THE IMPRECISION OF BODY WEIGHT REGULATION IN RESPONSE TO A LACK OF COMPENSATION TO IMPOSED ENERGETIC CHALLENGES

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THE IMPRECISION OF BODY WEIGHT REGULATION IN RESPONSE TO A LACK OF COMPENSATION TO IMPOSED ENERGETIC CHALLENGES

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Obesity and associated pathologies of being overweight is now the number one preventable cause of death and is a serious public health threat. Research indicates the cause of obesity is due to a chronic hypercaloric intake, ergo, treatment and prevention should be targeted at eating behaviors. While many believe in the Set Point theory, that is, body weight is tightly regulated and programed to be a specific value, evidence suggests otherwise. Data show that there is poor regulation of body weight (fat) and physiological mechanisms do not precisely correct for energy imbalances. This dissertation examines the precision of body weight regulation and attempts to identify practical strategies to prevent weight gain.

First a review of the literature discusses various energetic challenges and examines how precisely humans compensate. Furthermore, the dissertation seeks to quantify the range of energetic error before physiological mechanisms correct for the energy imbalance. A pilot study was conducted to investigate if a daily 12-hour fast would prevent weight gain and affect sleep behavior. Due to poor adherence, we were unable to draw conclusions about time restricted feeding (TRF). A larger TRF study among adults was conducted to test TRF as a weight management tool and sleep aid. TRF did not cause significant weight loss, but it did significantly improve sleep quality.

No research has investigated the feasibility or acceptability of TRF as a lifestyle, so individual interviews were conducted among 21 TRF participants. Experiences with TRF were

mixed. The largest positive aspect was an improved sense of control and self-efficacy. The largest negative aspect reported was a hindrance on socializing. Mixed experiences indicate TRF may not be a feasible lifestyle for everyone. Future research should attempt to identify characteristics of individuals who may be more successful at TRF.

Finally, a blind cross-over portion reduction study attempted to find the point at which participants compensate for a reduced portion and increase intake of another food. At no point (up to 25% reduction) did participants compensate and increase consumption of dessert. This study was the first to directly measure effects of portion reduction in a within-meal setting.

BIOGRAPHICAL SKETCH

Anna Marie Sewall studied Dietetics at Cornell University. She received a Bachelor's of Science degree in May of 2014 with a double major in Nutritional Sciences and Exercise Physiology. From 2014 to 2018 Anna was enrolled in Division of Nutritional Sciences' doctoral program at Cornell University in the combined Doctor of Philosophy/Registered Dietitian position. From. 2015 to 2016 she completed the Cornell Dietetic Internship program, in which she earned her certification as a Registered Dietitian.

During the summer of 2013, Anna became a certified Personal Trainer through the National Academy of Sports Medicine. In 2018 she completed a clinical research internship at the National Institute of Health in Bethesda, Maryland. Most recently, Anna defended her doctoral dissertation and earned her PhD, advised by Professor David Levitsky, in the Division of Nutritional Sciences.

Anna's future plans include continuing physiology research. She plans on working as the Chief Executive Officer of Iron Sage Consulting to translate the latest research into practical recommendations for athletes and clients looking to improve their health. She enjoys lifting weights, cooking, taking her dog Bentley for walks, swimming, biking, and spending time with her wonderful boyfriend, friends and family.

This dissertation is dedicated to Dr. David Levitsky. David took me under his wing and shared his knowledge and passion for teaching, research, discovery, and academia. I am forever grateful for his guidance and mentorship, he is an exemplary role model.

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My greatest thanks go to my parents, Charles and Penne Sewall. I would not be where I am today with what I have accomplished without all of your love and support. You encouraged me to pursue my dreams and supported me along every step of the way. You went above and beyond as parents and I am forever grateful for all you have done for me, thank you.

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CHAPTER 1: QUANTIFYING THE IMPRECISION OF ENERGY INTAKE OF HUMANS TO COMPENSATE FOR IMPOSED ENERGETIC ERRORS: A CHALLENGE TO THE PHYSIOLOGICAL CONTROL OF HUMAN FOOD INTAKE

Introduction

The preponderance of studies of the control of food intake has been devoted to illuminating the biological signals and pathways that are involved in energy intake. A PubMed search of the literature containing the words "food intake" in the title from the year 2000 to the present yielded 457 English titled review articles, of which 79% discussed some aspect of the biological control of food intake. Only 11% were devoted to exploring environmental or behavioral determinants of eating behavior.

Although biological theories of food intake can be traced to the classic work of Walter Cannon (Cannon & Washburn, 1912), Edward Adolph (Adolph, 1947), and Curt Richter (Richter, 1927), the current resistance to accept the power of biological determinants to explain eating behavior emanated from the framework of a Set-Point Theory of the control of body weight first established by Gordon Kennedy more than a half century ago (Kennedy, 1953).

The concept of a Set-Point for body weight (fat) was quickly accepted by (a) clinicians who used it to explain their failure at developing effective methods to produce sustained weight loss, (b) physiologists and psychologists who avidly subsumed it as a unifying mechanism bridging the gap between physiological sensors and behavior and by (c) pharmacologists who viewed it as the ultimate rationale to allow them to search for the substances that would signal the brain with information as to how much fat was on the body.

Shortly after the Set-Point theory was introduced, theorists began modifying the theory to explain why certain conditions such as the effect of the seasons or changes in hormonal level seem to move body weight to different levels that appeared to be regulated. Mrosovsky and Powley (Mrosovsky & Powley, 1977) began speaking of Set-Point**s,** rather than a Set-Point to explain these phenomena. Others pointed out that multiple set-points for body weight reduce the explanatory power of the Set-Point Theory and imposes several theoretical problems for the Set-Point Theory as an explanatory concept (Davis & Wirtshapter, 1978). Further complexities for a simple Set-Point Theory of body weight were added with the idea that, in addition to a physiologic homeostatic system that regulates body weight around a biological set-point, a non-homeostatic (hedonic) system coexists that modulates food intake through pleasure of taste and eating that may have its own neurochemical system in the brain. (Berridge, 2007, 2009; Berthoud, 2006).

More recently, alternative models to the Set-Point Theory have been proposed to account for not only the stability of human body weight over long periods of time, but also to explain perturbations of a fixed body weight during holiday eating (Cooper & Tokar, 2016; Schoeller et al., 2014; Yanovski et al., 2000) or periodic fasting (Heilbronn, Smith, Martin, Anton, & Ravussin, 2005; Trepanowski et al., 2017; Varady et al., 2015). Collectively, these theories are known as Dual Intervention Point models (Herman & Polivy, 1984; Levitsky, 2002; Speakman et al., 2011). What the models of eating behavior have in common is the idea that human body weight is bound by two limits: an upper and a lower limit, as shown in Figure 1. Biological mechanisms that modulate the food intake are activated only when body weight exceeds the upper limit of the settling zone in the form of excessive body fat. Similarly, if body weight drops below the lower boundary, an increase in energy intake and a decrease in energy expenditure would occur. However, within these two limits, eating is determined, not by physiological factors, but rather by environmental factors and habit ((Levitsky, 2005; Levitsky & Pacanowski, 2011; Wansink, 2004). Genetics may determine where on the body weight continuum the "Settling Zone" will be set. But within this zone of body weights, intake is not determined by physiological signals, but rather by environmental cues.

The width of this "Settling Zone" is important to both theory and practice. If the zone is very small, then it will be impossible to lose and maintain a reduced body weight because to do so requires a continuous battle with the physiological signals that drive body weight to return to its programed value. A narrow "Settling Zone" would mean that the solution to the obesity and overweight problem will depend on discovering and understanding the biological mechanisms that control eating behavior. On the other hand, if the zone is wide, then it should be possible to alter body weight for long periods of time and possibly avoid many of the expensive medical treatments that would be required to treat excessive body fat and obesity.

One way to estimate the size of this Settling Zone is to determine the extent to which energetic errors (deviations from homeostatic calorie intake and expenditure) imposed on humans need to accumulate before adjustments in either energy intake or energy expenditure are initiated to prevent further weight gain or loss. We could find no previous attempt to estimate the size of the energetic error where humans are challenged with energy surfeits or energy deficits and the degree to which energy intake matched the energetic challenge was measured. The purpose of this paper is to systematically review the published literature where humans were subjected to various energetic challenges and the changes in energy intake were measured.

Research Protocol

Search strategy and eligibility criteria

We conducted eight systematic reviews of studies which examined some challenge to energy balance and measured its effect on the amount of energy consumed. The databases used for the search was Google Scholar, PubMed, and Web of Science. The search terms were: “exercise”, “energy”, “consumption”, “intake”, “appetite”, “energy expenditure”, “overfeeding”, “breakfast”, “skipping”, “alternate day”, “activity”, “feeding”, “hunger”, “compensatory”, “compensation”, “energy restriction”, “underfeeding”, “portion size”, “diet”, “snacks”, “satiety”, “energy density”, “eating”, “lunch”, “dilution”, “meal”, “reduced fat”, “refeeding”, “expenditure”, “fast”, “deficits”, “substitutes”, and “restricted”.

Selection process and data analysis

The inclusion criteria for the weight loss and prevention studies included: (1) that the study was published between 1980 and the present, (2) food intake was measured in energy, or body weight values are presented from the beginning to the end of the intervention, and (3) a control group not subjected to the treatment was used. In addition, the following information was provided: the percent females, study duration, and sample size. If the study did not have all of this information and was not published in English, it was excluded. The studies were classified into one of these eight categories: (a) Alternate day fasting, (b) Diet Composition (c) Exercise, (d) Overfeeding, (e) Portion Size, (f) Meal Skipping, (g) Sugar or Fat Substitute and (h) Underfeeding.

Calculation of expected intake

The calculation of the expected and observed energy intake was made for each study. Expected intake is an estimation of the energy ingested if complete energetic compensation had occurred through the adjustment of energy intake. For studies categorized as alternate day fasting, the expected intake was the amount consumed on the *ad libitum* feeding day plus the difference between the usual consumption and the amount consumed on the semi-fasting day. This was done because one would expect an individual to consume the typical eating plus any additional calories missed on the fasting day. For the dietary composition studies, the expected intake was the non-intervention energy intake plus the difference in energy content between the energy dilution or the energy surfeit as a result of the changed caloric density and the non-intervention intake. For the exercise studies, the expected intake was the energy intake in the absence of the intervention plus the energy cost of the exercise. The expected intake for the overfeeding studies was calculated as energy intake without the intervention minus the difference between usual intake and the overfeeding. Similarly, the expected intake for the underfeeding studies was energy intake without the intervention plus the difference between usual intake and the underfeeding. The expected intake for the portion size studies was equal to amount consumed on the next smaller portion served. For the studies that involved restriction of meals, the expected intake was the caloric intake without the intervention plus the energy deficit caused by the dietary restriction of the previous meal.

Several studies did not include measured intake but did contain weight loss curves with sufficient data of the participants to use the formula of Hall (Kevin D. Hall et al., 2011) to estimate energy intake for the observation period. Also, for several of the studies the actual values for energy intake or expenditure were extracted from the figures. This was accomplished by using a Graph Digitizing Software, Un-Scan-it (version 7.0, Silk Scientific Corporation, Orem, UT, 84059).

The Energetic Error was determined for each group of studies and was equal to (Expected Mean Energy Intake to maintain weight – Observed Mean Energy Intake in the intervention) / Expected Mean Energy Intake to maintain weight. Essentially, energetic error is the deviation (either positive or negative) from a baseline or expected intake.

The statistics were determined using the statistical software JMP (JMP Pro 12.0.1, 2015 SAS Institute Inc.). A multiple linear regression was used to determine the contribution of percent females, sample size, and the duration of the study to the Energetic Error. Linear regressions were also performed to determine the significance and the slope the function relating observed intake as a function of the expected intake. All functions had the intercept set at zero and was compared to a slope of one as the indicator of complete compensation.

The selection of studies to be included as the initial estimation of the Energetic Error was performed by eight members of the Levitsky research group in addition to the author and double checked by David Levitsky.

Results

A total of 713 studies were identified by searching titles and abstracts, from which data was extracted from 197 studies and subjected to analysis. Studies were not included in the analysis because they did not meet all of the inclusion criteria. The mean and 99th percentiles of the Energetic Errors are presented in Table 1 and displayed graphically in Figure 1.

	Studies	Groups	Participants	Energetic Error	Lower 95% CI	Upper 95% CI
Alternative Day Fasting	10	20	402	-0.3270	-0.3950	-0.2590
Composition	33	147	3194	0.1362	0.0709	0.2015
Exercise	74	176	3526	-0.2008	-0.2311	-0.1705
Overfeeding	14	43	908	0.3999	0.26474	0.5350
Portion Size	9	28	988	0.2903	0.13851	0.4420
Skipping Meals	15	26	873	-0.2456	-0.3287	-0.1624
Caloric Substitutes	28	72	1793	-0.2032	-0.2708	-0.1355
Underfeeding	14	32	482	-0.2040	-0.2871	-0.1208
Total	197	544	12166			

Table 1 Energetic errors

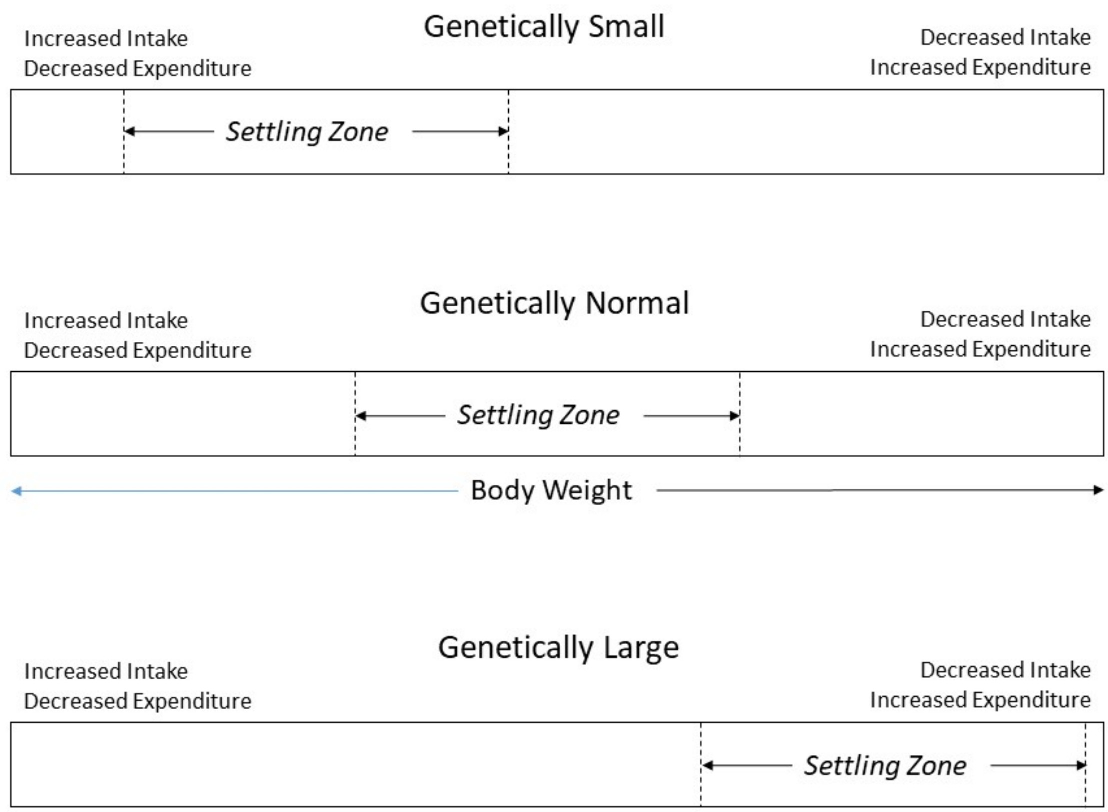

Figure 1. Schematic diagram of the Settling Zone.

As displayed in Figure 2, the Energetic Error for any category of intervention did not overlap with zero. Regardless of how the Energetic Error was induced, the change in energy intake was never sufficient to fully overcome the imposed energetic surfeit or deficit. The multiple linear regression analysis indicated sex had a significant effect on compensation in every category except Underfeeding and Portion Size. The duration of the study had no effect on the degree of compensation in any category.

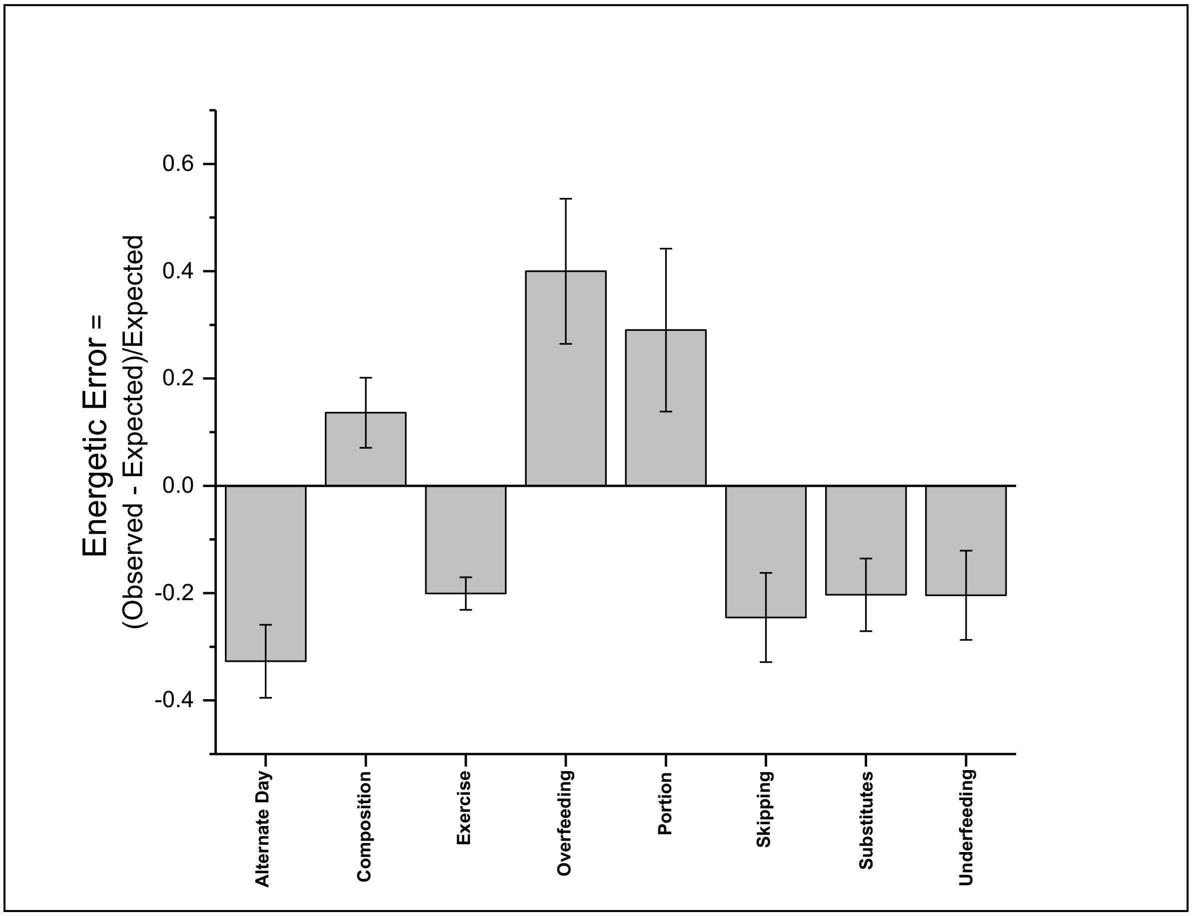

Figure 2. Mean difference between Expected Intake and Observed Intake for each of the eight kinds of energetic challenges.

A greater sense of the imprecision of human food intake to adjust to imposed energetic errors can be obtained from Figure 3, which depicts the regression of Observed Intake against the Expected Intake for each of the eight categories of studies where the energetic challenges required an increase energy intake to achieve perfect energy balance. The solid line in each figure represents perfect energy balance where the increase in energy intake would completely offset the energy deficit. The dotted line shows the actual linear regression. Each point on the graphs represents the mean of each individual group from every study that met the criteria for inclusion. The figures further demonstrate that whenever an increase in energy intake was required to compensate for an energy deficit, the increment was never sufficiently precise to completely compensate for the energy deficit, resulting in a negative energy balance. The *p*-value in each graph indicates the probability that the slope of the regression (dotted line) of the observed responses to the energetic challenges is significantly different from perfect compensation (solid line).

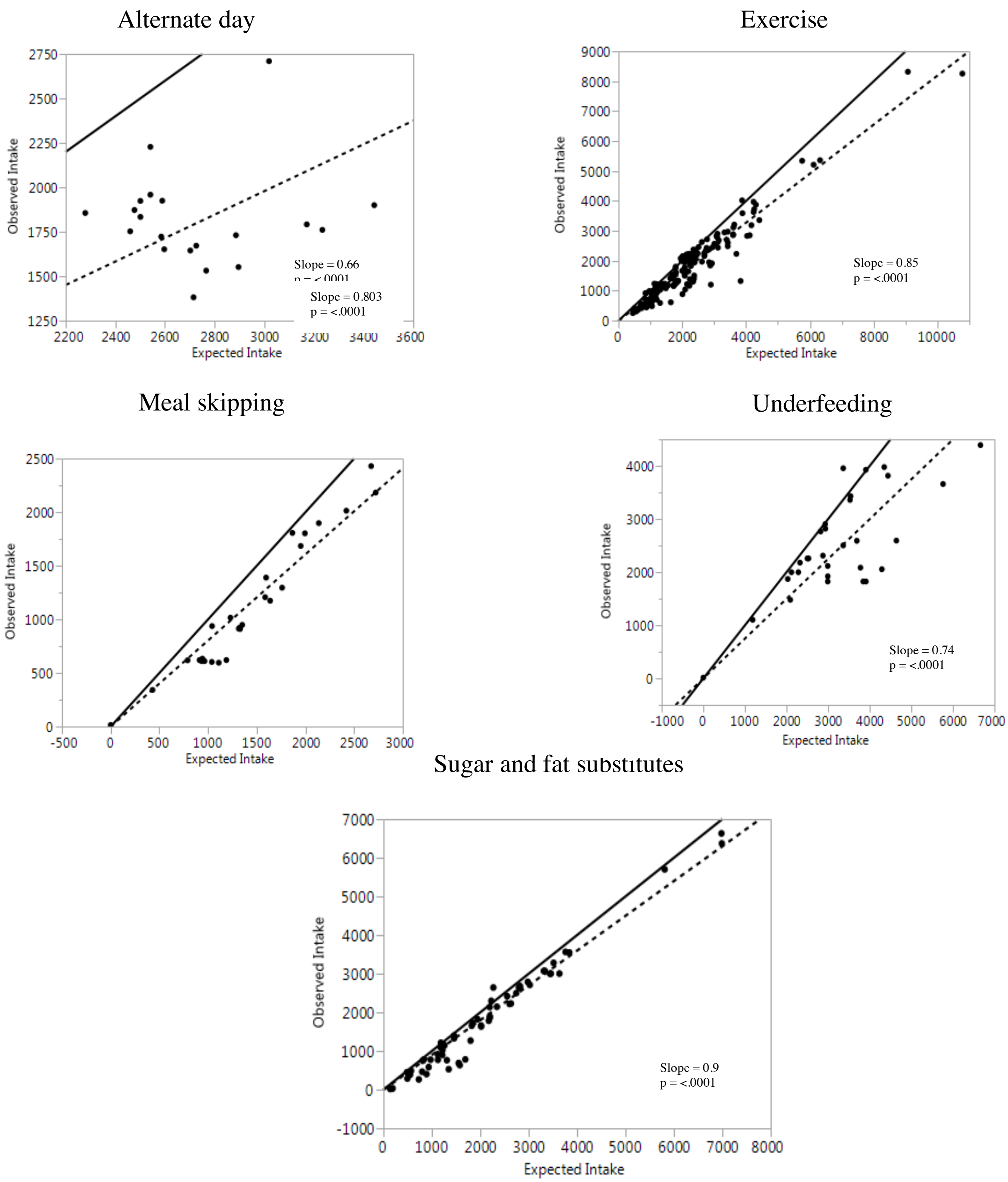

Figure 3. A scatter plot for each of the five categories of energetic challenge studies that required an increase in energy intake to compensate for the energetic error. The solid line represents complete compensation.

