedule.

- Drink plenty of water. You can drink plain water at any time, not just during your 10 hour eating window. But remember, drinking any beverage besides water will 'start the clock' on your daily 10-hour eating window, so make sure any coffee/tea/juices are only consumed within your window.

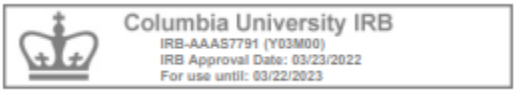
- Track everything that you eat and drink in the mCC App!

Try not to focus too much on mistakes. If you have a bad day, try to get back on track the next day!

Questions? Contact us!

Alison Garbarini
ag4415@cumc.columbia.edu
(212) 851-5581

Leinys-Santos Baez
lss2181@cumc.columbia.edu
(212) 305-2203



Supplemental Document 2: Sleep Log

Participant ID: _____

NY TREAT STUDY

AT HOME 14-DAY SLEEP LOG

Instructions for the sheet: Use this sheet to record what time you go to bed at night (turn the lights off to go to sleep) and what time you wake up (get out of bed in the morning).

	Date	Time you went to bed (lights off)		Date	Time you woke up (out of bed)	How would you rate your sleep quality? Please circle an option each day 1) Very Poor; 2) Poor; 3) Satisfactory 4) Good 5) Excellent				
Night 1			**Morning 1**			1	2	3	4	5
Night 2			**Morning 2**			1	2	3	4	5
Night 3			**Morning 3**			1	2	3	4	5
Night 4			**Morning 4**			1	2	3	4	5
Night 5			**Morning 5**			1	2	3	4	5
Night 6			**Morning 6**			1	2	3	4	5
Night 7			**Morning 7**			1	2	3	4	5
Night 8			**Morning 8**			1	2	3	4	5
Night 9			**Morning 9**			1	2	3	4	5
Night 10			**Morning 10**			1	2	3	4	5
Night 11			**Morning 11**			1	2	3	4	5
Night 12			**Morning 12**			1	2	3	4	5
Night 13			**Morning 13**			1	2	3	4	5

Supplemental Document 3: Questions asked using Visual Analog Scales.

VAS questions are presented on a 150 mm scale that is anchored from “Not at all” to “Extremely”. VAS are asked before and after each meal and before snack on Day-13 visits, and under fasting condition at Day-1 during the 12-month visit.

1. How energetic did you feel when you got up this morning?
2. How tired did you feel when you got up this morning?
3. How vigorous did you feel when you got up this morning?
4. How energetic do you feel this evening?
5. How rested did you feel when you got up this morning?
6. How drowsy did you feel when you got up this morning?
7. How satisfied are you with your sleep quality?
8. How hungry do you feel right now?
9. How full do you feel right now?
10. How much do you think you can eat right now?
11. How much do you crave something sweet right now?
12. How much do you crave something salty/savory right now?
13. How much can you resist late-night snacking?
14. How tired do you feel this evening?
15. How active do you feel this evening?
16. How vigorous do you feel this evening?
17. Do you feel bloated or have a swollen/tight feeling in the stomach right now?
18. How often do you suffer from acid reflux (heartburn)?
19. How satisfied are you with your bowel movements?
20. How many bowel movements do you usually have in a week? (please circle)

