

Study Title: Study of Time-restricted Eating on Weight Loss. A Randomized Controlled Trial of the Effects of Time-restricted Eating on Weight Loss in Obese Subjects.

NCT: 03393195

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Experimental Design:

This is a pilot study to examine the metabolic effects of TRF in overweight/obese humans. 100+ overweight/obese (BMI>27, <43kg/m²) male and female subjects over the age of 18 will be recruited to participate in this study. Participants will receive an iHealth Bluetooth connected scale to use during the study. Participants will be randomized to one of two eating plans. 1) **8-hour eating window:** TRF group instructed to limit daily calorie intake between 12:00pm and 8:00pm each day (only water and black coffee/tea permitted outside of eating window); or 2) **Consistent meal timing:** participants are instructed to eat three structured meals each day during specified eating windows (7:00am-11:00am, 11:00am-3:00pm, 4:00pm-10:00pm) Group allocation will be provided to subjects using the Eureka mobile research platform, and no recommendation on total calorie or macronutrient intake was provided. Participants will be instructed to use their iHealth scales daily, preferably in the morning before their first meal (Table 1). The Eureka app will also send adherence surveys, sleep questionnaires, and food attitude surveys to participants throughout the study.

Participants who live within 60 miles of UCSF were invited to participate in in-depth metabolic testing at UCSF. Immediately prior to study start, participants will go to the Clinical and Translational Science Institute (CTSI) clinical research center at the University of California, San Francisco (UCSF) in order to collect baseline values for the measurements listed in Table 2. Since fasting glucose and insulin measurements will be collected, participants will be instructed to fast from 8:00pm the night before. Additionally, iPhone users will be given the option to use the Oura ring for sleep and activity tracking. After 12 weeks, participants will come to the CTSI clinic to repeat the baseline measurements.

Table 1. Measurements to be collected by subjects at home.

Measurement	Mode of Collection	Frequency
Weight	Bluetooth Scale	Daily
Adherence Survey	Eureka	Daily
Sleeping habits (PSQI)	Eureka	Monthly
Food Attitudes (RED Scale)	Eureka	Monthly

Table 2. Measurements to be acquired at baseline and 12-week follow-up (local subjects only)

Questionnaire: Age, Sex, Ethnicity, SES, BMI,
Physical Anthropometry: Waist Circumference, Waist-to-Hip-Ratio (WHR), Mid-thigh girth, bicep girth
DXA Direct Adiposity Measures: Fat mass (arms, legs, trunk, total), Lean mass (arms, legs, trunk, total), percent fat (arms, legs, trunk, total), Volumes (arms, legs, trunk, total), muscle mass (appendicular, total)
DXA Derived Adiposity Measures and Indices: Visceral Adipose Tissue (VAT), Subcutaneous Abdominal Adipose Tissue (SAT), Trunk fat to leg fat ratio, Trunk to leg volume ratio, fat mass index (FMI), fat-free mass index (FFMI)
DXA Bone Measures: Bone mass (arms, legs, lumbar spine, total), Bone Mineral Density (spine, total)
Biochemical and Hormonal Markers in Fasting Blood
Albumin, amylase, bilirubin, BUN, CO ₂ , CPK, creatinine, GGT, LDH, total protein, uric acid
Insulin Resistance & IGFs: glucose, insulin, HbA1C, BHBA
Lipid Profile & Lipid-soluble Micronutrients: TG, total cholesterol, HDLC, LDLC, Ca, Cl, Fe, K, Mg, Na, Phosphate,
Liver Enzymes: ALT, AST, ALK
Questionnaire-based Behaviors on Dietary Intake, Physical Activity, and Cognitive Eating
Dietary Intake (MEC Quantitative Food Frequency Questionnaire): nutrients, food items, food groups
Physical Activity (MEC Physical Activity Questionnaire): total METs, METs for moderate/vigorous activities
Cognitive/Psychological Eating Behaviors (Weight-Related Eating Questionnaire): scores for emotional eating, eating in response to external cues, eating with compensatory restraint (eating less before/after a big meal), eating with routine restraint (holding back at meals, counting calories, dieting)
Meal frequency and times
Weight cycling history and parental body shape information
Strength Isokinetics and Isometrics: peak torque, average peak torque, total work, average power, AGON/ANTAG ratio
Hangrip Strength
Doubly labeled water technique: Total energy expenditure
Resting Metabolic Rate

Statistical Analysis Plan:

The primary outcome will be percent change in weight since baseline, measured daily via iHealth, in the overall cohort of 100 participants. To estimate the intention-to-treat effect of treatment assignment, we will use a linear mixed model (LMM) with fixed effects for treatment assignment, days since baseline (as a continuous variable), and their interaction, and random effects for participant and day, with unstructured covariance matrix. The treatment effect will be estimated by the fixed effect for the treatment by day interaction, capturing the between-group divergence in weight loss trajectories. In sensitivity analyses, we will repeat the analysis after Winsorizing outliers, which will be defined as points more than 1.5 times the interquartile range below the 25th or above the 75th percentile of the overall distribution. No adjustment will be made to p-values or confidence intervals for multiple comparisons for the primary outcome.

Our secondary outcomes will include body fat, lean mass, fasting glucose, insulin, and HbA1c levels, resting metabolic rate, and total energy expenditure, assessed at the baseline and 12-week clinical visits for a subset of 46 participants. To estimate the intention to treat effect of treatment assignment on changes in these outcomes, we will use LMMs with fixed effects for treatment assignment, an indicator for the 12-week visit, and their interaction, and a random effects for participant. The treatment effect will be estimated by the interaction. In sensitivity analyses, we will repeat these analyses Winsorizing any outliers, defined as in the primary analysis. P-values and confidence intervals will be Bonferroni-corrected for 7 comparisons.

All other outcomes measured at the baseline and 12-week clinical visits will be considered exploratory and analyzed using the methods described for the secondary outcomes, without penalization for multiple comparisons.