Figure 4 shows a similar plot for the three studies that required a decrease in energy intake to counter an increase in energy intake caused by the energetic manipulation. In every situation, the decrease in energy was never sufficiently precise to offset the surfeit of energy consumed caused by the energetic challenge.

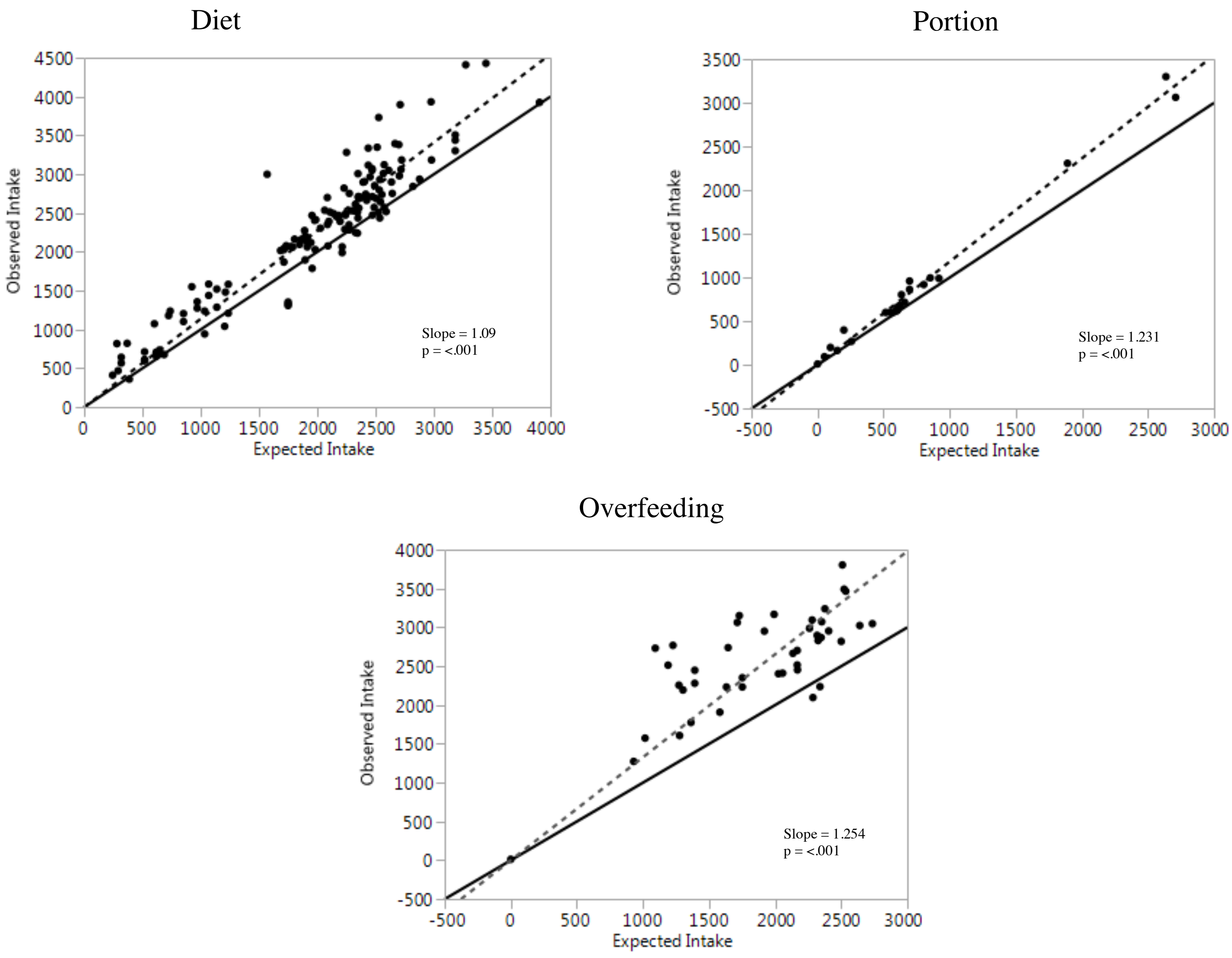

Figure 4. A scatter plot for each of the three categories of energetic challenge studies that required a decrease in energy intake to compensate for the energetic error. The solid line represents complete compensation.

Discussion

The purpose of this study was to estimate the degree to which energetic challenges in humans are met with compensatory changes in energy intake. The results show, quite clearly, that regardless of how the energetic challenges are produced, humans do not respond by precisely compensating for the energetic error by adjusting energy intake.

This review purposely avoided the literature of the control of energy expenditure as a mechanism for controlling body weight. Indeed, there is considerable evidence that changes in energy expenditure may compensate for perturbations in energy balance (Leibel, Rosenbaum, & Hirsch, 1995) and thus offset errors in energy balance. However, the point of this paper was to estimate how the precision of the control of human energy intake to compensate for imposed energetic errors to order to maintain energy balance and a constant body weight.

The Dual Intervention Point Theories of body weight postulate that a range of body weights exist for each individual, a Settling Zone (Speakman et al., 2011), within which the physiological control of energy intake does not operate. From this review, the magnitude of this Settling Zone appears to be quite large. The average (absolute) energetic error derived from all the energetic challenges reviewed in this study is about 25%. A 25% increase in the average American daily energy intake (2800 kcal) would results in energy intake of the average American to be about 700 kcal. Using the energetic equations of Kevin Hall (K. D. Hall, 2017), such a large energetic error, if repeated daily, would result a weight gain of about 50 lbs. in one year. This gain in weight far exceeds the weight gain in longitudinal studies.

In a recent study by Dutton *et al.,* the average annual weight gain between the ages of 18 until 55 is approximately 0.65 kg (1.4 lbs.) for males and 0.68 kg (1.5 lbs.) per year for females (Dutton *et al*., 2016). Because the increase in body mass (about 5000 calories) is relatively small compared to the average amount of calories we ingest each year (about 800,00 kcals), it is frequently argued that a physiological control system must be operating (Harris, 1990; Leibel et al., 1995).

This reasoning, however, may not be correct. It is possible to have daily energy intake determined by random environmental forces and still maintain body weight relatively constant. Consider the following alternative model of energy intake based on two assumptions. First, total daily energy intake and daily energy expenditure are determined by random, normally distributed, environmental events. Second, energy expenditure increases with increasing body mass. This latter assumption is quite well-founded because many have shown that lean body mass increases with increasing body weight and lean body mass has a high energy expenditure (Forbes, 1987; Janssen, Heymsfield, Wang, Ross, & Wang, 2000). Skeletal muscle comprises a great deal of lean mass, among bones and organs, and increases as body weight increases because it takes more force to move a larger object. Moreover, simple physics tells us that carrying a larger body mass requires more energy than carrying a small body mass.

In addition, habit may also play a large role in reducing the variability of an individual's daily energy intake. It is well established that humans consume a rather constant daily energy intake over long periods of time (Edholm et al., 1970; Edholm, Fletcher, Widdowson, & McCance, 1955; Levitsky et al., 2017) and is frequently expressed as a higher within subject correlation of successive daily intake than between subject correlations (Mcgee, Rhoads, Hankin, Yano, & Tillotson, 1982; Obarzanek & Levitsky, 1985; Sempos, Johnson, Smith, Gilligan, & Johnson, 1985; Tarasuk & Beaton, 1991). Such a model as the one proposed above plus the damping action of habit could produce a stable body weight over long periods of time without the necessity of using a physiological control mechanism.

The only study which purports to have demonstrated precise compensation of energy intake for increases in energy loss was published recently by Polidori *et al.* (Polidori, Sanghvi, Seeley, & Hall, 2016). They reported a one-year study where a negative energy balance was imposed in participants who were taking a daily dose of Canagliflozin, a drug that caused a loss of glucose (calories) through the kidneys. Using mathematical equations and the rate of decline in mean body weight they inferred that an increase in energy intake must have occurred to offset the loss of energy from the body. However, no direct measurement of energy intake was made. We will have to wait to see if such calculations can be substantiated through subsequent studies.

One limitation of this review is that almost all the studies measured energy intake over relatively short periods of time. It is possible that energetic errors require more than several days to correct the energy imbalance. Most of the studies measured tracked energy intake at most for only a few days. Indeed, only long-term recovery trials in response to imposed energetic errors can truly answer this question. What we can say, however, that physiological signals have little influence over short-term mechanisms involved in the control of food intake.

In conclusion, a review of 197 published results from various kinds of studies where an energy deficit or energy surplus have been imposed in humans and energy intake was measured, the overwhelming result is that compensation is never precise.

CHAPTER 2: PILOT STUDY

Introduction

Kennedy (1953) introduced the pervasive idea that people can precisely regulate body weight through biological control of food intake. This theory, set-point theory (SPT), is rooted in control theory. SPT researchers suggest a feedback mechanism regulates body weight (i.e., total lipid volume) to maintain a predetermined weight (i.e., the set-point) (Wirtshafter & Davis, 1977). Deviations from the set-point generate an error signal in the brain that alters behaviors (e.g., eating, activity) to correct the energetic error and return the body to homeostasis. An energetic error is considered an over- or under-consumption of calories to maintain body weight. The result is a relatively constant body weight. SPT aligns well with modern understandings of the brain's role in maintaining other biological variables (e.g., blood pressure, blood glucose). These variables rely on feedback mechanisms to maintain homeostasis; regulation of body weight may be similar. SPT accurately reflects body weight regulation, but there are phenomena of over- and under-eating that the theory cannot explain.

Body weight of people around the world is increasing so drastically that it is an epidemic (Muller *et al*, 2018). The obesity epidemic is contrary to SPT. Young adults in the United States gain weight faster than older adults, gaining approximately 0.45-0.9 kg per year, and continue past adolescence into mid-life with the fastest rate of weight gain between the ages of 18 to 25 years old (Arnett, 2000; Wing et al., 2016). According to SPT, the set-point in these individuals must be either labile or inoperative under certain conditions. SPT also fails to account for periods of reduced body weight (Speakman et al., 2011). If there was a specific set point, the individuals would compensate to maintain their weight and prevent weight loss. There are several methods to reduce energy intake (EI) and body weight, thus challenging the SPT. Methods to induce a calorie deficit include: decreasing the energy density of food, decreasing portion size, limiting social facilitation, reducing the variety of foods, and skipping meals or snacks (Casazza et al., 2016).

One method to manage calorie intake is intermittent fasting (IF). IF is a broad term that encompasses several fasting protocols that manipulate the timing of eating using short-term fasts or semi-fasts (Tinsley & LaBounty, 2015). IF may include elimination of meals or snacks to reduce EI. Skipping meals or snacks has been shown to be effective for reducing calorie intake (Levitsky & DeRosimo, 2010; Levitsky & Pacanowski, 2011, 2013). In a randomized crossover trial, participants consumed either no breakfast, a high carbohydrate breakfast (335 kcal), or a high fiber breakfast (360 kcal) on three separate occasions and ate an *ad libitum* lunch. There was no difference in intake at lunch between skipping and eating breakfast nor did the type of breakfast matter (Levitsky & Pacanowski, 2013). Skipping breakfast resulted in a net caloric deficit of 408 kcal that contributed to weight loss. Hence, skipping a meal does not result in complete energy compensation at subsequent meals (Levitsky & Pacanowski, 2013).

More drastic calorie restrictions also have poor energetic compensation (Levitsky & DeRosimo, 2010). Twenty-two women underwent a randomized calorie restriction one day per week for four weeks. Monday to Friday participants ate measured food from a metabolic kitchen. There were three groups and on Monday they either ate 1) *ad libitum* 2) a 1200 kcal meal, or 3) fasted. They ate *ad libitum* Tuesday through Friday. Body weight decreased with a 1200 kcal diet and decreased further with fasting, but did not decrease in the *ad libitum* group. Recovery of body weight occurred in all groups without increasing spontaneous food intake; control of food intake was not the primary mechanism of body weight homeostasis (Levitsky & DeRosimo, 2010).

A final demonstration of poor caloric compensation is the use of meal replacements (Levitsky & Pacanowski, 2011). Seventeen participants consumed a portion-controlled lunch replacement instead of eating *ad libitum* for two weeks, ~250 kcal reduction. Levitsky and Pacanowski (2011) found no sign of caloric compensation and a significant (0.51 $\pm$ 0.17 kg) loss of body weight because participants did not compensate. Reducing the time a person has available to eat during the day may result in eliminating snacks or meals. Consuming fewer meals or snacks decrease calorie intake and increase weight loss. Hence, restricting eating time may be a method to reduce calorie intake to cause weight loss because the body does not compensate. This chapter includes details from literature regarding an understudied area of energetics: reducing the hours in a day that one eats (i.e., IF).

Forms of Intermittent Fasting

There are various forms of intermittent fasting ranging from alternate day fasting (ADF) in which participants alter days of *ad libitum* intake with a fasting day (0-25% of daily calorie needs) to time restricted feeding (TRF) that limit the hours of eating throughout the day. A 2019 Google search of *intermittent fasting* yielded 48,300,000 results. However, there is a dearth of evidence-based research supporting IF as a safe and effective public health practice. This gap in the literature warrants the present investigation.

Ramadan and Body Weight

One natural study of the effect of TRF is Ramadan, the ninth month of the Islamic calendar, a month of fasting. During Ramadan, Muslims fast from sunrise to sunset and consume all food and beverages at night. The duration of fasting changes annually based on the lunar calendar. Researchers consistently find that people lose weight during Ramadan (Khattak et al., 2012; Mansi & Amneth, 2007). Mansi and Amneth (2007) evaluated the effect of Ramadan fasting on 42 healthy Jordanian male students (mean age 21 $\pm$ 1.6 years). Mean weight changed from 76.64 $\pm$ 9.53 kg one day before Ramadan to 72.66$\pm$ 9.2 kg the fourth week of Ramadan (Mansi & Amneth, 2007). Similarly, Khattak et al. (2012) studied the energy and nutrient intakes of male university students by taking anthropometric measurements one day before Ramadan and on day 21 of Ramadan. Participants kept food records and Khattak et al. (2012) analyzed the averages of their energy and macronutrients intakes. There was a significant ($p < 0.05$) decrease in body weight despite no change in reported calorie intake. These results question the accuracy of the participant food records. A study of 57 young Jordanian women measured body weight and body composition during Ramadan; body weight and body mass index (BMI) decreased significantly ($p < 0.05$) during the fasting period (Al-Hourani & Atoum, 2007).

Worldwide, changes in body weight occur during Ramadan; fasting results in significant weight loss, averaging 3 pounds overall for both men and women (Sadeghirad et al., 2014). People regain this weight a few weeks after Ramadan after returning to their previous eating habits (Sadeghirad et al., 2014). Recovery of body weight implies a decrease in EI during the fasting period. Such fluctuations in body weight refute the idea of precise body weight regulation (SPT). If body weight regulated automatically, there would have been no, or very insignificant weight loss during the fasting period. Participants would consume adequate calories to maintain their weight at their set-point, but this was not the case. Body weight regulation is not precise enough to cause participants to sufficiently increase calories during the fast to maintain their weight. In all Ramadan studies, researchers measure body weight using a scale and estimate calorie intake from food records (Al-Hourani & Atoum, 2007; Khattak et al, 2012; Sadeghirad et al., 2014). Generalizing results to a broader population is difficult. Foods consumed during Ramadan are not typical parts of the diet beyond the holiday and eating occurs only at night (Reilly & Waterhouse, 2007). The variability in fasting time and dietary habits makes generalizing about changes in body weight and diet composition during Ramadan difficult (Trepanowski & Bloomer, 2010).

Alternate Day Fasting (ADF) and Body Weight

The most extreme version of IF is ADF. ADF is consuming an *ad* libitum diet on one day (known as the feed day) and fasting (or only eating one small meal) on the subsequent day (known as the fast day). The feed and fast days are alternated, hence the name alternate day fasting. There are few randomized clinical trials of ADF in humans. Trepanowski et al. (2017) compared the effects of ADF and daily calorie restriction on weight loss, weight maintenance, and cardiovascular disease risk indicators in a clinical trial of obese adults, and concluded that 21 ADF participants lost weight (-6.8% [95% CI, -9.1% to -4.5%] ADF vs -6.8% [95% CI, -9.1% to -4.6%] DCR) over the six month intervention and regained some weight after the treatment ended during a six month follow-up period (-6.0% [95% CI, -8.5% to -3.6%] ADF vs -5.3% [95% CI, -7.6% to -3.0%] DCR). Similarly, Catenacci et al. (2016) conducted a randomized pilot study used an ADF diet that consisted of zero calories on the fasting days and *ad libitum* intake on alternate days. Fourteen obese adults (BMI > 30) ages 18 to 55 completed an 8-week ADF intervention and achieved a 376 kcal/day greater energy deficit than the daily calorie restricted group, resulting in a mean weight loss of 8.2 $\pm$ 0.9 kg (Catenacci et al., 2016). Weight loss in both groups supports non-compensation.

If SPT was correct, the ADF group would not have lost weight because they would have consumed adequate calories on the *ad libitum* day to compensate for the calorie deficit on the fasting days. On fast days, average EI was 44.4 kcal and 2565.5 kcal on *ad libitum* days. Therefore average daily calorie intake was 1,304.9 kcal/day. Participants regained weight only after terminating the treatment (Catenacci et al., 2016). Weight regain after the study ended indicates participants likely reverted to previous eating habits, at least partially. If participants would have maintained the ADF regime, they likely would have maintained their weight loss achieved during the study.

In addition to randomized controlled trials, many ADF human studies suggest an association between ADF and weight loss (Bhutani et al., 2010; Bhutani et al., 2013; Donahoo et al., 2009; Eshghinia & Mohammadzadeh, 2013; Heilbronn et al., 2005; Johnson et al., 2007; Klempel et al., 2013; Varady et al., 2009; Varady et al., 2011; Varady et al., 2013). Protocols varied in experimental design, duration, participant characteristics (e.g., age, gender, and weight), and caloric intake on fasting days. All participants lost weight after ADF regardless of protocol. Based on the limited number of studies, ADF is effective for weight loss in obese individuals with as little as two weeks and up to six months, but is an extreme approach, not eating for an entire day every other day. A higher dropout rate in ADF compared to a daily calorie restriction implies that a less restrictive version could provide similar results with better adherence (Catenacci et al., 2016).

Time Restricted Feeding and Body Weight

TRF is not religious fasting or ADF. IF has positive results for weight loss (Varady et al., 2013). Only eight human trials examined a less restrictive eating period, TRF, in a non-religious setting (Sutton et al., 2018; Byrne et al., 2018; Betts et al., 2014; Chowdhury et al., 2016; Gill & Panda, 2015; LeCheminant et al., 2013; Moro et al., 2016; Gabel et al., 2019). Fifty-one obese men were randomized to 16 weeks of either continuous or intermittent energy restriction for a total of 30 weeks (Byrne et al., 2018). Participants in the intermittent group had greater fat mass moss (12.4 ± 4.8 vs 8.0 ± 4.2 kg). Furthermore, Sutton et al. found early time restricted feeding lowered the desire to eat in the evening, which may facilitate weight loss among other health improvements even in the absence of weight loss (Sutton et al., 2018). Moro et al. (2016) examined the effects of eight weeks of an eight-hour feeding window in 34 normal weight, resistance-trained males and reported a significant ($p < 0.007$) decrease in fat mass in the TRF group compared to the control (CON) group. Chowdhury et al. and Betts et al used the same protocol but in two different study populations. Chowdhury et al. (2016) studied obese participants and Betts et al. (2014) studied normal weight individuals. Lean participants did not compensate for fasting and lost weight; obese participants in the fasting group overcompensated and gained weight (Betts et al., 2014; Chowdhury et al., 2016). It is plausible that the obese participants were more likely to binge during the feeding window compared to lean individuals.

LeCheminant et al. (2013) eliminated evening intake and showed a decreased short-term EI and an increased weight loss in 29 men (20.9 $\pm$ 2.5 years old) who underwent a two-week night eating restriction that limited calorie intake to 13 hours per day. There was a -0.4 $\pm$ 1.1 kg weight loss relative to the control treatment (+0.6 kg $\pm$ 0.9); however, the study only included young male athletes, which limits generalizability (LeCheminant et al., 2013). Another TRF strategy is to allow participants to choose their own fasting/feeding time. Gill and Panda (2015) allowed participants to select an eating period of 10-12 hours each day without further instructions regarding food quality or quantity. Participants logged food pictures for 16 weeks and reduced their eating duration by an average of four hours and 35 minutes, resulting in a reduction in total body weight of 3.27 $\pm$ 0.9 kg (Gill & Panda, 2015).

The most recent TRF study found a decrease in body weight among 23 obese individuals of 2.6% $\pm$ 0.5 relative to a historical matched control group over a 12-week period with an ad libitum feeding between 10:00-18:00 (Gabels et al., 2018). Existing studies provide inadequate data regarding whether an ad libitum diet with mildly restricting eating periods to a self-selected time results in weight loss.