Supplemental Table 1: Questionnaires

Questionnaire Name	Number of questions	Scoring System	Outcome
Insomnia Severity Index (ISI)[47]	7	Each question ranked on a scale of 0-4 (0 = best; 4 =worst). The total score is the sum of these rankings.	**No clinically significant insomnia**: 0-7, **Subthreshold insomnia**: 8-14, **Clinical insomnia** (moderate severity): 15-21, **Clinical insomnia** (severe): 22-28
Pittsburgh Sleep Quality Index (PSQI)[48]	9	The 9 questions on sleep habit result in 7 component scores, which are summed for a global PSQI score.	**Adequate sleeper:** Global sum <5, **Poor sleeper**: Global sum ≥5
Berlin Questionnaire[52]	10	10 items, covering 3 categories associated with sleep apnea risk, are scored individually according to the key. The items within each category are summed, for a total score in each category. For categories 1 and 2, if the score is ≥2 then the category is considered positive. Category 3 is positive if the answer to the 10th item is yes, or if the patient's BMI is ≥ 30kg/m^2.	**High Risk:** ≥2 categories with a positive score. **Low Risk:** ≤ 1 category with a positive score.
Morningness-Eveningness[49]	19	19 Likert-type and time-scale questions about chronotype. The Likert-type questions offer 4 choices, and the lowest value indicates definite eveningness. The time-scale questions are divided into 15-minute sections of a 7-hour timeframe. Each section has a value of 1-5. The total scores for each item are summed for a global score.	**Definitely morning type:** 70–86, **Moderately morning type:** 59–69, **Neither type:** 42–58, **Moderately evening type:** 31–41, **Definitely evening type:** 16–30
International Physical Activity Questionnaire (IPAQ)[53]	7	The responses to 7 items about PA within the last week are used to calculate the total MET-minutes in a week. This is the sum of: • Time spent walking (3.3 METs x No. of minutes/day x No. of days/week) • Time spent in moderate intensity activity (4.0 METs x No. of minutes/day x No. of days/week) • Time spent in vigorous activity (8.0 METs x No. of minutes/day x No. of days/week) The total MET minutes/week can be used to determine activity level on a descriptive scale.	**Low PA Level:** No activity, or activity that is not high enough for Categories 2 or 3. **Moderate PA Level:** either→ ≥3 days vigorous activity, at ≥20 minutes/day; ≥5 days moderate-intensity activity or walking ≥30 minutes/day; ≥5 days of walking, moderate or vigorous-intensity activities with ≥600 MET-minutes/week. **High PA Level:** either→ ≥3 days vigorous-intensity activity, with ≥1500 MET-minutes/week; ≥7 days of walking, moderate or vigorous-intensity activities, with ≥3000 MET-minutes/week
Beck Anxiety Inventory (BAI)[50]	21	Each of the 21 items measuring anxiety is rated on a 4-point scale of 0-3, with 0 = symptom not at all bothersome; and 3 =symptom severely bothersome. The rankings of the 21 items are summed for the total score.	**Low Anxiety:** 0-21, **Moderate Anxiety:** 22-35, **Potentially Concerning Levels of Anxiety:** ≥36
Beck Depression Inventory II (BDI-II)[50]	21	Each of the 21 items is rated on a 4-point scale of 0-3, with 0 = least severe and 3 = the most severe. The rankings of the 21 items are summed for the total score.	**Minimal Depression:** 0-13, **Mild Depression:** 14-19, **Moderate Depression:** 20-28, **Severe Depression:** 29-63
Socioeconomic Status (SES) Survey	12	*N/A*	Collection of social demographic information
Three-Factor Eating Questionnaire	51 total : 21 on dietary restraint, 16 on disinhibition, 14 on perceived hunger.	The survey consists of Part I and Part II questions. Each numbered item is worth one point. For all questions, the Factor (1,2, or 3) that is being measured is noted. For each factor, points for each question measuring that factor can be summed for the factor's total score. In Part I: The underlined response for the true/false questions indicates that this response should receive 1 point, while the alternative response receives no points. In Part II: Items are labelled with either a '+' or '-' . Each item consists of 4-6 potential response choices, each labelled with a 0,1,2,3, 4, or 5. If the item is labelled '+', responses 0, 1, or 2 receive no points, while responses 3,4, or 5 receive 1 point. For items labelled '-', responses 0, 1, and 2 receive 1 point, while responses 3,4, and 5 receive no points.	**Factor 1:** Dietary restraint is measured with a score range of 0 (low) to 21 (high). **Factor 2:** Disinhibition to eating is measured with a score range of 0 (low) to 16 (high). **Factor 3:** Perceived hunger is measured with a score range of 0 (low) to 14 (high).
Participant Post-Intervention Survey	TRE group: 6 HABIT group: 4	*N/A*	Measures participant satisfaction and experience during the 3-month intervention
Participant Exit Survey	TRE group: 11 HABIT group: 6	*N/A*	Measures participant satisfaction and experience during the study after 1 year

HABIT= habitual eating. MET = metabolic equivalent of task; PA = physical activity; TRE = time-restricted eating.

Supplemental Table 2: Biomarkers

Biomarkers	Assay method
Metabolites	
Glucose	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Glycated hemoglobin (HbA1C)	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Total cholesterol (TC)	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Low density lipoprotein (LDL)	Integra (INT) systems assay (Roche, COBAS INTEGRA)
High density lipoprotein (HDL)	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Triglycerides	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Free Fatty Acids (FFA)	Liquid Chromatography-Mass Spectrometry (LCMS)
β-hydroxyl-butyrate	Colorimetry
Glycerol	Colorimetry
Hormones	
Insulin	IMMULITE immunoassay system (Siemens, Immulite)
C-Peptide	IMMULITE immunoassay system (Siemens, Immulite)
Adipokines	
Leptin	Radioimmunoassay (RIA)
Adiponectin	Radioimmunoassay (RIA)
Inflammation biomarkers	
hsCRP	Integra (INT) systems assay (Roche, COBAS INTEGRA)
Interleukin 6 (IL-6)	Enzyme linked immunosorbent assay (ELISA)
Tumor necrosis factor alpha (TNF-a)	Enzyme linked immunosorbent assay (ELISA)
Receptor for Advanced Glycation End product (RAGE)	Enzyme linked immunosorbent assay (ELISA)
Oxidative stress markers	
8-Isoprostane	Liquid Chromatography-Mass Spectrometry (LCMS)