Calorie Consumption Timing and Body Weight

People consume more food as the day progresses (Gill & Panda, 2015) and associate evening hours with snacking and high calorie consumption (Striegel-Moore et al., 2006). Epidemiological data suggests that consuming more calories later in the day leads to weight gain (Andersen et al., 2004; Baron et al., 2011; Eng et al., 2009; Gluck et al., 2008; Tholin et al., 2009). Night eating is not possible with TRF, which requires ending calorie consumption in the early evening. TRF is an opportunity to test body weight regulation by eliminating evening calories. It is unknown whether individuals compensate for missed evening calories the following day. Existing data suggest missed evening calories are not compensated for the subsequent day. Sutton et al. (2018) found that early TRF (consuming all calories by 14:00) led to a lower desire to eat in the evening, which may facilitate weight loss (Sutton et al., 2018)

Not all data support the association between night eating and weight gain. Waller et al. (2004) instructed overweight and obese participants to consume cereal with 2/3 cup fat-free milk (total of ~200 kcal) instead of their usual evening snack. The CON group consumed their typical evening snack without restrictions. The treatment group lost an average of 1.85 $\pm$ 3.56 pounds in four weeks; the CON group lost an average of 0.39 $\pm$ 3.1 lbs. (Waller et al., 2004). Night eating may have some benefits such as increased protein synthesis and reduced appetite the following morning, which could affect body weight. Human trials have shown increases in muscle mass after night eating compared to CON groups (Figueroa et al., 2014; Groen et al., 2012; Kinsey et al., 2014; Madzima et al., 2014; Ormsbee et al., 2015; Waller et al., 2004). These researchers did not record long-term weight measurements, except for Waller et al. (2004). Therefore, limited data is available regarding how the timing of calorie consumption affects body weight. Controlled trials do not show weight gain with the exception of Chowdhurry et al (Chowdhury et al., 2016). Observational data only provides correlation, not causation, and there is no evidence that calorie intake at night causes weight gain. Calories consumed at night may contribute to weight gain due to an energy surplus rather than a physiological predisposition to lipogenesis in the evening. That is, even though insulin sensitivity and glucose tolerance are higher in the morning than at night, energy balance is the determinant of weight gain or loss. Another contributing factor to weight gain from night eating is calorie density, which increases as the day progresses (LeChiminant et al., 2014).

Sleep

Cross-sectional and observational studies suggested a positive correlation between unintentional sleep curtailment and chronic high EI (Cappuccio et al., 2008). However, experimental evidence is equivocal at best.

As of 2019, 14 studies assessed the effect of partial sleep deprivation (PSD) on energy balance (Al Khatib et al., 2017). Of the 14 studies, seven noted an increase in EI and seven found no significant change in EI. Gupta et al. (2002) found that obese participants experienced less sleep than non-obese participants ($p < 0.01$) and for each hour of sleep lost, the odds of obesity increased by 80%. These data support the connection between sleep and EI. Similarly, a 2008 systematic review of 36 studies found that in both cross-sectional and cohort studies of young adults and children, short sleep duration is “strongly and consistently associated with concurrent and future obesity” (Patel & Hu, 2008, p. 643). Observational data suggests an inverse correlation between sleep duration and BMI; experimental data only partially suggests an increase in EI as a result of sleep deprivation (Patel & Hu, 2008).

Sleep duration is not the only variable that affects body weight and EI; sleep quality also has an effect on body weight. Individuals who have poorer sleep consume more calories and gain weight compared to when they have better quality sleep (Gonnissen et al., 2013). Researchers measure sleep quality using the Pittsburgh Sleep Quality Index (PSQI), a self-report questionnaire to assess sleep quality over a one-month interval by calculating a global score (Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). Another method of measuring sleep quality is actigraphy, a non-invasive methods of monitoring rests and activity cycles during sleep.

Subjective sleep quality increases the likelihood of weight-loss success by an average of 33% in overweight and obese women enrolled in a two-year randomized clinical trial of a weight loss program (Thompson et al., 2016). Sleep was measured using the Pittsburgh Sleep Quality Index. Partial sleep disturbance may increase EI and improved sleep quality may facilitate weight loss and promote weight control after a weight loss intervention has ended (Thompson et al., 2016).

Observational and cross-sectional data support an inverse relationship between BMI and sleep, but experimental studies fail to consistently show detrimental effects of poor sleep on EI or weight. There is little data on how TRF affects sleep. Only three TRF studies investigated sleep (Chowdhury et al., 2016; Gill & Panda, 2015; Gabel et al., 2019). Chowdhury et al. (2016) found no effect of prolonging nighttime fasting on wake time, bed time, or sleep duration in 23 adults (44 $\pm$ 10 years old; BMI 33.7 $\pm$ 4.9 kg/m^2). Gabel at et. Found no change in subjective measure of wake time, bedtime, and sleep duration among the 23 obese participants who fasted for 16 hours per day for 12 weeks.

Gill and Panda (2015) did not directly report wake time, bed time, or sleep duration; however, when investigating intake relative to fasting, they found “the total overnight fasting duration paralleled the time of inactivity (sleep) at night” (p. 793). Based on this finding, restricting feeding to 12 hours may increase sleep duration by shifting onset of sleep to earlier in the evening because people will not spend time eating in the evening. Our study is similar to Gill and Panda (2015) who found that fasting increased sleep duration and quality.

Few researchers have addressed the question of how TRF affects body weight in free-living adults, and previous work has been limited to very small study (Gill and Panda, 2015; Gabel et al., 2019). Thus it has not yet been well established whether TRF impacts sleep quantity. In addition, sleep deprivation has been shown to cause weight gain (Al Khatib et al., 2017). Therefore, TRF may reduce obesity by promoting weight loss and improve sleep quantity and quality.

The aim of this research was therefore to examine the impact of TRF on body weight and sleep in young adults. Young adults were chosen because there was a large interest in participating in such a study. In light of current evidence, we hypothesized that participants would lose weight and go to bed earlier, hence increasing sleep duration during TRF.

Methods

A randomized crossover trial was conducted among 40 young adults in Ithaca, New York. Participants weighed twice daily (once upon waking and once after their final calorie intake of the day, recorded wake and bedtimes, and photographed all food and caloric beverages before and after consumption for four weeks. No other form of dietary record was kept. For two of the four weeks participants consumed all calories within a self-selected 12-hour feeding window (TRF phase). Participants were randomized to begin in the TRF or control phase (CON). After two weeks, they switched phases. Therefore participants either completed TRF then CON or CON then TRF. Figure 5 provides details of the progress through the phases of the parallel randomized trial of the two groups of participants.

Study Population

40 participants were recruited for this crossover nutrition intervention via an in-class PowerPoint advertisement (Appendix A). Inclusion criteria included being at least 18 years of age, enrollment in NS 1150 for the fall semester of 2016, and ownership of a smart phone. Exclusionary criteria included any history of an eating disorder or diabetes. All 40 interested participants met eligibility criteria and provided written, informed consent prior to participation. The Cornell University Institutional Review Board (IRB) approved all study materials and protocol.

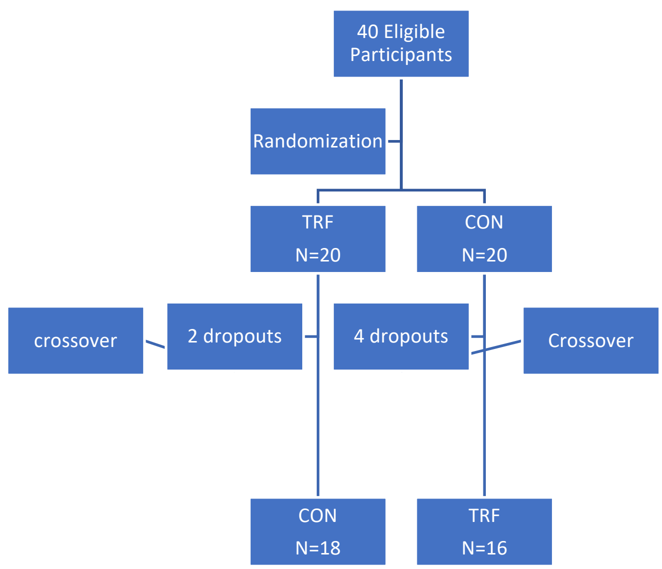

Figure 5. A flow diagram of the progress through the different phases of the parallel randomized trial of the two groups of participants. Dropouts were lost to follow-up and did not provide reasons for not completing the study.

Procedure

Participants reported to the Human Metabolic Research Unit to receive study materials and have their weight taken as a baseline measurement. Body weight was measured on a calibrated Seca (no model number available) scale and height was measured using a stadiometer (no brand or model number available). Participants removed shoes for height and weight measurements but remained clothed. Participants received a Withings body scale (WS-50 Smart Body Analyzer, Withings) with Wi-Fi and Bluetooth capabilities. They downloaded the Withings app and paired their smart phone with the scale. Usernames and passwords were obtained to access participant weight data from their individual scales during the study.

Participants were instructed to step on the scale provided to them immediately upon waking and after voiding every morning for four weeks. Weights transmitted wirelessly to a database and research personnel collected the data from individual Withings accounts after participants provided his or her username and password. After consuming the last food of the day, participants weighed themselves again. This second measurement was an indicator of their adherence to the TRF eating schedule. If a morning weight was higher than the previous evening's weight, the researcher considered it non-compliance. Participants recorded the time they awoke each day and what time they went to bed.

Participants also downloaded an app called *Eat Cornell* that captured food and beverage consumption data. The Department of Consumer Science developed the *Eat Cornell* app for this study to capture food and beverage intake with as little participant burden as possible. It was a simple app that used a camera to capture a "before" photo by tapping the before button, and an "after" photo by tapping the "after" button. Given the demographics of the study population, a photo-based food record would have better adherence and greater accuracy than a paper food log. Participants placed their student ID card (a fiducial marker) next to food items, took a *before* picture using the app, and when finished, took an *after* photo. This created a digital food record to document calorie intake. Photos were not stored in the phone but rather directly transmitted to the research database. Hence, participants could not access previous intake photos.

The researcher assigned half of the participants to begin with the TRF phase followed by two weeks of the CON phase; the other half of participants began in the CON followed by TRF phase. The CON phase consisted of daily weighing (once upon waking and once after the final intake of the day, recording wake and bedtimes, and photographing all food and beverages before and after consumption. During the TRF phase, the participants completed all aspects of the CON phase plus adhered to a 12-hour feeding window from 7:30 to 19:30 during which they could eat and drink *ad libitum*. They could drink water and non-caloric beverages *ad libitum* throughout the study without any time restriction. The researcher selected 7:30 to 19:30 as the feeding period for two reasons: (a) almost all participants (85%) relied on the dining halls for meals and the dining halls did not open until 7:30; and (b) ending calorie intake by 19:30 would eliminate night-time eating yet allow participants who played sports to consume a last meal in the dining hall before it closed at 19:00. Moreover, the researcher collected data on meal plan ownership because it was thought that eating in the dining halls may affect weight changes. Participants eating in the dining hall may not lose as much weight as those who cook for themselves due to social facilitation of eating.

Statistical Analyses

The researcher ran a repeated measures of analysis variance for body weight, wake- and bedtimes (RM-ANOVA) in SPSS (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY; IBM Corp.) to test for differences between groups over time. The labels TRF and CON are just that, labels. RM-ANOVAs look for differences in the data over the entire 28 days. The researcher checked Levene’s test of equality (Schultz, 1985) of error variances for all 28 measures of weight in the study. Significance was defined as a p-value of < 0.05 and results are presented as (mean ± standard error) because the data was not normally distributed. There were no violations of Levene's test for any of the measures, $p < .05$. The data indicated a violation of Box's test of equality (Olson, 1976) of covariance matrices ($p < .05$). The researcher defined a weight as adherent if a participant recorded it by 20:30, one hour after the end of the eating period during TRF. The researcher calculated the percent of compliant weights by dividing the number of evening weights before 20:30 by the total number of evening weights.

Results

Participants

Participants were 19.1 ± 1.15 years old and on average overweight (25.55 ± 3.98 kg/m^2). Table 2 and Figures 6-10 show participants' baseline characteristics. Of the 40 participants, 34 (85%) completed all components of the study. The researcher did not include the six participants who did not complete the study in the data analysis. Individuals who did not complete the study were on average 19.66 years old, 22.8 kg/m^2, and non-Caucasian. There was no significant difference in age ($p = 0.29$) or BMI ($p = 0.11$) between individuals who did and did not complete the study.

Table 2

Participant Baseline Characteristics

Variable	n = 34 Mean ± SE	n = 18 TRF/CON	n = 16 CON/TRF	*p*-value
Age (years)	19.1 ± 1.15	18.77 ± 1.06	19.25 ± 1.06	0.20
Height (cm)	166.7 ± 8.17	166.91 ± 9.02	166.73 ± 7.09	0.95
Body Weight (kg)	70.4 ± 13.24	74.17 ± 16.55	68.54 ± 10.23	0.26
BMI (kg/m^2)	25.45 ± 4.08	26.48 ± 4.91	24.60 ± 3.01	0.21
Female n (%)	17 (50)	9 (50)	8 (50)	
Male n (%)	17 (50)	9 (50)	8 (50)	

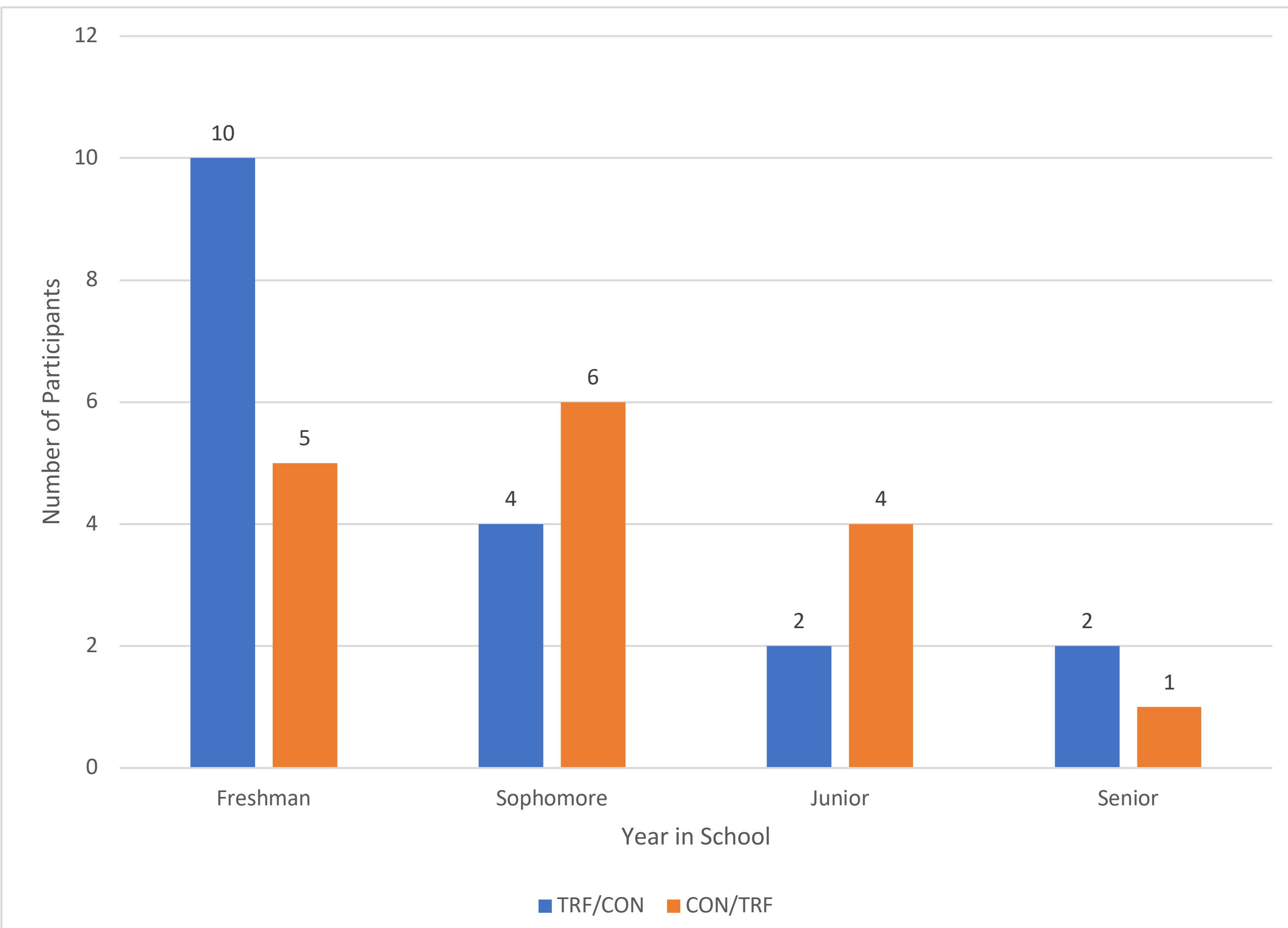

Figure 6. Class year in school of study population.

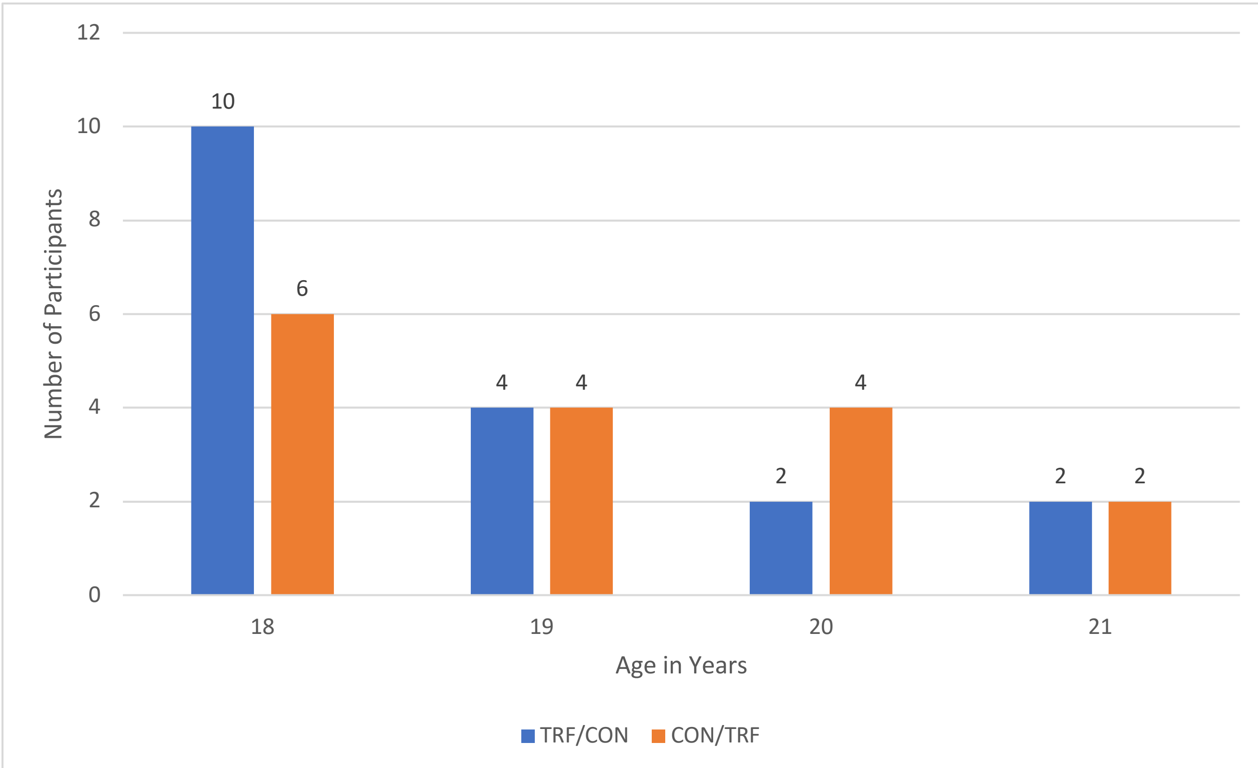

Figure 7. Study population age in years.

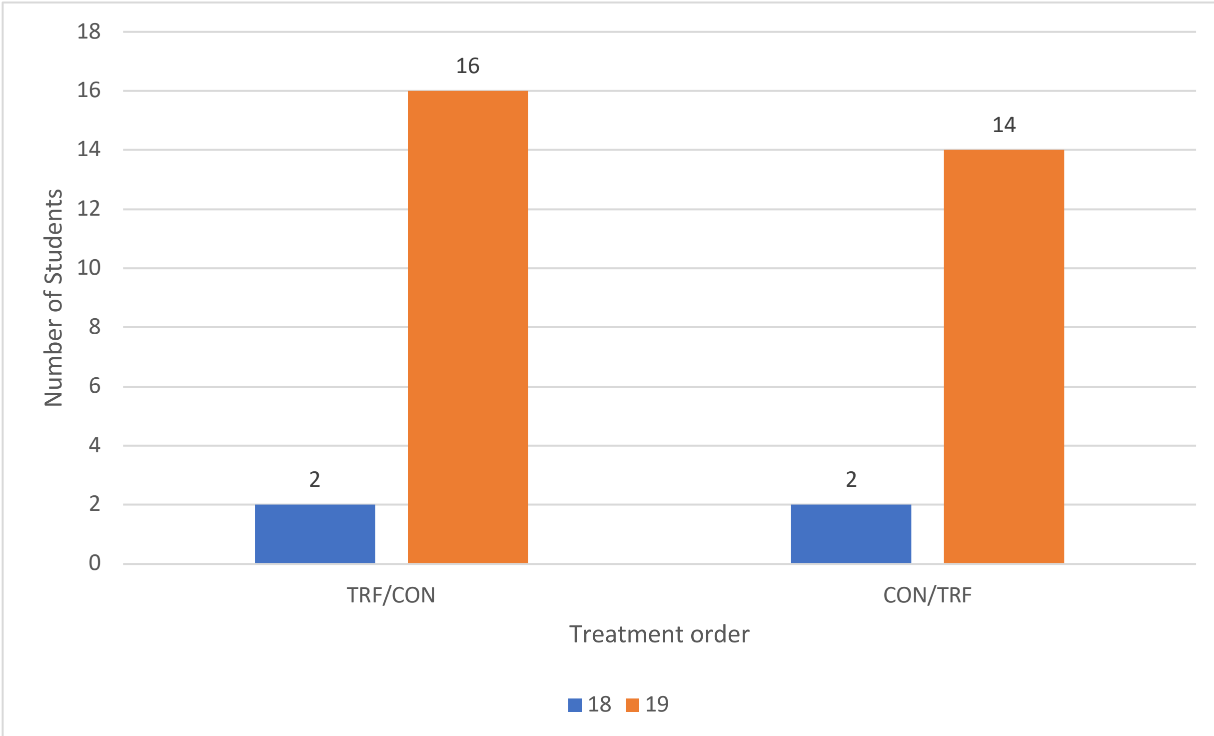

Figure 8. Meal plan ownership of study population.

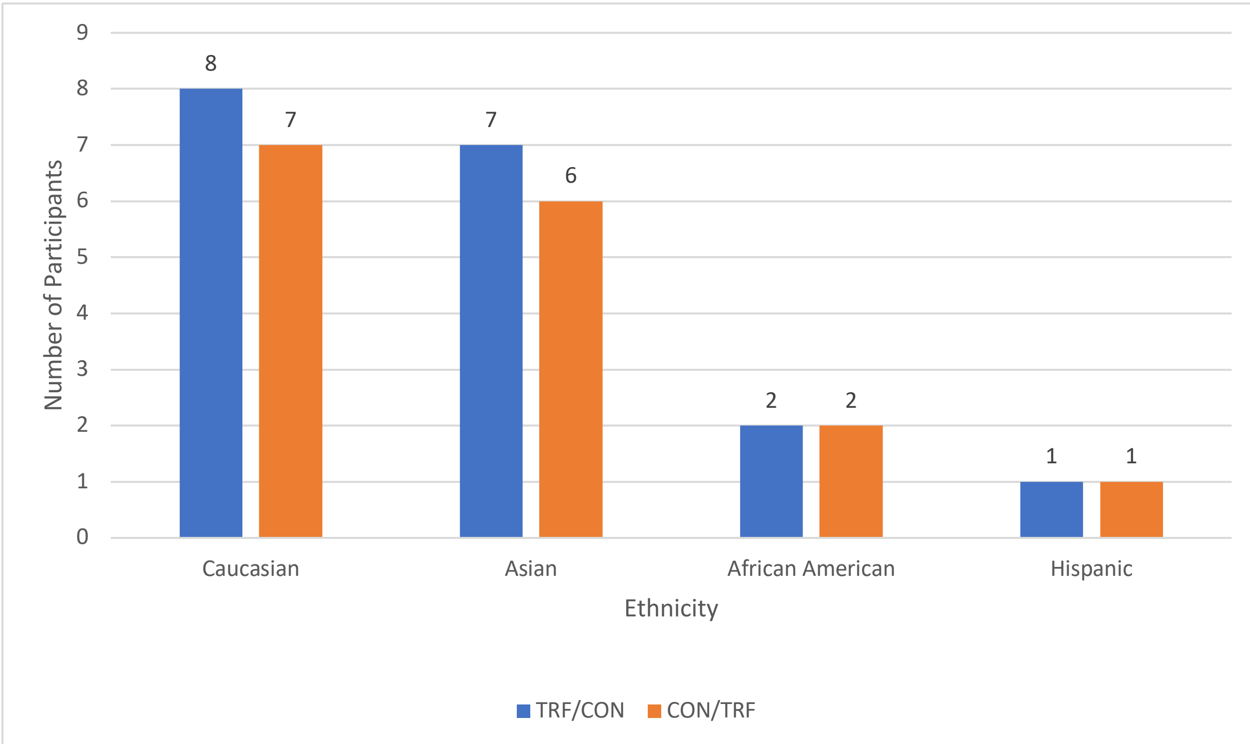

Figure 9. Study population ethnicity.

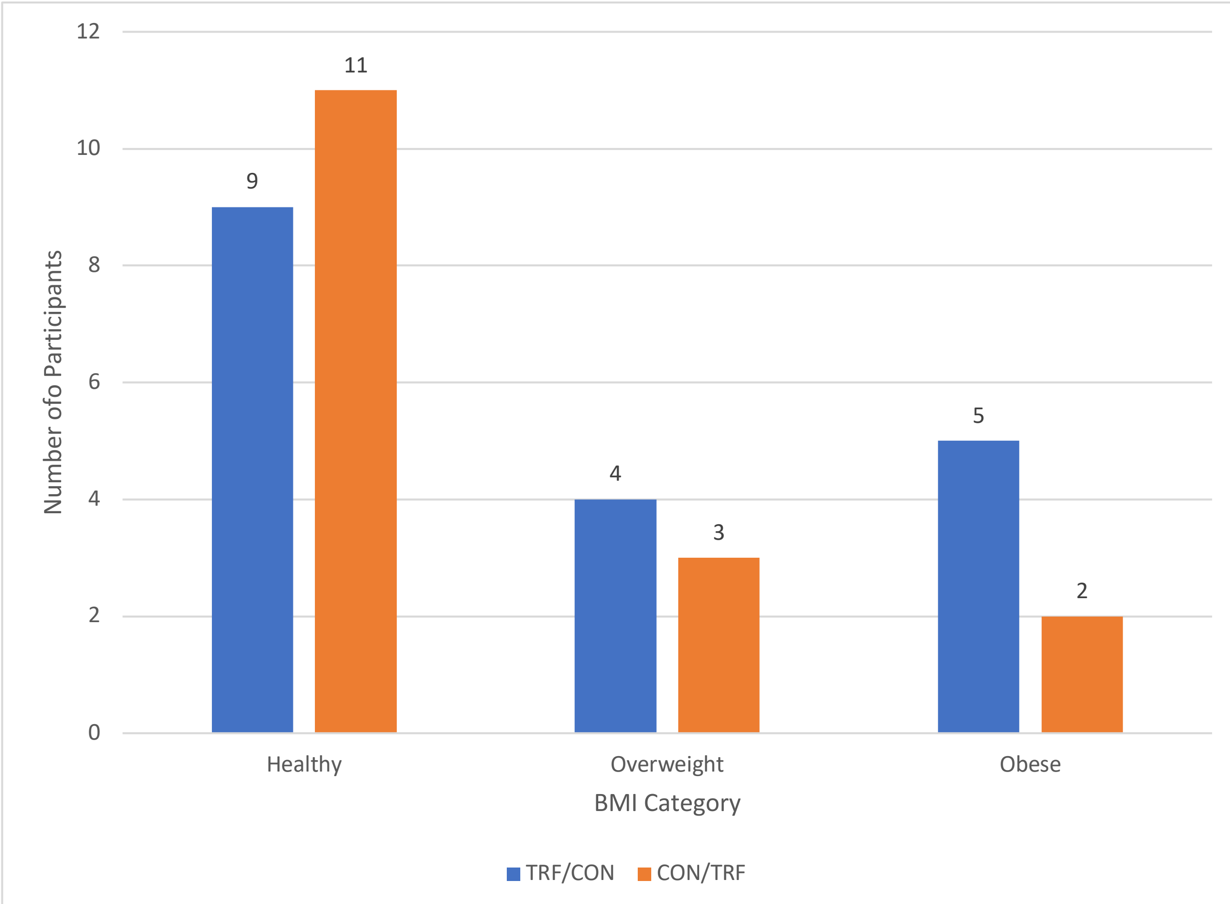

Figure 10. Study population body mass index (BMI). Healthy BMI is 18.5-24.9, overweight is 25-29.9, and obese is ≥ 30 (Bell, 2006).

Body Weight

Only six respondents had enough data to analyze thoroughly (See Figure 11). There other 28 participants had missing data (primarily evening weights). Data presented in Figure 11 is based on morning weights, which was more complete data (n = 34). Adherence was defined as having an evening weight by 20:30, one hour after the end of the feeding window. The between group differences in weight were not significant, there was little to no change in weight over time for each group. The marginal mean is the mean weight based on treatment (TRF or CON).

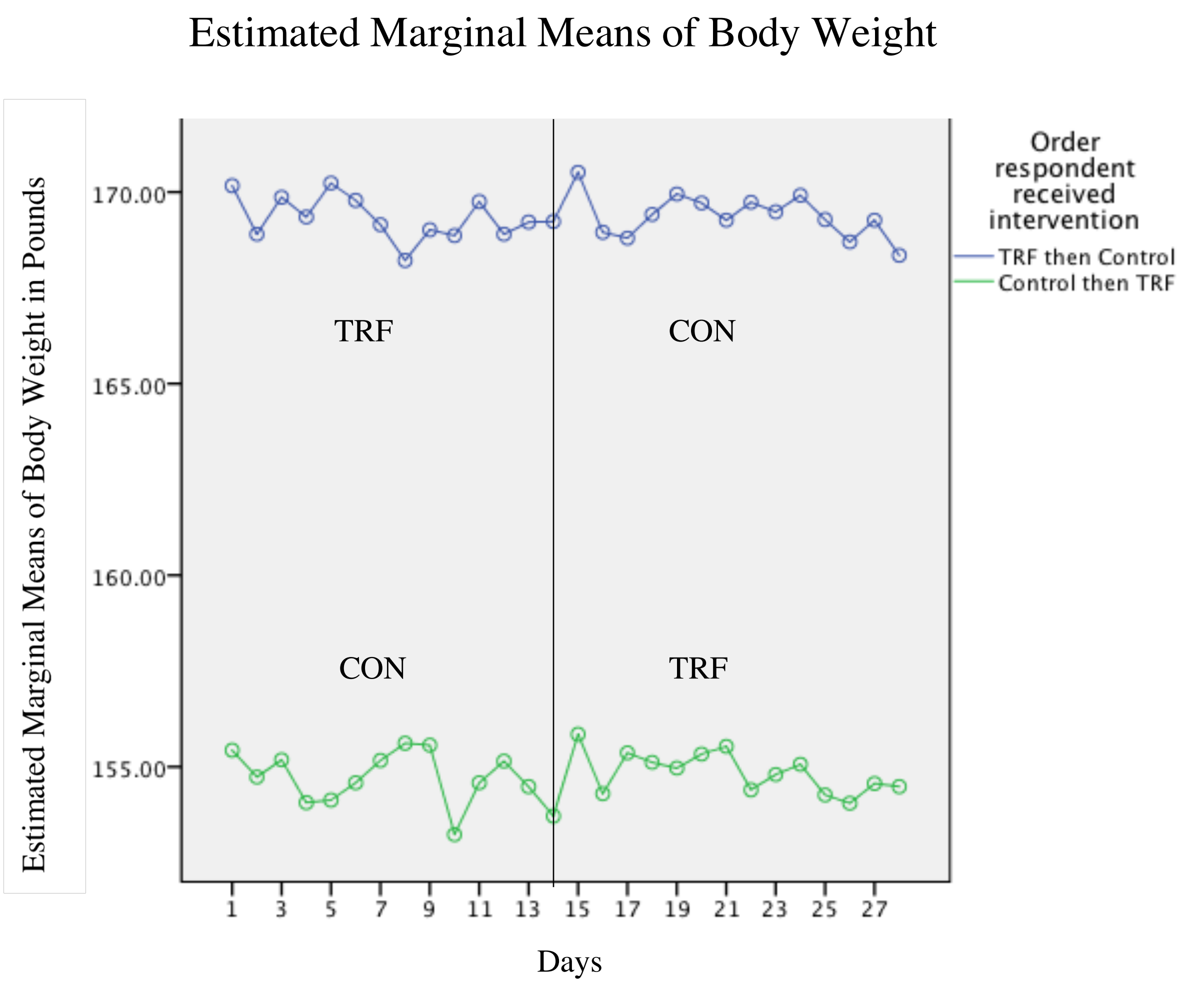

Figure 11. Weight change over time for pilot study respondents. Crossover occurred at day 14.

Sleep

There was no significant interaction effect between the order of intervention and sleep duration, $\lambda = .101$, $F\ (27, 3) = .988$, $p = .597$. Likewise, there was no significant main effect for differences in sleep duration in the respondents over time, $\lambda = .086$, $F\ (27, 3) = 1.182$, $p = .519$. However, there was a significant main effect for differences in sleep duration in the respondents over time between the groups based on intervention: $F\ (1, 29) = 6.832$, $p < 0.014$.

Taken together, the lack of significant differences over time and the significant differences between the CON vs TRF suggest that the CON and TRF phases are different and that intervention order did not drive the difference. Figure 12 shows the mean sleep duration differences between participants during the pilot study.

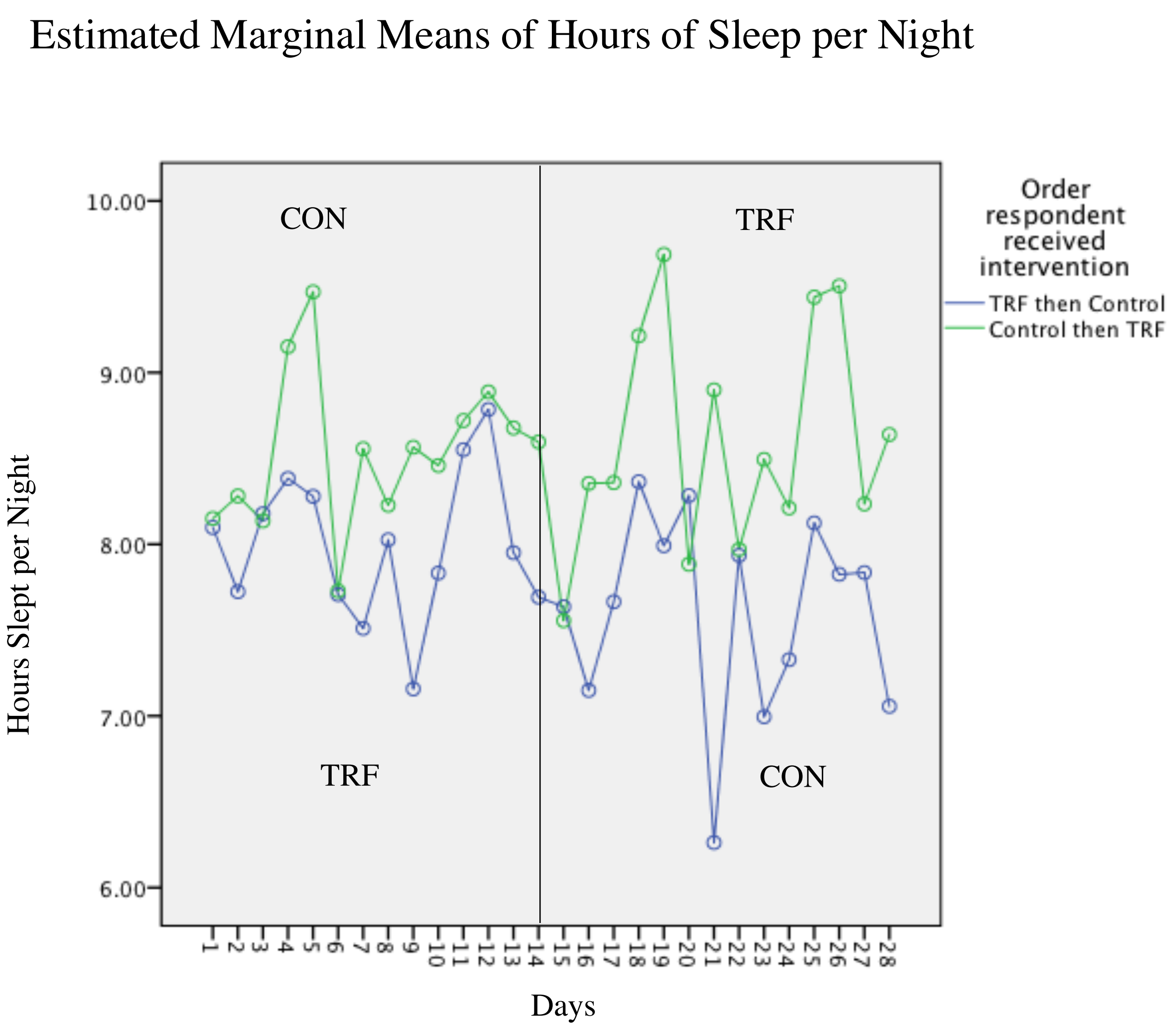

Figure 12. *Mean sleep duration differences by pilot respondents.*

There were no significant interaction effects between the order of intervention and bed time in hours over the 28 day study, $\lambda = .068$, $F\ (27, 3) = 1.531$, $p = .412$. There was not a significant effect for changes in bed time over time, differences over time from time 1 to time 28 days, $\lambda = .160$, $F\ (27, 3) = .584$, $p = .812$. Figure 13 shows the bed times of respondents during the study.

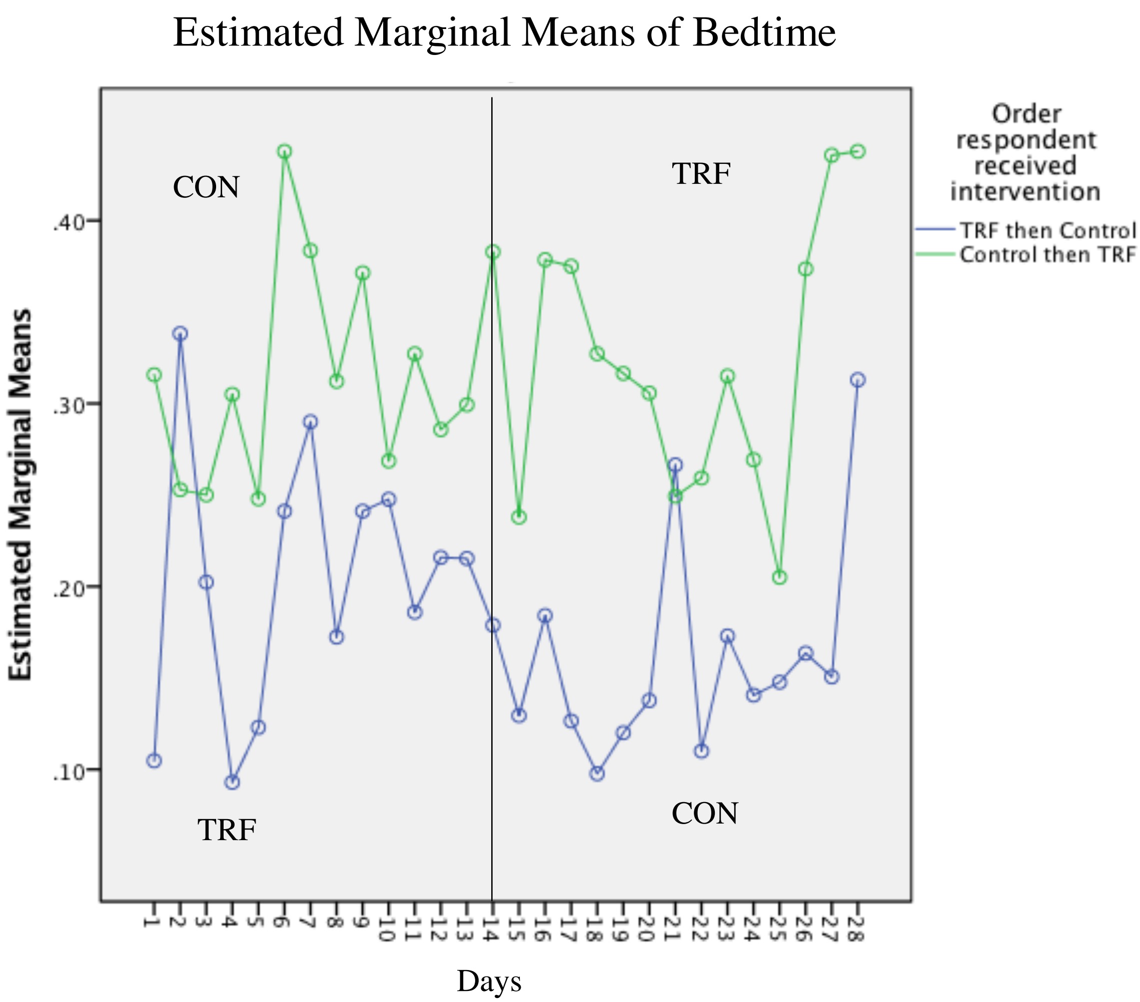

Figure 13. Bed time over time of pilot study respondents.

Similarly, there was no significant interaction effect between the order of intervention and wake time over time, $\lambda = .096$, $F(27, 3) = 1.041$, $p = .575$. There was not a significant effect for changes in wake time over time, differences over time from time 1 to time 28, $\lambda = .078$, $F(27, 3) = 1.310$, $p = .475$. Figure 14 shows the wake times of participants during the study.

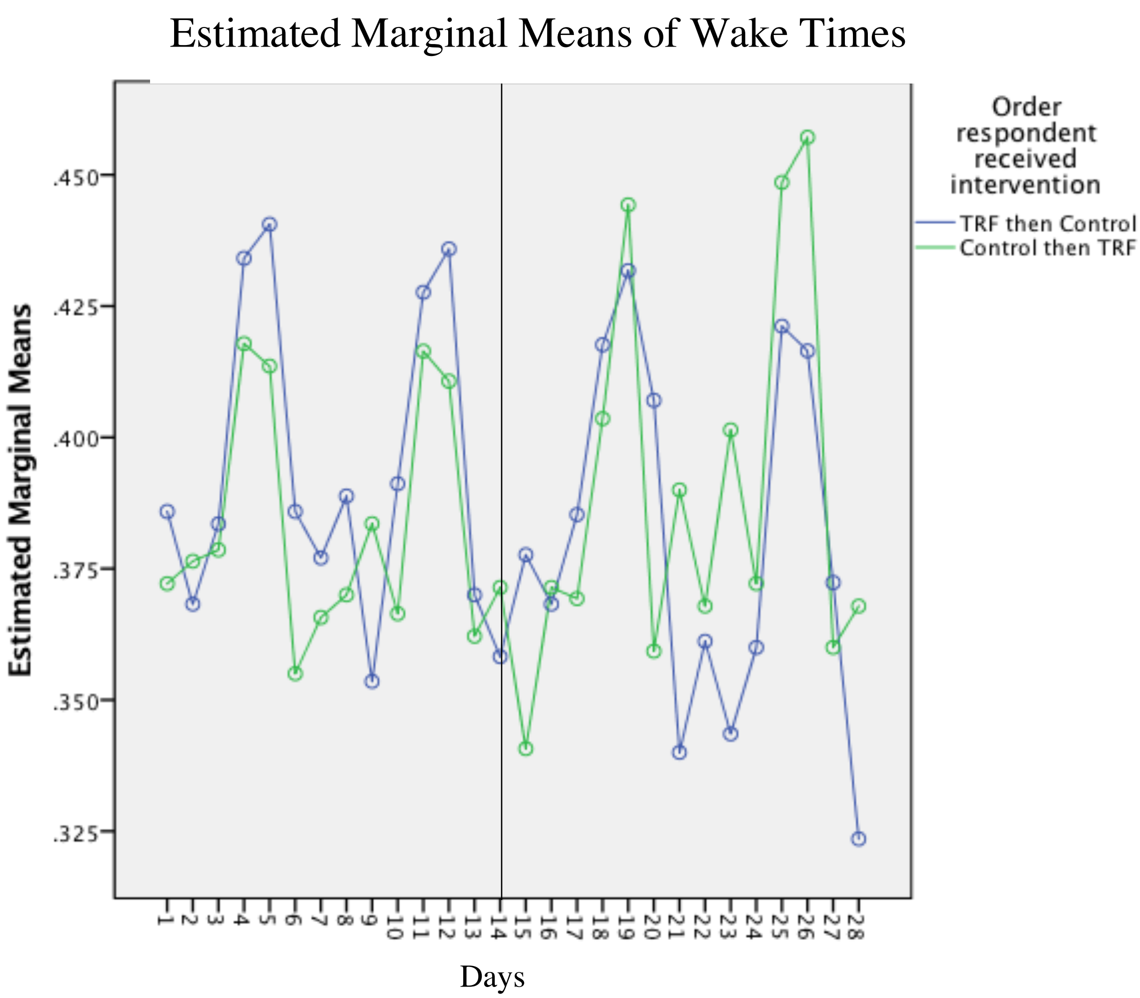

Figure 14. Wake time over time of pilot study respondents.

Calorie Intake

The Eat Cornell app estimated calories consumed at each meal with a time stamp. Unfortunately, the app was unable to support all the photos participants took and it failed after participants submitted photos. Researchers were unable to retrieve the photos and there were no paper records. Therefore, no data is available on what time eating occurred or the number of calories consumed.

Adherence

The researcher defined weight data as adherent if the participant recorded it by 20:30, one hour after the end of the eating period during TRF. The researcher deemed 155 evening weight recordings during the TRF phase as adherent to the protocol out of a possible 504 weights (30.75%). The average evening weight time is defined as the time of day participants weighed themselves after their last calorie intake of the day. It was 22:31 $\pm$ 160.7 minutes. Four participants properly adhered to the protocol, however six had sufficient morning and evening weight data to analyze. Ten participants had 50% compliant evening weight recordings. Four participants did not have a meal plan, so the researcher allowed a 60-minute grace period to return to the dorm and weigh in after finishing a meal (assuming the meal finished by 19:30). The remaining participants failed to weigh immediately after their final meal and some reported bedtimes earlier than recorded weight measurements (Figure 15).