Supplemental Table 3: Primary and secondary outcomes

Type	Name	Time Frame	Brief Description
Primary	Body weight	0, 3, 12 months	Measured to the nearest 0.01 kg on calibrated scale
Primary	Fat mass by QMR	0, 3, 12 months	QMR is performed on Day-1 and Day-14 of ambulatory assessment, concurrently to DLW measures, and at 12 months; it can detect at little as 50 grams change in fat mass
Secondary	DLW	0, 3 months	To calculate EI and EE (kcal). EI is calculated from total daily EE measured by DLW and changes in body energy stores (ΔES), measured by QMR, over two weeks [EI (kcal/d) = EEDLW + ΔES]
Secondary	Adherence score	0, 3, 12 months	Number of days with good logging (both groups) and number of days meeting target eating window (≤10-hours) and mean reduction in duration of eating window (TRE only)
Secondary	Glucose levels (mg/dl)	0, 3 months	Total and incremental 24-hour glucose AUC from ambulatory CGM and from OGTT
Secondary	Glucose variability (GV, MAGE, LAGE)	0, 3 months	Calculated from CGMS data using EasyGV 8.6 software
Secondary	Insulin resistance HOMA-IR	0, 3 months	[fasting insulin (mU/mL) x fasting glucose (mmol/L)]/22.5
Secondary	Insulin resistance Matsuda index	0, 3 months	Fasting and OGTT glucose and insulin levels are used to calculate the Matsuda index:10,000/ ([fasting insulin (mU/mL)x fasting glucose (mmol/L)]x[mean OGTT insulin (mU/mL) x mean OGTT glucose (mmol/L)])
Secondary	Insulinogenic index	0, 3 months	AUC insulin 30 min/AUC glucose 30 min during OGTT
Secondary	Sleep	0, 3, 12 months	Bedtime, waketime, total sleep time, sleep onset latency, sleep efficiency, and wake after sleep onset will be recorded during each 2-week ambulatory assessments by actigraphy
Secondary	ASA24 macronutrient composition	0, 3, 6, 9, 12 months	On 2 non-consecutive weekdays and one weekend day during each ambulatory assessment and 10-day logging periods of months 6 and 9.
Secondary	Inflammation markers (hsCRP, IL6, TNF α), RAGE, Lipids (TC, HDL, LDL, TG), Glycerol, FFA, β-OH-butyrate	0, 3, 12 months	Fasting blood sample
Secondary	Blood pressure (SBP, DBP)	0, 3, 12 months	Measured with an automatic blood pressure monitor (Spacelab Healthcare, Snoqualmie, WA)

AUC = Area Under the Curve. DBP = Diastolic Blood Pressure. DLW = Doubly Labelled Water. EE = Energy Expenditure. EI = Energy Intake. HDL = high-density lipoprotein. LDL = low-density lipoprotein. Kg = kilogram. OGTT = Oral Glucose Tolerance Test. QMR = Quantitative Magnetic Resonance. RAGE = Receptor for Advanced Glycation End Products. SBP = Systolic Blood Pressure. TC = total cholesterol. TG = triglycerides. TNF alpha = Tumor Necrosis Factor alpha.

Supplemental Figures 1a and 1b

Item	Picture Number
Activia Strawberry Yogurt	1
Almonds	2
Applesauce (sweetened)	3
Baked Naked V'nilla Yogurt	4
Carrots	5
Chips Ahoy! Chewy Chocolate Chip Cookie	6
Coffee	7
Fruit Cup	8
Lean Cuisine Comfort Meatloaf with Mashed Potatoes	9
Mixed Vegetables: Broccoli, Cauliflower, Carrots	10
Pretzels	11
Sabra Hummus	12
Tea	13
Weight Watchers Smart Ones Chicken Parmesan	14

1


2


3


4


5


6


7


8


9


10


11


12


13


14


Item	Picture Number
Almonds	1
Applesauce (unsweetened)	2
Broccoli	3
Cheerios	4
Chips Ahoy! Chewy Chocolate Chip Cookie	5
Chobani Low Fat Greek Yogurt	6
Coffee	7
Fruit Cup	8
Lean Cuisine Butternut Squash Ravioli	9
Lean Cuisine Mac & Cheese	10
Mixed Vegetables: Broccoli, Cauliflower, Carrots	11
Mozzarella Cheese Stick	12
Pistachio Nuts	13
Pretzels	14
Raisins	15
Tea	16

1

6

11

2

7

12

3

8

13

4

9

14

5

10

15

16