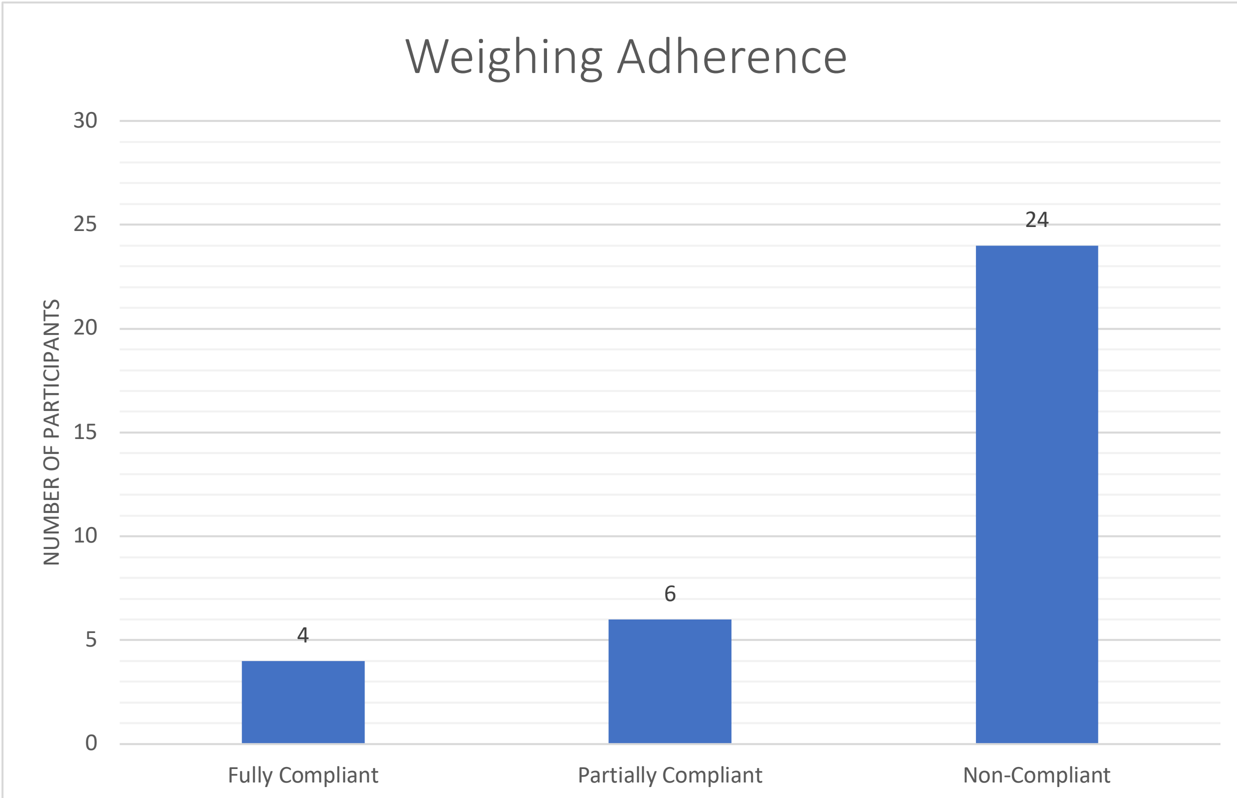

Figure 15. Adherence of evening weighing during the TRF phase.

Note. Evening weight compliance is defined as weighing within one hour after the final evening snack or meal. Partially compliant indicates some of the evening weights were within one hour of the final meal/snack, non-compliant is defined as having a weight more than one hour after the end of the eating phase.

Discussion

Major Findings

The current study was a first attempt at examining the effect of TRF on body weight and sleep in young adults. Contrary to Gill and Panda (2015) and LeCheminant et al. (2013), there was no evidence that two weeks of TRF altered body weight or sleep in young adults, which is consistent with the findings of Gabel et al. who found no change in wake time, bedtime, or sleep duration during a 12-week TRF protocol (Gabel et al., 2019). Nevertheless, the study does provide valuable insights for future TRF research.

Body weight. There was no significant difference in body weight between TRF and CON phases of the trial. Most literature (Betts et al., 2014; Gill and Panda, 2015; LeCheminant et al., 2014; Moro et al., 2016; Sutton et al., 2018; Gabel 2018; Byrne et al., 2017) supports TRF as an effective weight loss strategy except for Chowdhury et al. (2016) who reported weight gain in obese subjects in the TRF group who fasted until 12:00; the CON group gained more weight than the TRF group. Chowdhury et al. (2016) attributed the weight gain to overcompensation and poor intake regulation in obese subjects. A higher body weight does not explain the lack of weight loss in the present study, however; 65% of participants had a normal BMI. Other studies of normal weight participants still reported weight loss in as little as two weeks (Betts et al., 2014; LeCheminant et al., 2013; Moro et al., 2016).

The lack of weight loss is perplexing because the protocol was extremely similar to that of LeCheminant et al. (2013). Notable differences include: (a) twice daily weighing; (b) using an app rather than written food record; (c) no washout period; (d) using both men and women. The study population was extremely similar in age and lifestyle and the fasting time was only one hour different. During TRF, participants in the study by LeCheminant et al. (2013) decreased EI by approximately 239 kcal/day, resulting in significant weight loss of 0.4 ± 1.1 kg. When obese subjects fasted for 12-14 hours per day, caloric intake decreased by approximately 20.26%, which resulted in an average weight loss of 3.27 kg (95% CI: 0.9081–5.624 kg) over a 16-week intervention (Gill & Panda, 2015). TRF could result in weight loss because humans consume heterogeneous food types in a time-of-the-day-dependent manner (e.g., coffee in the morning and alcohol in the evening). As a result, during TRF, foods consumed outside the feeding period would likely not redistribute to feeding times because those foods would seem temporally out of place.

One would expect weighing twice a day to lead to weight loss because daily weighing has been shown to cause weight loss (Pacanowski et al, 2015). However, the majority of participants did not adhere to the protocol and weigh twice a day, therefore we are unable to conclude that daily weighing was ineffective. Using an app to capture all food intake may have become burdensome for participants. LeCheminant et al used random 24-hour recalls twice a week to estimate energy intake, which would minimize participant burden (LeCheminant et al., 2015). Moreover no washout period may have compromised results in the second half of the study because any effects induced by the first half may have carried over into the second phase. The final difference in study design was the inclusion of women. One potential variable that may have affected weight was menstrual cycle fluctuation in water retention and hunger levels, which have been shown to increase, particularly in the late luteal phase.

There are three possible explanations for the lack of weight loss during TRF in the present study. Participants redistributed calories that they would typically consume during the fasting period to the feeding period. Caloric intake differences are not known so we cannot draw conclusions on how TRF affects calorie intake or expenditure. They sufficiently reduced physical activity (PA) to offset a decrease in calorie intake. Lastly, they did not adhere to the fasting protocol, which is the most likely explanation as evidenced by non-compliant weight times.

Sleep

The data revealed no effects of TRF on wake time, bedtime, or sleep duration. Like the effect of TRF on weight loss, the most logical reason for the lack of an effect may have been lack of compliance with the protocol. This was the first trial to investigate sleep in young adults participating in TRF. Gabel et al. found no difference in sleep duration, bedtime or wake time during 12 weeks of TRF (Gabel et al., 2018). The hypothesis was that TRF would improve sleep quality and duration, based on results from Gill and Panda (2015) who found that TRF improved sleep duration when restricting eating to 10-12 hours per day. Alternatively, the bedtime would shift slightly earlier because participants would not be eating at night, which could save time. A non-viable explanation may be that going to bed earlier may avoid hunger or boredom that participants previously filled by eating. However, there was no significant change in bedtime or wake time; therefore, the results do not support this explanation.

Adherence

One explanation for the contradictory results is the lack of protocol adherence in the present study. The current protocol instructed participants to weigh themselves immediately after eating. The researcher marked over 70% (n = 24) of participants' evening weights as non-compliant. Only 12% (n = 4) recorded all evening weights by the deadline of 20:30. For example, one participant reported going to bed at 22:00 but had a time-stamped weight recorded at 01:23. Participants repeatedly failed to weigh immediately after the final meal or snack in the evening.

Participants were not under observation and there was no reasonable method to monitor whether they ate after the feeding window ended. Taking an evening weight provided an objective, quantitative method to determine adherence to the time restriction. The lack of protocol adherence to weigh immediately after consuming the final evening meal or snack may explain the lack of adherence to eating within the time restriction itself. Participants may have consumed foods outside of the designated eating period. This hypothesis aligns with the lack of weight loss during the TRF phase, which other researchers found with similar time restrictions

(Gill & Panda, 2015; LeCheminant et al., 2014). It is also likely that that participants did follow the time restriction and simply did not weigh immediately after the final food intake of the day.

A 12-hour TRF was likely difficult to adhere to because the study population was university students whom do not accurately represent the general population. It may be that the lifestyle of university students make adhering to TRF more difficult compared to the general population. The present study included a 12-hour feeding window and participants could eat *ad libitum*, which should have made adherence easier than past studies. A longer feeding window should be easier to adhere to because it allows more eating opportunities and does not force participants to modify their normal eating pattern as drastically as a shorter feeding window, such as eight hours used in other studies (Moro et al. Sutton et al., 2018, and Gabel et al., 2018). The general population may have better adherence because they do not have the late-night social pressures of collage participants and more control of preparing meals versus eating in a dining hall. On the other hand, it may be easier for university students who eat in the dining hall because they do not have 24-hour access to a kitchen/food like the general population.

Limitations

There are several limitations to these results. First, each condition (TRF and CON) was only two weeks in duration. Therefore, it is impossible to make conclusions about long-term effectiveness of TRF for weight management. There was no initial weight loss; therefore, it is unlikely that a longer duration would exhibit different results. Typically, if a method is going to induce weight loss, it is evident in the first two weeks, which was not the case here (Levitsky D.A. and Pacanowski, C.R. 2013). This trial did not provide any insight into the practicality or feasibility of TRF as a lifestyle or long-term weight management tool, however it was not practical or feasible for the majority of participants for the short duration of this study, so it is unlikely that a longer period would be more feasible. The poor adherence to the protocol raised concern that it may not be a suitable lifestyle for a college student population. The study population consisted of undergraduate university students with lifestyles that limit external validity and prevent generalizing the findings to a broader adult population. Many participants failed to report data, deviated from the protocol, or reported data that was likely false as evidenced by contradicting data entries. Additional research is necessary in broader populations, particularly adults and individuals with more consistent schedules. Future studies should attempt to measure EI and energy expenditure as it is unclear how TRF affects these two crucial parameters and how these variables translate into modulations in body weight.

Strengths and Contributions

Despite these limitation, the present study has strength designs, but does not significantly contribute to the current TRF literature. It was the largest human trial to experimentally examine the influence of TRF on body weight and sleep in free-living, young adults. The study included both males and females, which is important because much TRF research only includes male participants. Moreover, the present trial did not provide food to meet energy requirements, unlike many previous TRF studies (Varady et al., 2014). This is a strength because it was a more natural environment for participants to eat as they normally would, rather than having food provided.

Conclusion

In conclusion, we are unable to draw conclusions of the effects of TRF because so few participants actually adhered to the protocol. Other participants who partially complied with TRF did not receive an adequate “dose” of the intervention. We can only conclude that a 12-hour TRF was not feasible for university students due to such poor compliance, which resulted in a lack of data. Additional research is necessary to determine the effectiveness of TRF as a lifestyle on weight management weight and sleep.

CHAPTER 3: RANDOMIZED CROSSOVER TRIAL

Introduction

A pilot TRF study of young adults was conducted to expand the literature regarding body weight, wake time, bedtime, and sleep duration (see Chapter 2). After reviewing the pilot study design, strengths, limitations, and data, it was evident there was no effect of TRF on bodyweight, bedtime, wake time, or sleep duration. Weaknesses in the methodology and gaps in the literature warranted further research. The objective of the present study is to examine the effects of TRF on body weight, sleep, PA, and calorie consumption timing. The hypothesis is that TRF causes weight loss, earlier bedtimes, longer sleep duration, and better quality of sleep due to an earlier final calorie intake in the evening.

TRF and Sleep

Very little is known about how TRF affects sleep in humans. Only three human trials have examined the effect of TRF on sleep (Chowdhury et al., 2016; Gill & Panda, 2015; Gabel et al., 2018). Chowdhury et al. (2016) randomized 23 obese participants to either a daily breakfast ($\geq$ 700 kcal before 11:00) or extended fasting/TRF (0 kcal until 12:00) for six weeks and found no effect of regularly extended fasting on wake time, bed time, or sleep duration. Similarly, Gabel et al (2018) examined the effects of TRF on 23 obese adults who followed an 8-hour TRF for 12 weeks. They too found that TRF does not alter sleep quality or duration (Gabel et al., 2018).

However, not all TRF studies agree that TRF has no effect on sleep. Gill and Panda (2015) reported that total overnight fasting duration paralleled sleep duration at night in eight overweight adults who self-selected a 10-12 hour feeding window for 16 weeks. They measured sleep via a CamNTech Motionwatch 8, a device that measured activity and light. Time in bed was scored as a nighttime drop in activity and an absence of light. Participants subjectively rated their sleep quality on a scale of 1 to 10. After the 16 weeks of TRF, sleep scores significantly increased ($p < 0.05$ paired t-test) from 5.625 ± 0.78 to 7.125 ± 0.81. Hence, there is no consensus in human trials regarding whether TRF affects sleep duration.

All three studies (Gabel et al., 2018; Chowdhury et al. 2016; Gill and Panda, 2015) used relatively small (n = 23 and n = 8) and obese samples. Consequently, the effects of TRF on sleep in a non-obese population is unknown. The current study was the first to examine the effects of TRF on body weight, wake time, bed time, sleep quality, and sleep duration in non-obese, free-living adults.

TRF and Physical Activity

A common side effect of a hypocaloric state is decreased physical activity (PA) (Redman et al., 2009). TRF does not necessarily induce a hypocaloric sate, however there is scant research on how TRF affects PA. Betts et al. (2014) found that PA thermogenesis was markedly higher (442 kcal/day) in a CON group who consumed breakfast compared to a TRF group that fasted until noon. Morning food intake may affect spontaneous behaviors more than conscious decisions to participate in PA or exercise. Nevertheless, the effect of calorie intake on PA may be direct and immediate rather than secondary to accumulated physiologic adaptations with sustained exposure to the presence or absence of calorie intake (Betts et al., 2014). Chowdhury et al. (2016) replicated this finding using the same protocol with normal weight subjects and found that the TRF group had lower PA expenditure during the awake, fasting period, indicating PA expenditure changed most with restricted EI. Thus it is important to better understand how TRF affects PA because a reduction in PA may reduce weight loss.

TRF and Calorie Consumption Timing

Additional research is necessary to clarify how TRF affects the timing of calorie consumption, which may affect food choices, and thus total calorie intake.

There is little data available regarding how TRF affects calorie consumption timing. Moro et al. (2016) reported no significant difference in nutrient distribution between CON and TRF groups, but they altered the time between meals for the TRF group. Subjects ate the same meals, but closer together, to accommodate for the 8-hour feeding window (Moro et al., 2016). Gill and Panda (2015) reported that TRF reduced eating duration by 4 hours and 35 minutes on average in a 10 to 12-hour TRF regimen and noted the time of last caloric intake was more variable than first caloric intake. Hence additional research is warranted to elucidate the effects of TRF on calorie consumption timing.

Methods

Participants

Participants were recruited for a randomized crossover TRF trial via an advertisement sent to Cornell employees on an email list serve called Life Digest in April 2017. See appendix for recruitment advertisement. Eighty-nine people responded to the advertisement. Exclusionary criteria included a diagnosis of diabetes, current or history of an eating disorder, binge eating, cancer, pregnancy or planning to become pregnant in the next six months, not owning a Bluetooth enabled device, or taking any of the following medications: steroids, antidepressants, antipsychotic, or mood stabilizers. Ten people were ineligible due to medication use and one person had binge eating disorder. Sixty-six adults provided written, online consent and completed a pre-study online questionnaire regarding demographics, eating behaviors, PA, and sleep. Survey responses were used as baseline data and no participants were excluded based on their responses. The Cornell University IRB for Human Participants approved all procedures and materials for this trial prior to the initiation of the study.

Procedures

In June 2017, participants reported to the Human Metabolic Research Unit and received a folder containing study instructions and a data collection sheet for wake time, bedtime, and body weight. See appendix for data collection sheet and study instructions. The primary investigator (PI) read the research description and consent form to all participants. Everyone had an opportunity to ask questions before providing written consent. Participants also received a Withings body Wi-Fi scale (Nokia, model WB-S05_03), downloaded the Withings app on their Bluetooth device, and established an account to capture weight measurements. Usernames and passwords were obtained from participants to access and pool time-stamped weight data.

After all participants collected study materials, a random number generator was used to assign individuals into the CON or TRF phase of the study. Half of the participants began a two-week TRF intervention followed by a two-week CON period; the other half followed the opposite order. Participants received email reminders when it was time to switch conditions. The researcher assessed the following outcomes during each condition: (a) body weight; (b) wake time; (c) bed time; (d) sleep duration and arousal (getting out of bed at night); (e) subjective sleep quality (f) night eating; (g) meal and snack frequency measured by the baseline survey; (h) PA.

Control condition Every morning, participants recorded what time they awoke on the data sheet. Next, they used the bathroom, removed any heavy clothing, and weighed themselves. Participants opened the Withings app, stepped onto the Withings body Wi-Fi scale, and waited for the weight measurement to register on the app. This is a similar protocol to other daily weighing studies (Wilkinson et al., 2017). Data transmitted via the Withings app for each participant's personal account. Participants weighed themselves using the same procedure again after consuming the last food of the day under similar clothing conditions as their morning weigh-in (i.e., either nude or in light clothing). The evening weight was an estimate of protocol adherence for the TRF phase. If a participant's morning weight was higher than the previous evening's weight, the researcher considered it non-compliance and assumed the participant ate outside their designated TRF eating window. Participants recorded weight measurements on the data sheet for both morning and evening weights as a backup to the Bluetooth transmitted data to ensure no weight measurements were absent. In the evening, participants recorded what time they went to bed on the data sheet.

TRF condition. For the two-week TRF phase, participants followed the same instructions as the CON phase in addition to restricting calorie intake to a 12-hour period. Individuals were free to choose any 12 hours between 5:00 and 8:00 and had to keep the same 12-hour eating period for the duration of the TRF phase. This time frame of no earlier than 5:00 start time and no later than 8:00 start time eliminated night-time eating. Typically, night eating is any eating after 19:00 (LeCheminant et al., 2013). However, the present study occurred around summer solstice; with extended daylight, it was more reasonable to allow participants to eat until 20:00. The researcher also predicted the extension might yield better compliance. Participants reported their twelve-hour eating time *a priori*. Meal and snack data were collected at baseline as part of the questionnaire and not collected daily. At the end of the study, 60 participants completed the post-study questionnaire; eight did not complete the questionnaire and were unavailable for follow-up.

Statistical Analysis

The data were subjected to an ANOVA using SPSS (version 25) to test for differences between groups over time. The Levene's test (O'Neill and Mathews; 2002) was used to test for equality of error variances for all 28 measures (only morning weight was used to track body weight) of weight and sleep as well as various measures from the pre- and post-questionnaires. There were no violations of Levene's test for any of the measures, $p < .05$. Additionally, Box's test of equality of covariance matrices (Box; 1953) for each research question variable was used to checked each variable for an interaction effect before proceeding to analyze and interpret the main effects. Statistical significance was set as $p < 0.05$. Time of eating occasions, wake time, and bedtime was converted to military time. Age was converted to a categorical variable and natural breaks within the sample created equally sized groups for analysis. The sample naturally broke into three groups with ages ranging from 20 to 38, 39 to 51, and 52+ years old. These categories were chosen due to the distribution of the sample.

Differences between groups were tested based on ethnicity across the dependent variables. Before conducting the analyses, a frequency analysis was run to determine distribution of the ethnic groups within the sample. Most of the sample is Caucasian (86%, $n = 52$). The other ethnic groups in the sample (e.g., Asian, Hispanic, and African American) are not large enough to be part of this analysis. Therefore, Asian, Hispanic, and African American groups were collapsed into a non-Caucasian ethnic group. Significance for all tests was set at $p < 0.05$.

Results

Study Population

A total of 68 participants enrolled at baseline and 60 (88%) completed the study. Eight participants did not complete the study. The final study population consisted of seven males (12%) and 53 females (88%) with a mean age of 46.6 $\pm$ 10.09 years old. The mean BMI was clinically overweight at 27.351 $\pm$ 5.5598 kg/m^2. Over 86% of participants identified as Caucasian. The mean household size was 2.85 $\pm$ 1.313 people per household with a median income of \$40,000-\$59,999 per year. Table 3 includes details of participants' baseline characteristics.

Table 1

Participants' Average Baseline Characteristics

	Mean $\pm$ SD; count (%)	TRF/CON	CON/TRF	*p*- value
Age (years)	46.6 $\pm$ 10.09	47.79 $\pm$ 1.87	45.48 $\pm$ 1.81	0.38
Race	African American 2 (3.33%)	1	1	
	Asian 5 (8.33%)	4	1	
	Caucasian 52 (86.66%)	23	29	
	Hispanic 1 (1.66%)	1	0	
Median Income (dollars)	\$40,000-\$59,000	\$60,000-\$79,999	\$60,000-79,999	
Gender	53 women (88%); 7 men (12%)	25 women 4 men	28 women 3 men	
BMI	27.351 $\pm$ 5.5598 kg/m^2	27.23 $\pm$ 1.04	27.38 $\pm$ 1.01	0.96

Body Weight

There was no significant interaction effect between the order of intervention and weight, $\lambda = .564$, F (27, 36) = 1.032, $p = 0.458$. The lack of significance in the interaction effect indicates that group membership did not drive additional differences across the dependent variable, weight. This result allows for the main effects to be interpreted, respectively. There was a significant effect for weight over time, differences over time, $\lambda = .410$, F (27, 36) = 1.920, $p < .05$. The effect for time was very large, $\eta^2 = .59$, which indicates a significant difference in weights over time, meaning there was no significant effect for treatment, F (1, 62) = .052, $p = .821$. This result suggests there were no differences between the groups in weight loss.

During the TRF phase, average weight change was -0.42 $\pm$ 0.10 kg and 0.16 $\pm$ .12 kg during the CON phase. TRF before CON did not lose more weight than the CON before TRF group. Differences between the groups on a total measure of weight, adding morning weights together across the 28 days were also tested. There were no significant differences between groups: t (62) = -.227, $p = .821$. This suggests that the groups are not significantly different. Instead, both groups lost weight over time (see Figure 16).

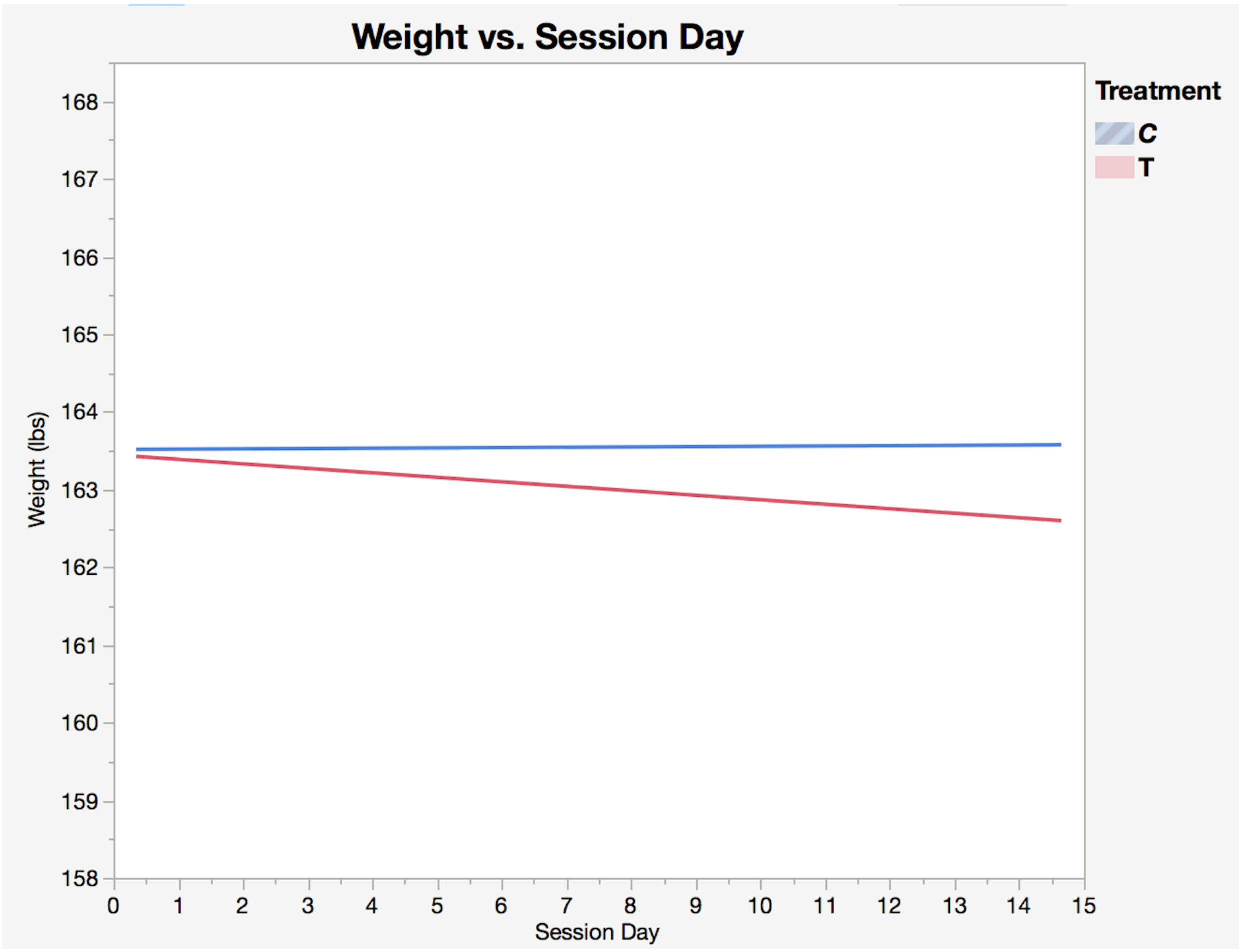

Figure 16. Weight loss over time by group.

There was no significant interaction effect between gender and weight loss over time: λ = .487, *F* (27, 36) = 1.403, *p* = 0.170. Additionally, there was no significant main effect for time by gender. Respondents of either gender did not significantly lose weight across time, both genders lost weight at the same rate: λ = .454, *F* (27, 36) = 1.602, *p* = .093. Finally, there was no significant main effect for differences between the genders: *F* (1, 62) = .968, *p* = .329, meaning gender did not significantly influence weight loss over time (see Figure 17).

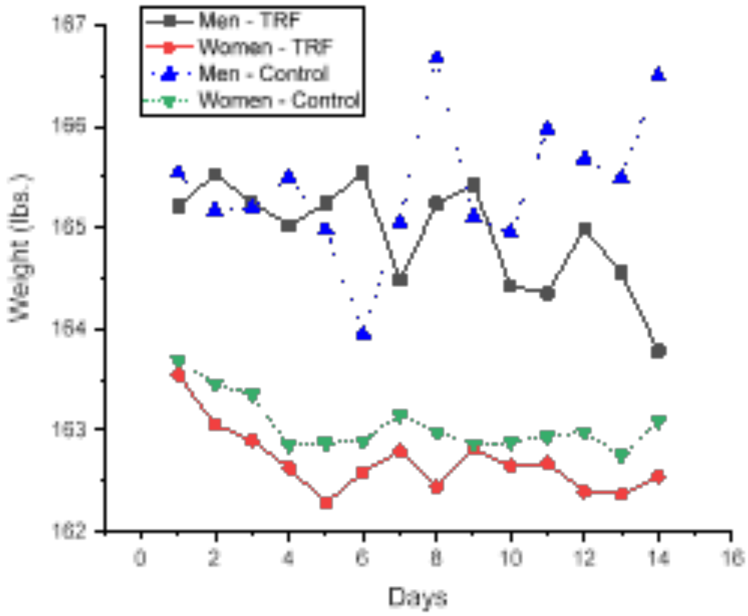

Figure 17. Body weight by gender.

There was no significant interaction effect between age and weight loss over time: $\lambda = .124$, $F\ (81, 103) = 1.281$, $p = .117$. Considering age, there was a significant main effect for time, regardless of age group membership. Respondents lost significant amounts of weight over time: $\lambda = .369$, $F\ (27, 34) = 2.151$, $p < .018$. However, there was no significant main effect for differences between groups based on age: $F\ (3, 60) = 1.793$, $p = .158$, which means age did not significantly influence weight loss over time (see Figure 18).

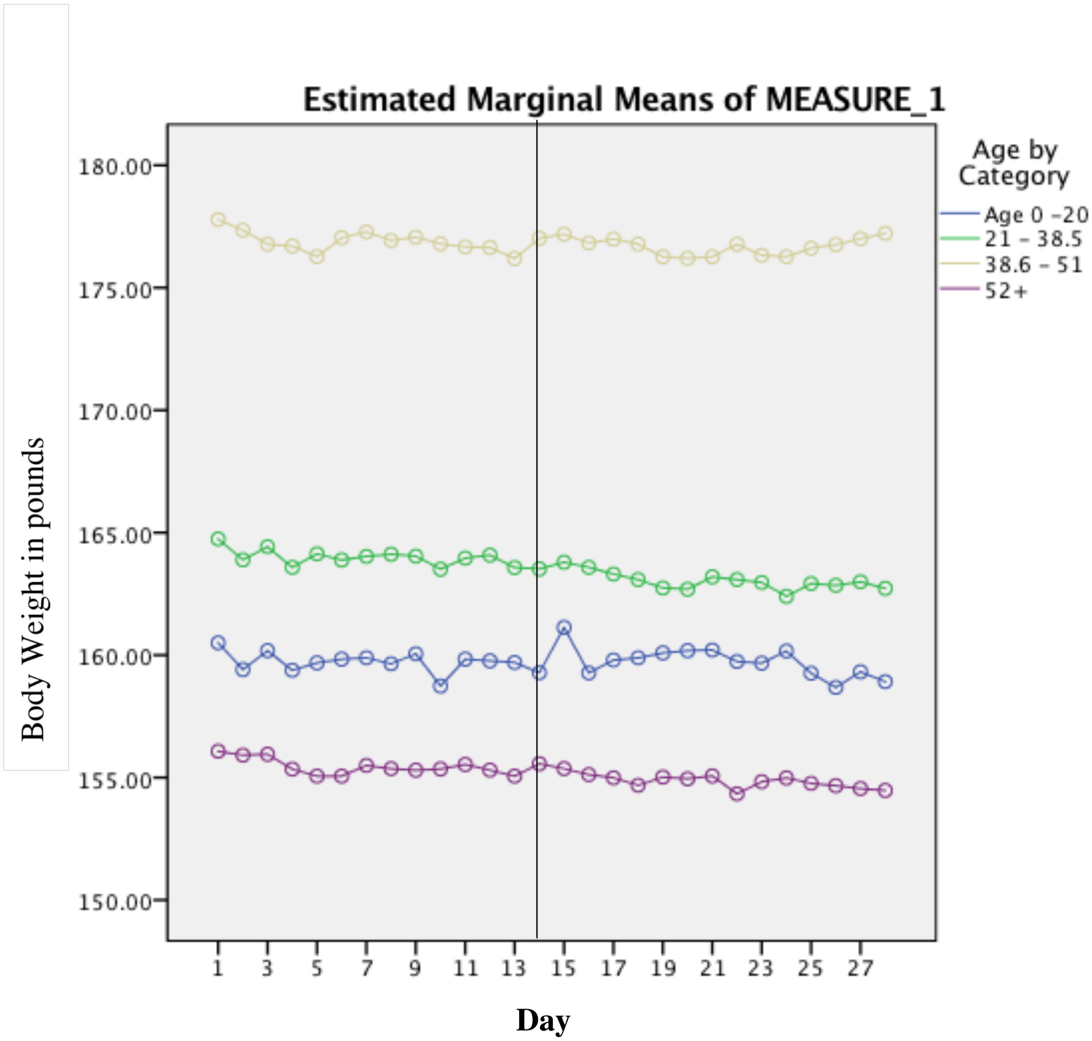

Figure 18. Weight over time by age.

There was no significant interaction effect between ethnicity and weight loss over time: λ = 0.497, F (27, 36) = 1.351, p = .197. There was a significant main effect for time, regardless of ethnic group membership. Respondents lost significant amounts of weight over time: λ = 0.417, F (27, 36) = 1.862, $p < 0.05$. However, there was no significant main effect for differences between groups based on ethnicity: F (1, 62) = 2.207, p = 0.142, which means ethnicity did not significantly influence weight loss over time (see Figure 19).

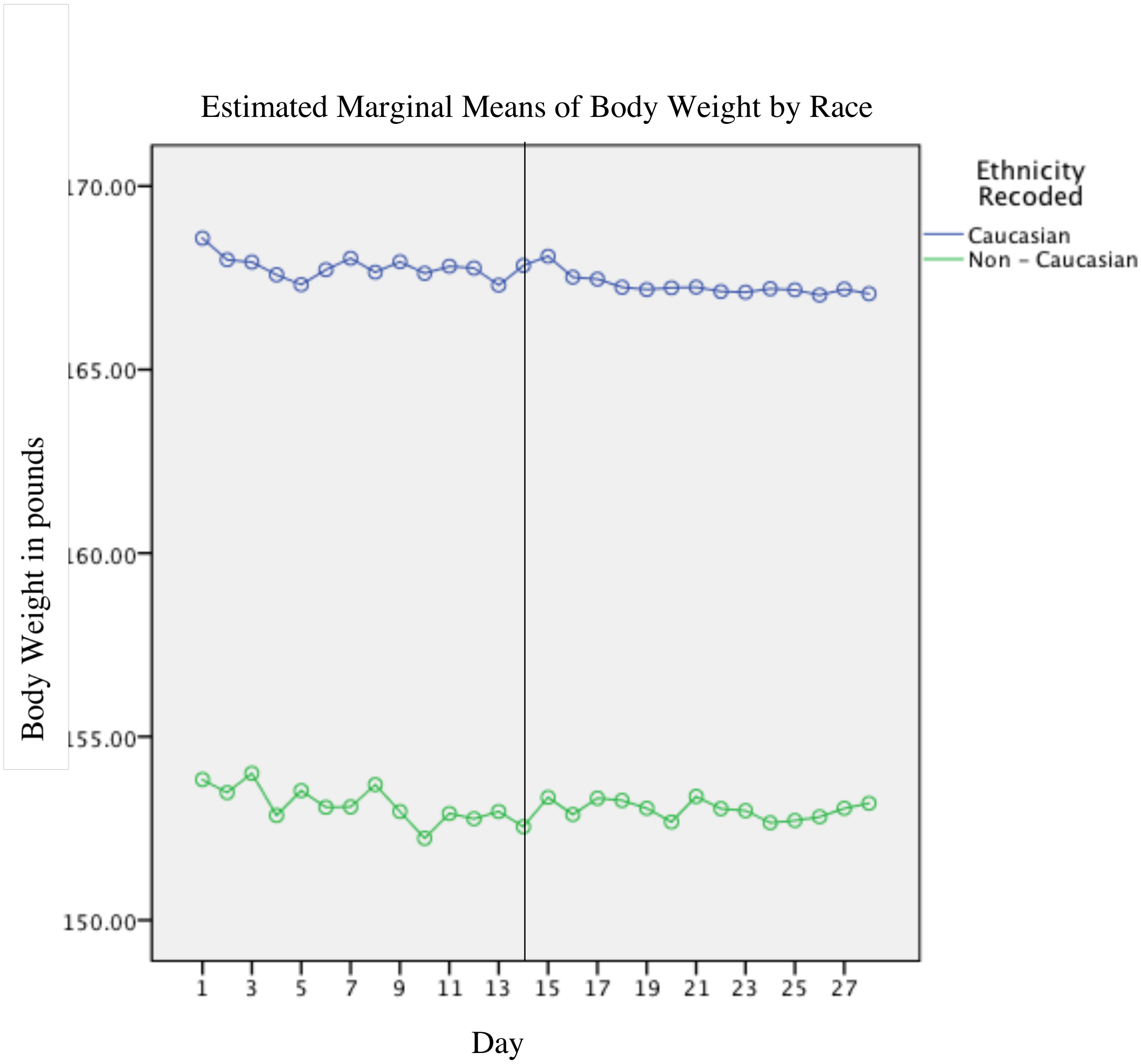

Figure 19. Weight loss over time by ethnicity.

Sleep

There was no significant interaction effect between the order of intervention and duration of sleep, $\lambda = .712$, F (27, 36) = .942, $p = .554$. The lack of significance in the interaction effect indicates that group membership did not drive additional differences across the dependent variable, sleep duration. Participants slept an average of 7.0 $\pm$ 0.09 hours during the CON phase and 7.08 $\pm$ 1.41 hours during the TRF phase. There was not a significant effect for sleep duration over time, differences over time from day 1 to day 28, $\lambda = .710$, F (27, 36) = .952, $p = .542$. This result indicated that there was not a significant difference in sleep duration over time. There were no significant differences between the groups: t (89) = 1.320, p = .190. This suggests that the groups are not significantly different (see Figure 20).

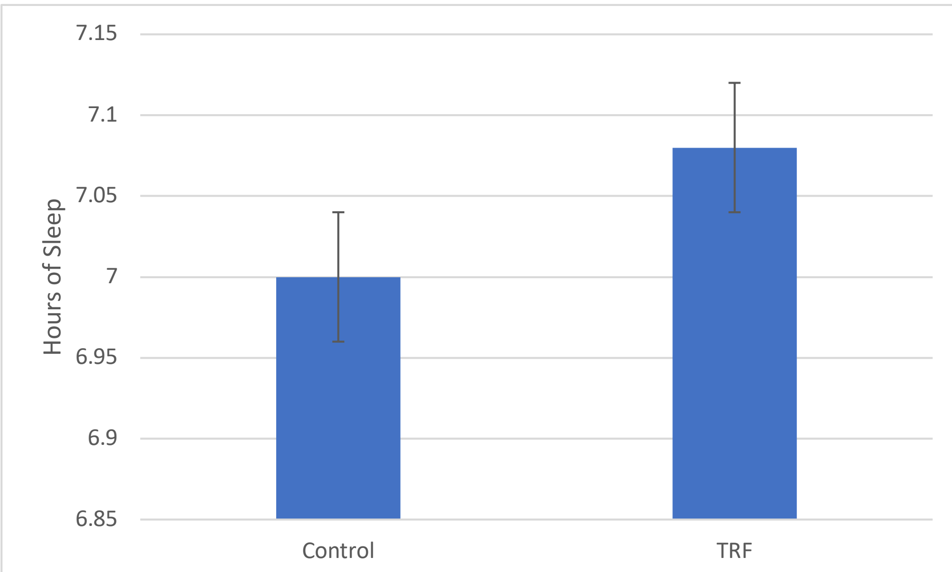

Figure 20. Average hours of sleep per night.

There was a significant interaction effect between age and sleep duration over time: λ = .570, F (27, 63) = 1.757, p < .034. However, participants did not significantly change sleep duration over time: λ = .692, F (27, 63) = 1.038, p = .438. Women slept an average of 7.08 $\pm$ 0.09 hours during CON and 7.13 $\pm$ 0.15 hours per night during TRF while men slept an average of 6.43 $\pm$ 0.29 hours during CON and 6.67 $\pm$ 0.70 hours per night during TRF. Lastly, there was no significant main effect for differences between the genders: F (1, 89) = .013, p = .911, indicating that gender did not significantly influence changes in sleep duration (see Figure 21).

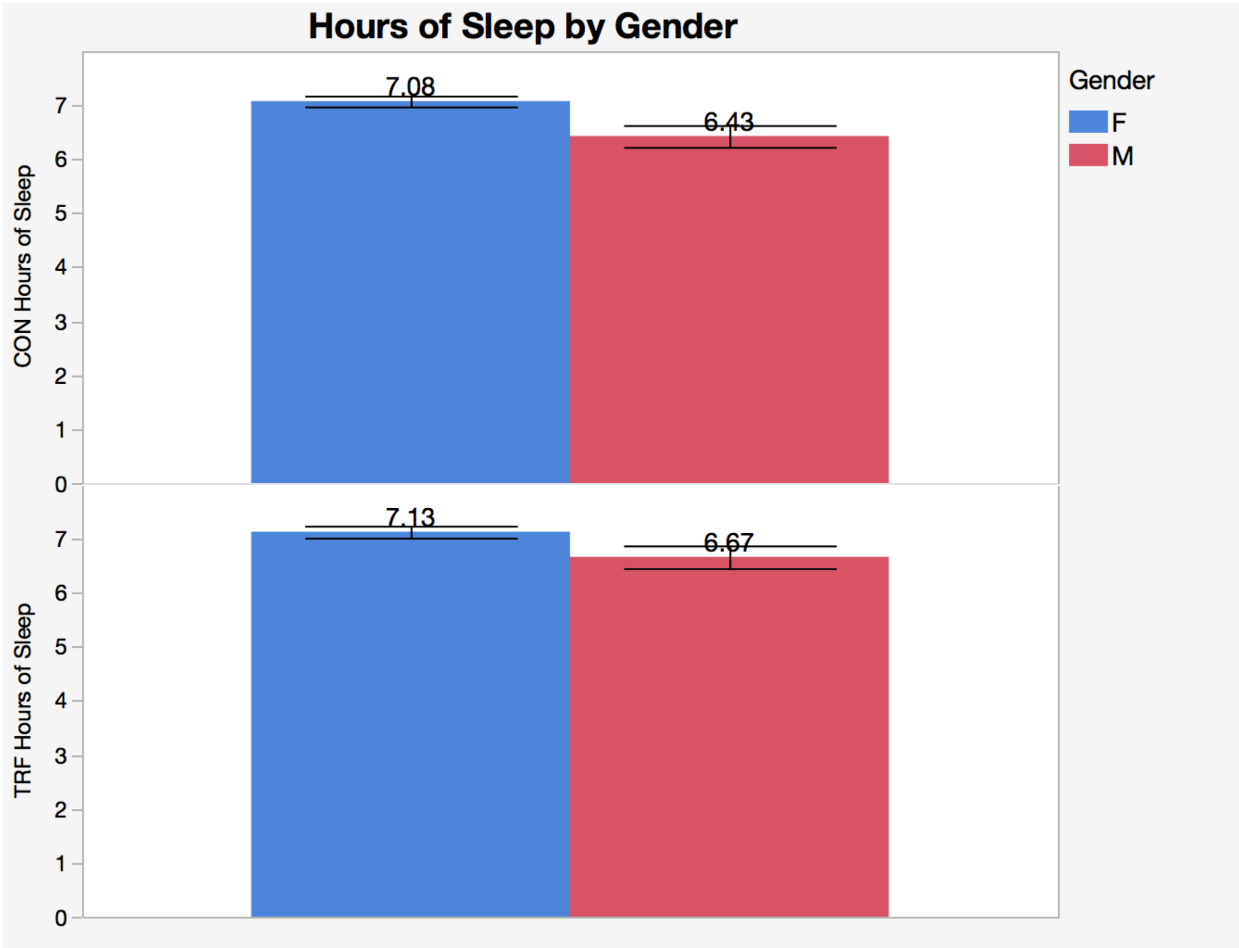

Figure 21. Sleep duration by gender.

There was no significant interaction effect between age and sleep duration over time: λ = .328, *F* (81, 183) = 1.022, *p* = .445. Additionally, there was no significant main effect for time. Regardless of age group membership, respondents did not experience changes in sleep duration over time: λ = .682, *F* (27, 61) = 1.051, *p* = .423. Lastly, there was no significant main effect for differences between groups based on age: *F* (3, 87) = 1.542, *p* = .209, which means age did not significantly influence sleep duration over time (see Figure 22).

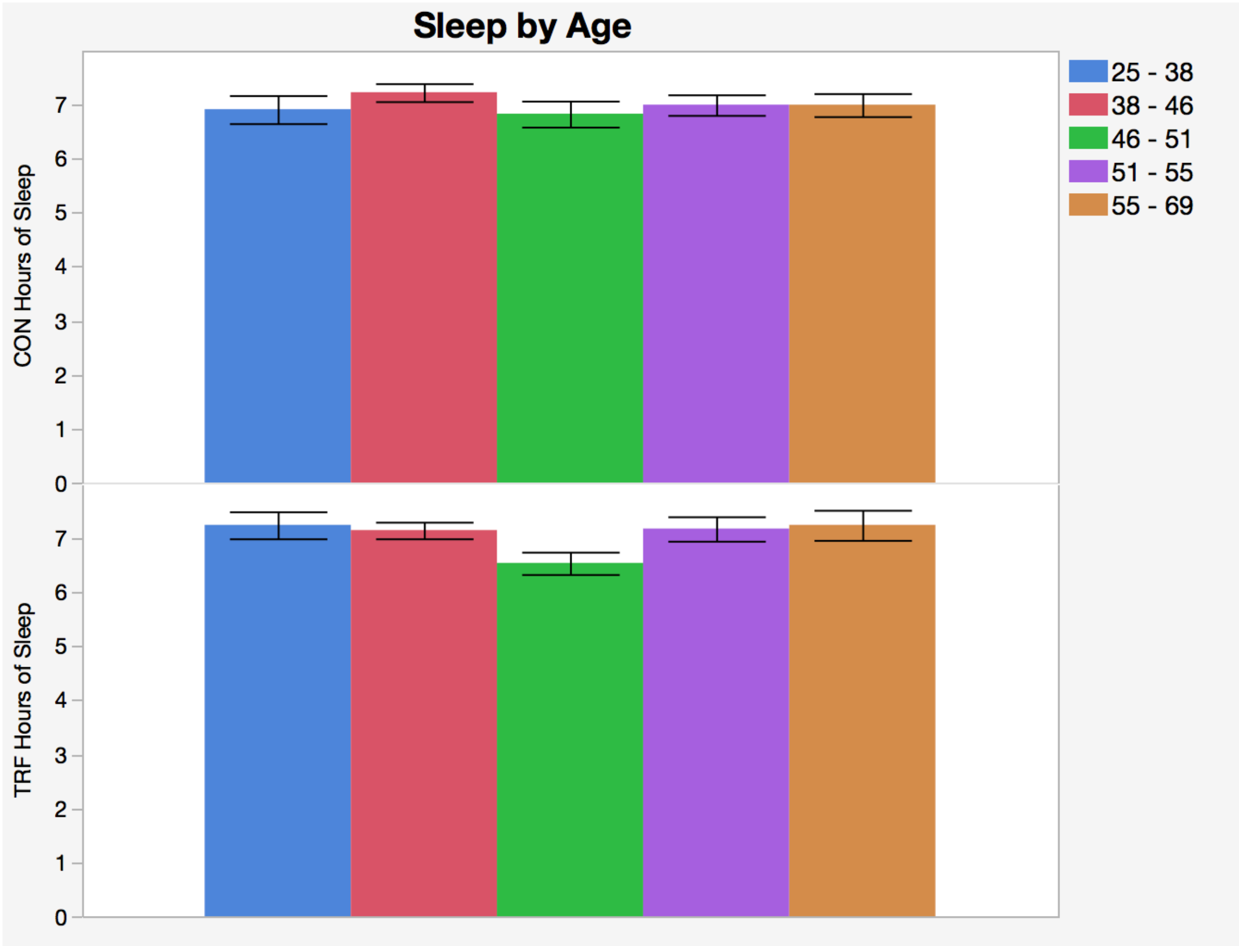

Figure 22. Sleep duration by age.

There was no significant interaction effect between the ethnicity and sleep duration over time: $\lambda = .735$, F (27, 62) = .826, $p = .703$. Additionally, there was not a significant main effect for time regardless of ethnic group membership and no significant changes in sleep duration over time: $\lambda = .709$, F (27, 62) = .943, $p = .554$. Finally, there was no significant main effect for differences between groups based on ethnicity: F (1, 88) = .046, $p = .831$, which means ethnicity did not significantly influence sleep duration over time (see Figure 23).

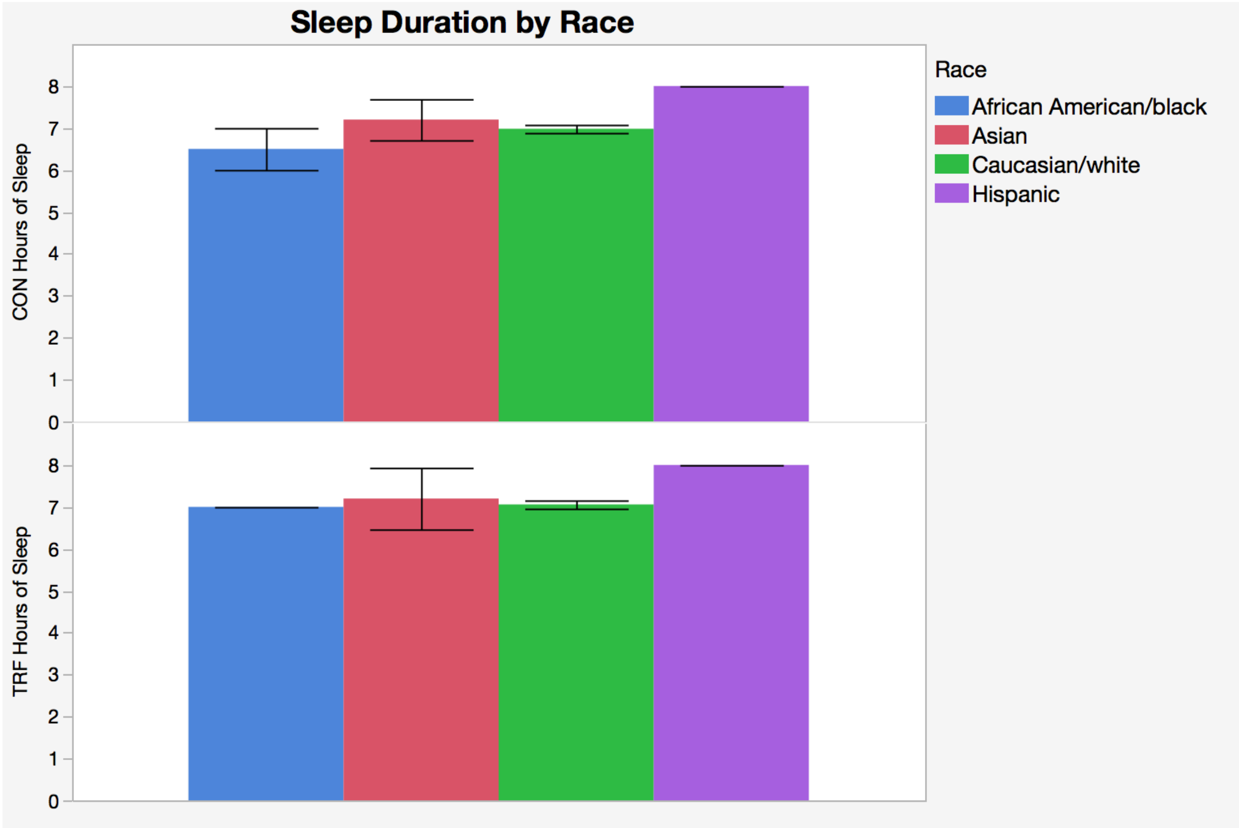

Figure 23. Sleep duration by race.

There were no significant interaction effects between the order of intervention and bed time over time, $\lambda = .490$, F (27, 32) = 1.235, $p = .282$. Moreover, there was not a significant effect for changes in bed time over time, differences over time from time 1 to time 28, $\lambda = .473$, F (27, 32) = 1.321, $p = .224$. There was a significant effect for group membership, F (1, 58) = 4.222, $p = .044$. The size of the effect was medium, $\eta^2 = .068$. This suggests the TRF then CON group was different from the CON then TRF group. The means plot indicated a greater variation in their bed times (see Figure 24). Participants went to bed an average of 83.86 $\pm$ 13.83 minutes before midnight during the CON phase and 49.23 $\pm$ 14.30 minutes before midnight during the TRF phase.

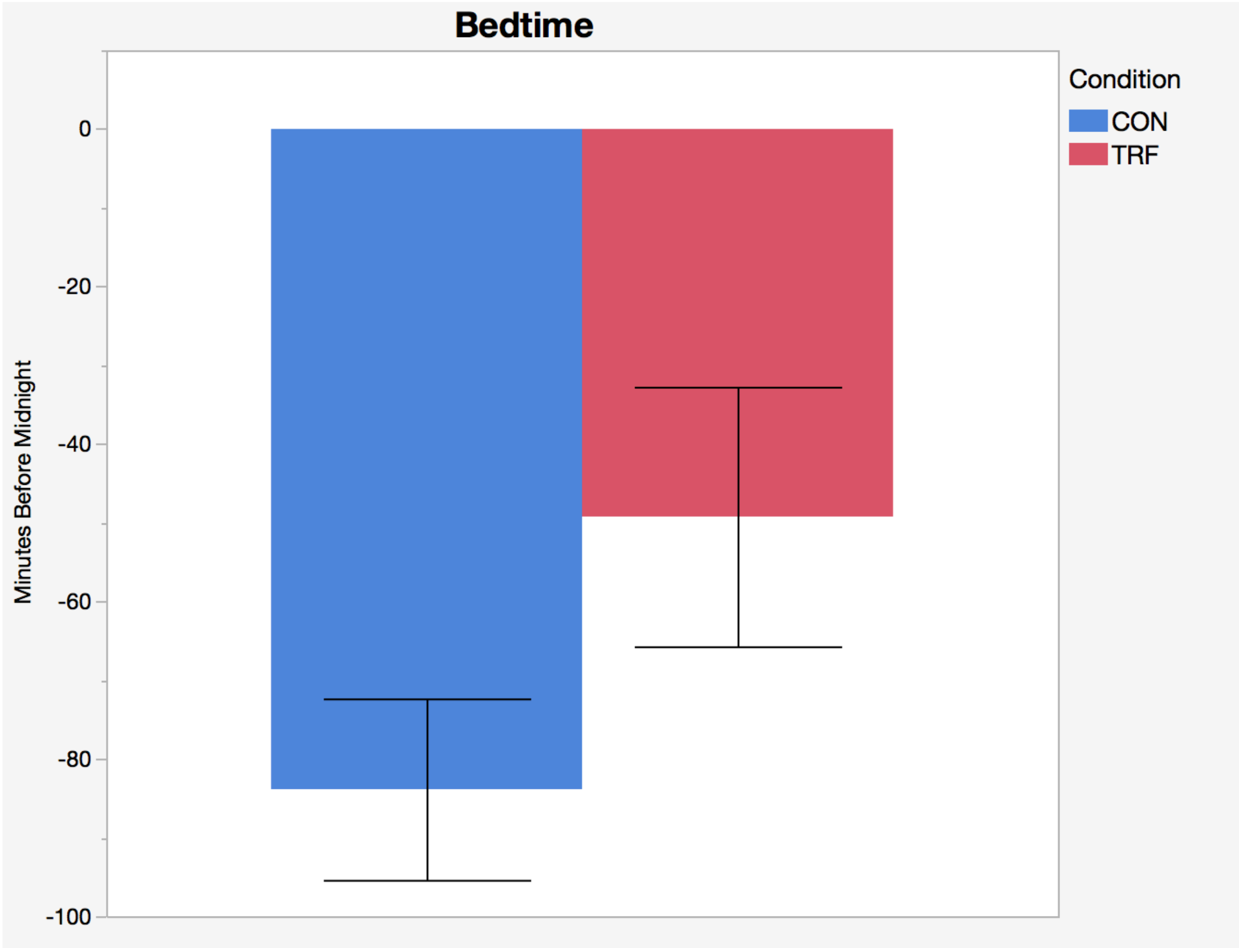

Figure 24. Bedtime in minutes before midnight .

There was no significant interaction effect between the order of intervention and wake time over time, $\lambda = .652$, $F\,(27, 32) = .633$, $p = .885$. There was a significant effect for changes in wake time over time, differences over time from day 1 to day 28, $\lambda = .210$, $F\,(27, 32) = 4.450$, $p < .001$. The size of the effect was large, $\eta^2 = .790$. This result indicated that there was a significant difference in change in wake time over time for the adult group (see Figure 25).

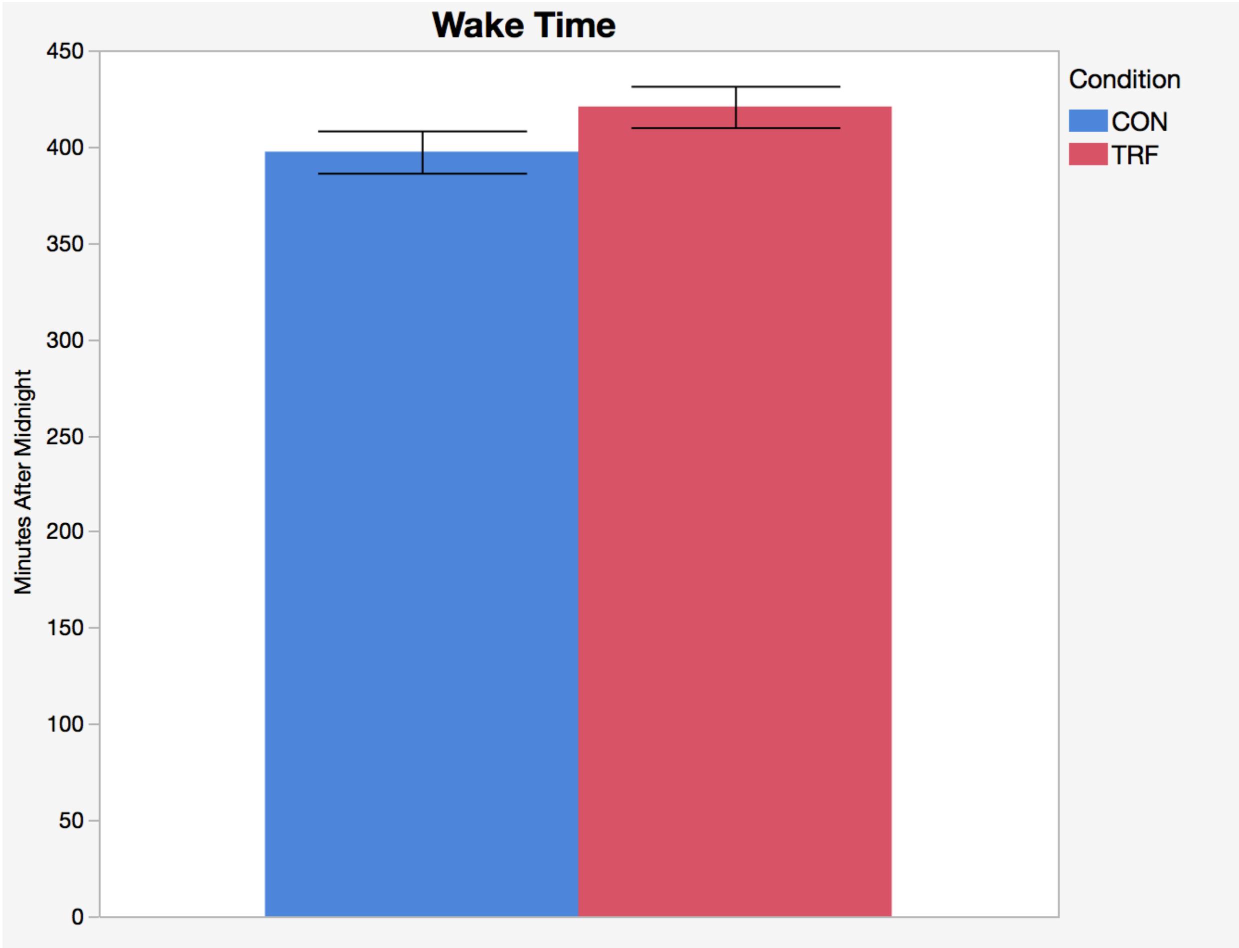

Figure 25. Wake time in minutes after midnight of adult respondents.

There was a significant effect for group membership, F (1, 58) = 5.403, $p < .05$. The size of the effect was medium, $\eta^2 = .085$. This result indicated that there were differences between the groups in wake time over time. There was no significant interaction effect between the order of intervention and sleep quality, $\lambda = 0.982$, F (1, 57) = 1.031, $p = 0.310$. There was a significant effect regarding sleep quality, pretest to posttest differences, $\lambda = 0.847$, F (1, 57) = 10.258, $p < .01$, and the effect was large, $\eta^2 = 0.15$. This indicated there was significant improvement in sleep quality after the intervention (see Table 4 and Figure 26).

Table 2

Pretest to Posttest Sleep Quality by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	72.61	16.12	76.43	16.50
Control – TRF	71.19	18.72	78.61	13.97

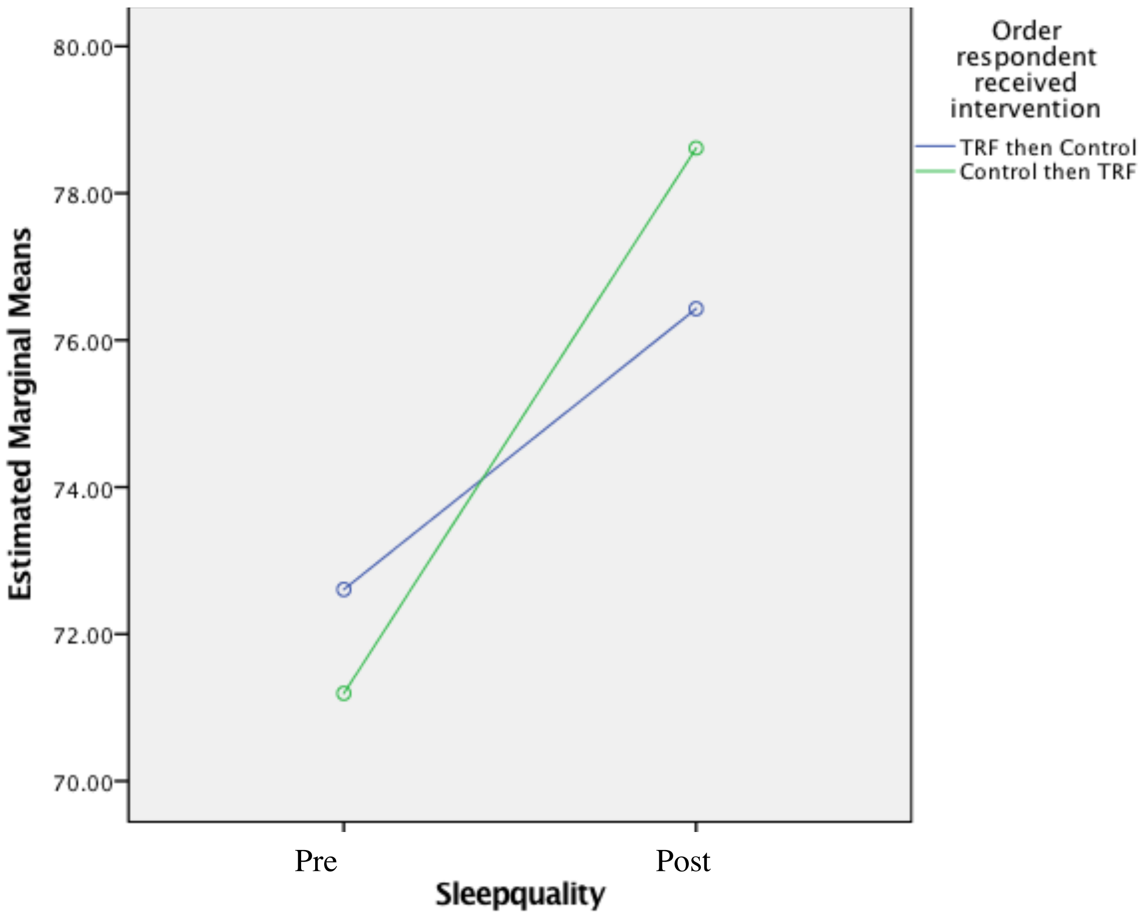

Figure 26. Pretest to posttest sleep quality by group.

There was a significant effect regarding number of times getting out of bed, pretest to posttest differences, $\lambda = .896$, $F\ (1, 56) = 6.518$, $p < .05$, and the effect was medium, $\eta^2 = 0.104$ (see Table 5 and Figure 27).

Table 3

Pretest to Posttest Getting Out of Bed by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	2.22	0.85	2.00	0.87
Control – TRF	2.35	0.75	2.10	0.87

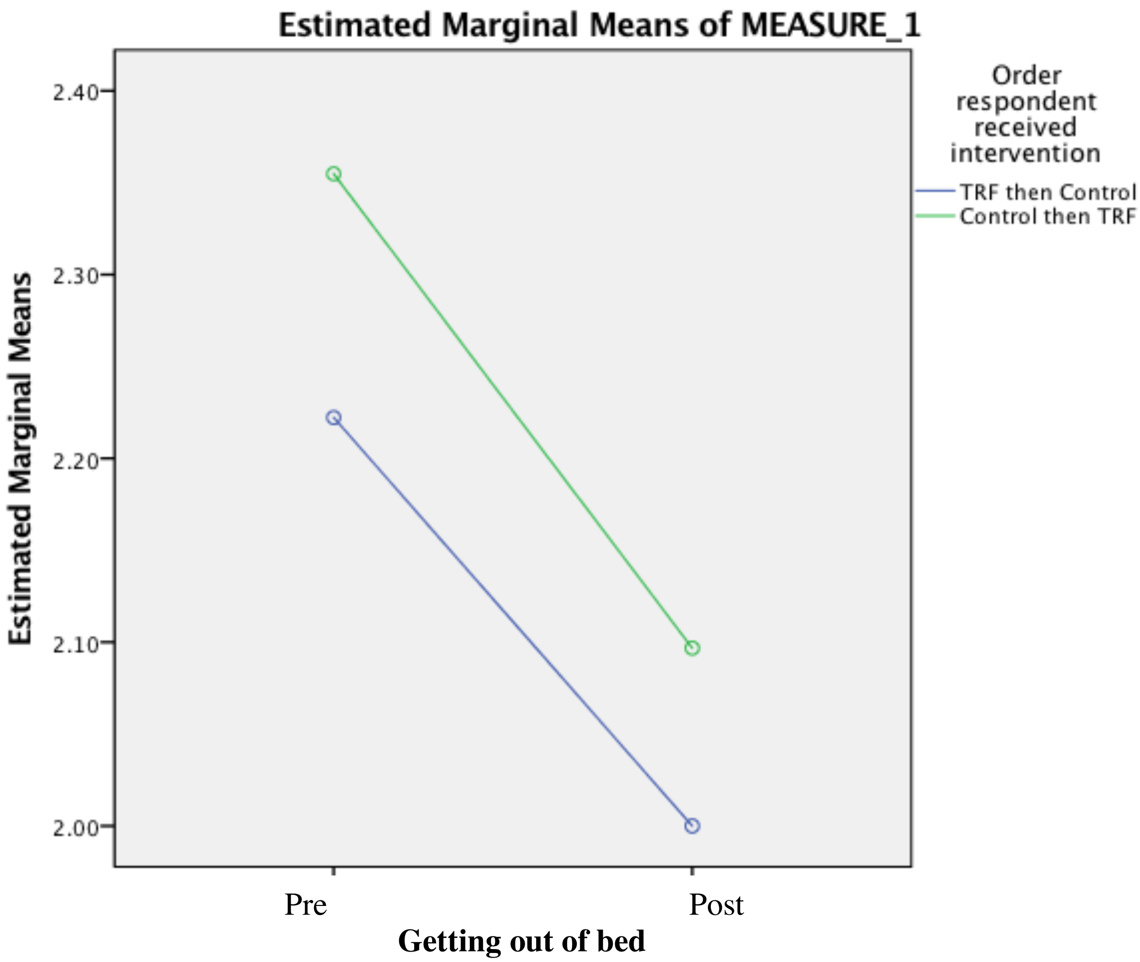

Figure 27. Pretest to posttest nightly bed exists by group.

There was no significant interaction effect between the order of intervention and pretest to posttest hours of nightly sleep, $\lambda = .999$, $F(1, 57) = 1.377$, $p = .246$ and no significant effect regarding hours of nightly sleep, pretest to posttest differences, $\lambda = .989$, $F(1, 57) = .663$, $p = .419$ (see Table 6 and Figure 28).

Table 4

Pretest to Posttest Hours of Sleep by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	6.86	0.71	7.04	0.92
Control – TRF	7.16	0.73	7.13	0.67

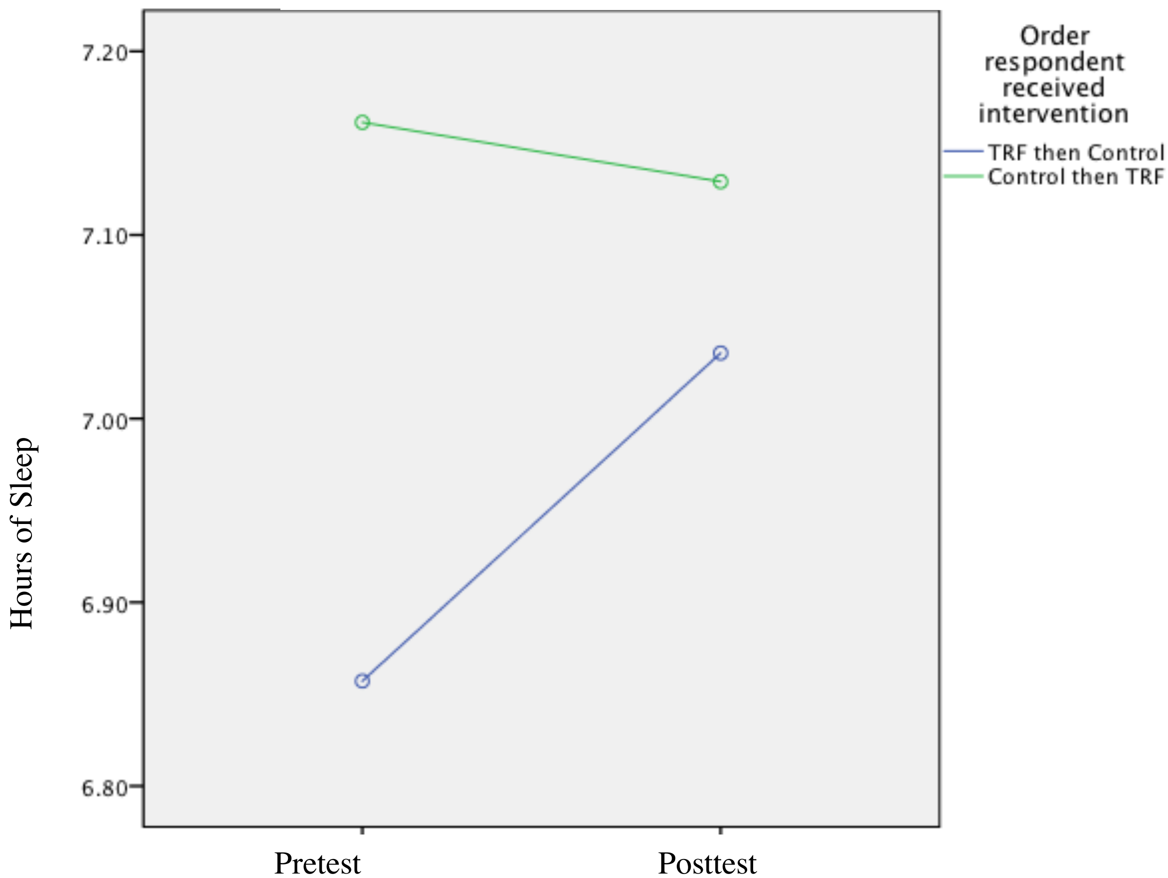

Figure 28. Pretest to posttest hours of nightly sleep by group.

Physical Activity

There was no significant interaction effect between the order of intervention and PA, $\lambda = .953$, F (1, 56) = 2.774, $p = .101$. This indicates group membership did not drive the effect and permits interpretation of the main effects. There was a significant decrease in PA, $\lambda = .751$, F (27, 36) = 18.579, $p < .001$. The effect of this difference was large, $\eta^2 = 0.29$ (see Table 7 and Figure 29).

Table 5

Pretest to Posttest Physical Activity by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	7.89	2.63	7.87	2.61
Control – TRF	7.21	2.90	6.33	2.86

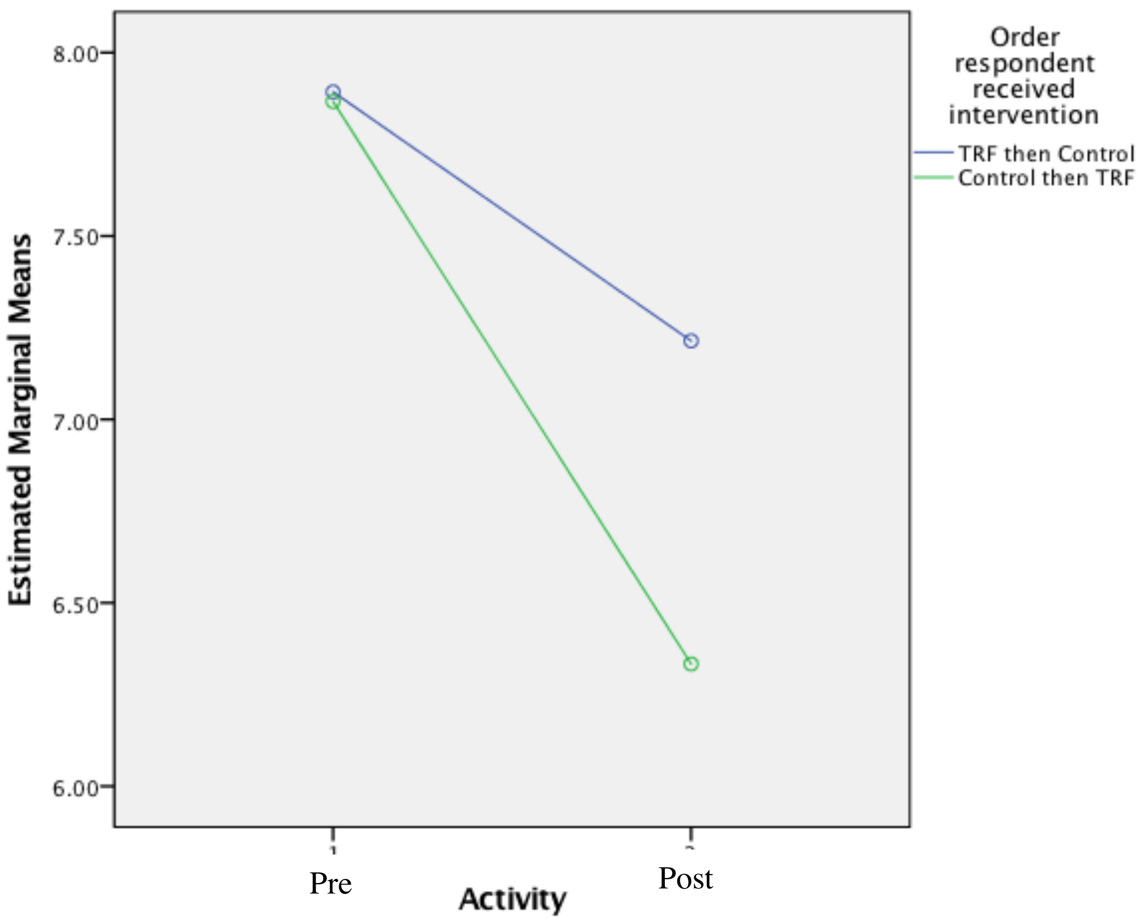

Figure 29. Pretest to posttest physical activity by group.

Timing of Calorie Intake

There was no significant interaction effect between the order of intervention and time the participants consumed the most food, $\lambda = .998$, $F(1, 57) = .104$, $p = .748$. This allows analysis of the main effects. There was not a significant effect regarding time of most food consumption, pretest to posttest differences, $\lambda = .998$, $F(1, 57) = .127$, $p = .722$ (see Table 8 and Figure 30).

Table 6

Pretest to Posttest Time of Most Food Consumption by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	17:18	2:39	17:38	2:22
Control – TRF	16:57	3:23	16:58	3:18

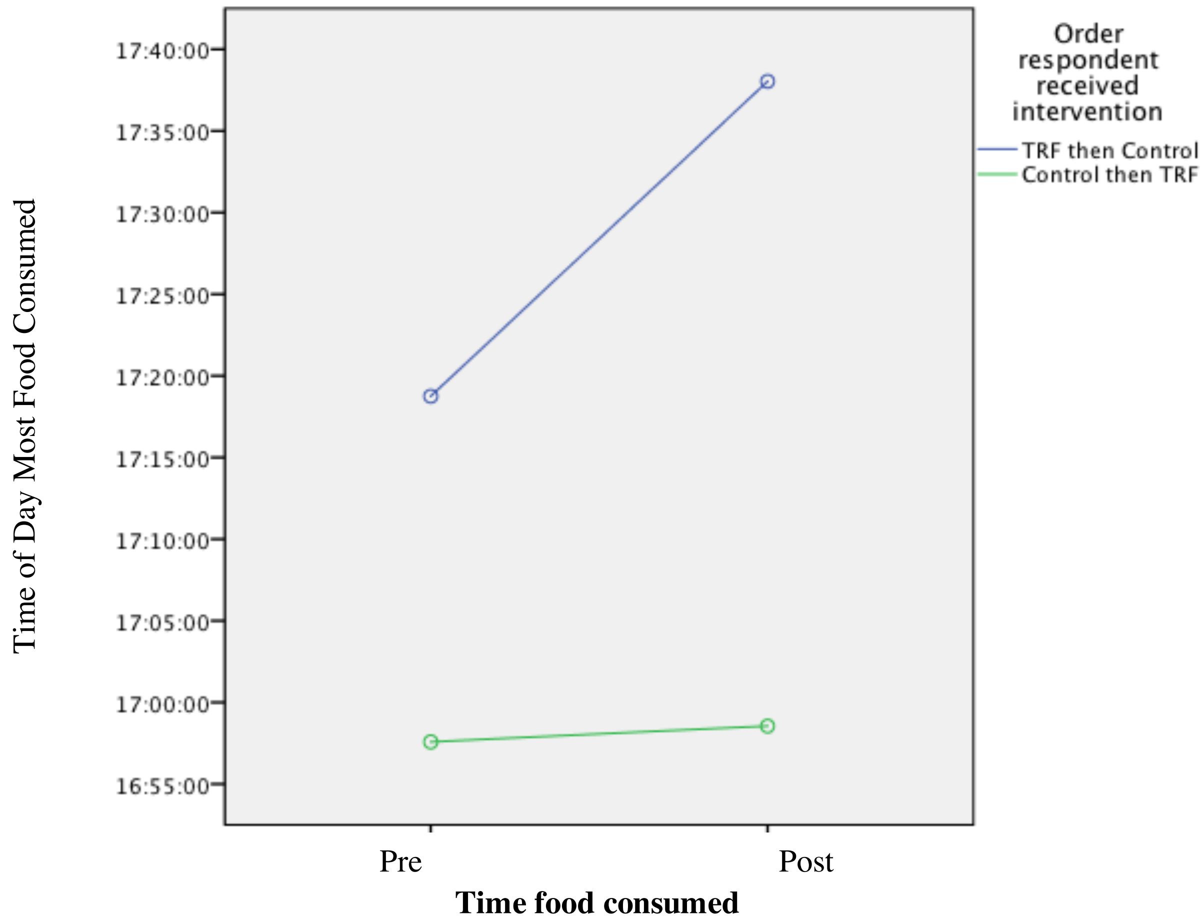

Figure 30. Pretest to posttest time of most food consumption by group.

There was no significant interaction effect between the order of intervention and time of consumption of first meal, $\lambda = .953$, $F(1, 57) = 2.830$, $p = .098$. There was not a significant effect regarding time of first food consumption, pretest to posttest differences, $\lambda = .999$, $F(1, 57) = .037$, $p = .848$ (see Table 9 and Figure 31).

Table 7

Pretest to Posttest Time of First Food Consumption by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	8:09	1:43	8:23	1:22
Control – TRF	8:08	1:26	7:58	0:57

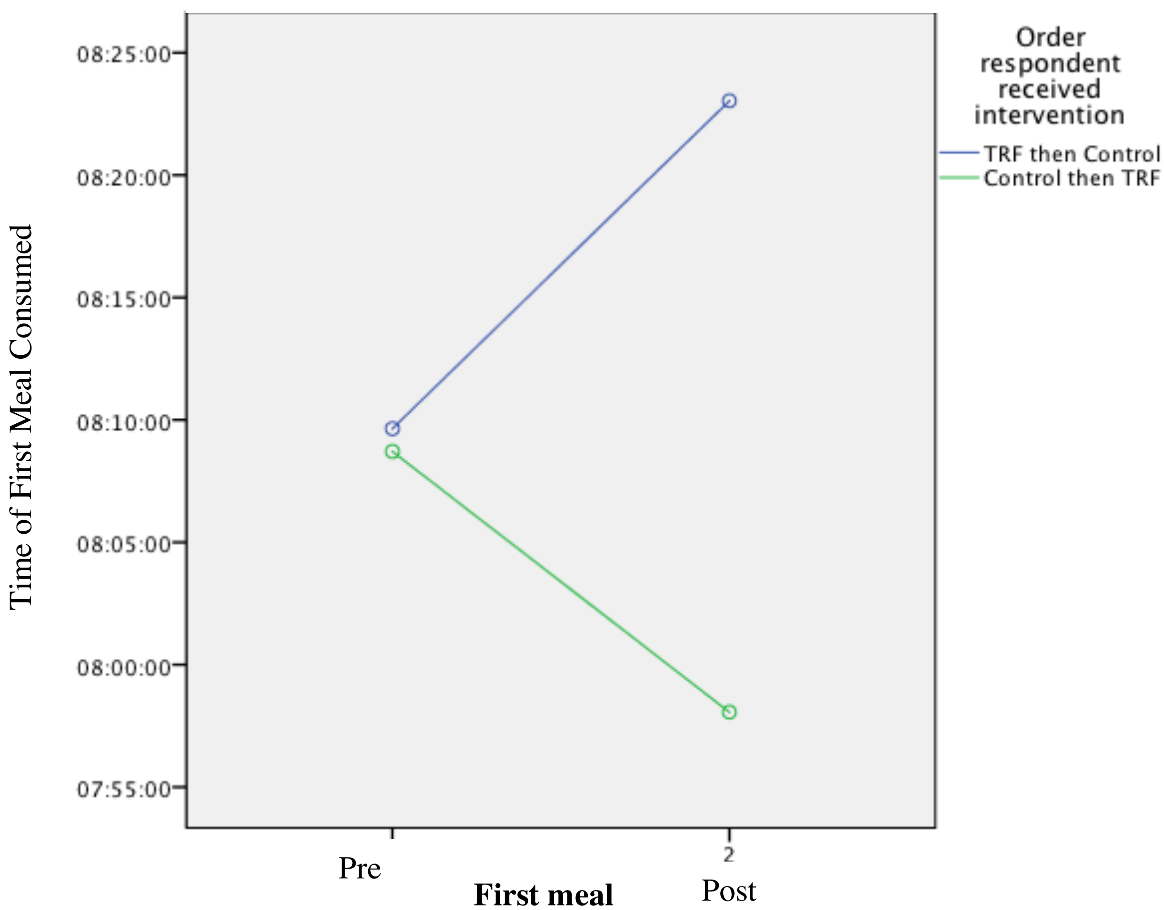

Figure 31. Pretest to posttest time of first food consumption by group.

There was no significant interaction effect between the order of intervention and time of last meal consumption, $\lambda = .999$, $F(1, 56) = .053$, $p = .818$. The lack of significance in the interaction effect indicates that group membership did not drive additional differences across the dependent variable, pretest to posttest time of last food consumption. There was a significant effect regarding time of last food consumption, pretest to posttest differences, $\lambda = .745$, $F(1, 56) = 19.131$, $p < .001$. The effect was large, $\eta^2 = 0.26$ (see Table 10 and Figure 32).

Table 8

Pretest to Posttest Time of Last Food Consumption by Intervention Order

Group	Pretest		Posttest	
	M	*SD*	*M*	*SD*
TRF – Control	20:10	1:34	19:11	0:40
Control – TRF	19:55	1:42	19:02	1:07

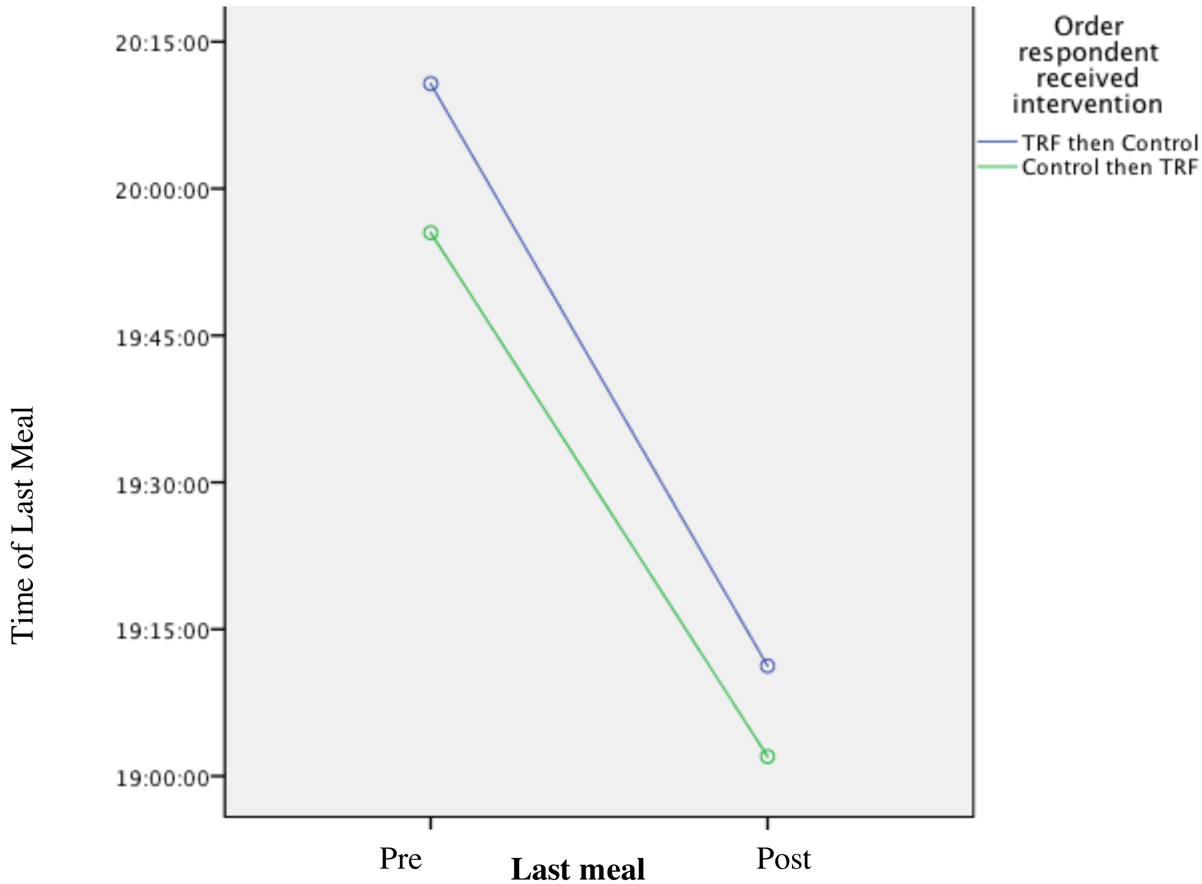

Figure 32. Pretest to posttest time of last food consumption by group.

Of the 60 respondents, three responded to a follow-up question asking what time they added additional meals during the TRF phase after indicating they added at least one meal per day during the TRF phase. The answers were 15:00, 16:00, and 19:15. Similarly, participants were asked if they skipped any meals during the TRF phase and if so, what time they would have normally eaten those meals. Nearly 75% (n = 44) of respondents did not answer this question. Of the nearly 25% (n = 16) of respondents who did answer, most indicated they skipped a meal starting after 19:00. Most indicated skipping meals after 20:00. The follow-up questionnaire also included details regarding adding or eliminating snacks during TRF. Forty percent (n = 24) did not respond to this question; 48% (n = 27) reported eating fewer snacks during TRF. Most respondents reported they would have been snacking after 20:00. Of the respondents who reported eating more snacks (n = 9) during TRF, most reported eating them in the afternoon after 14:00. Each respondent provided a unique time. Table 11 includes details of this data.

Table 9

Times Snacks Eaten

Variable	N	%
Specific Time	21	100%
After 19:00	2	9%
After 20:00	10	48%
After 21:00	7	33%
After 22:00	2	9%

There was no difference in weight loss between groups, suggesting that the order of intervention did not have a measurable effect on weight loss. There was a significant improvement in sleep quality, but not sleep duration, and a decrease in the number of times participants were out of bed during the night. There was also a significant decrease in PA. Time of first calorie intake did not change, but there was a significant change in time of last calorie intake. The time of largest calorie consumption did not change.

Discussion

Major Findings

These results suggest that two weeks of TRF does not cause significantly more weight loss than a CON period in free-living adults who weigh themselves daily and consume an *ad libitum* diet. Nevertheless, TRF seemed to improve sleep quality without altering sleep quantity and reduced time out of bed during the night. The TRF phase significantly reduced PA and altered the time that participants consumed their last meal.

Body weight

Participants lost weight regardless of the phase of the study, which means TRF was not more effective for weight loss than merely participating in a health-related study and weighing oneself daily. These results have several implications. First, they emphasize the strength of behavior change elicited by participating in research. Participants lost weight despite instructions to maintain their normal lifestyle during the CON phase. Second, the results corroborate previous research suggesting daily weighing as an effective tool for weight management. Moreover, if PA increased, weight loss could be attributable to greater expenditure, but this was not the case. Participants lost weight despite exercising less. Therefore we can extrapolate that weight loss was caused by decreased calorie intake rather than increased exercise. Weight loss may explain the decrease in PA. Research shows energy expenditure may decrease during a calorie deficit (Henslemen, 2016). Alternatively, participants may have rearranged their schedules to accommodate new eating patterns and therefore reduced or excluded PA. Decreased PA may be a detrimental effect of TRF if not counterbalanced by decreased calorie intake.

The present results contradict most other non-religious, TRF studies that included an *ad libitum* phase (Gabel et al., 2018; Betts et al., 2014; LeCheminant et al., 2013; Gill & Panda, 2015; Moro et al., 2016; Gabel et al; 2018; Sutton et al., 2018; Byrne et al., 2018). Other studies showed a significant weight loss during TRF while the present study did not find a significant weight loss during TRF. These researchers reported significant weight loss, ranging from 0.4 kg-3.27 kg, over two to 16 weeks. The primary discrepancy of the present study from these studies was daily weighing versus a pre- and post-intervention weight. All other TRF studies took a baseline weight before the intervention and a final weight after the study ended; the current study incorporated daily weighing collect sufficient weight data to determine weight trends during the study. However, daily weighing likely influenced weight loss throughout the study; therefore, the difference in weight loss between TRF and CON was not great enough to reach statistical significance. Other studies observed weight loss with a longer feeding period (13 hours), leaner subjects (BMI = 24.4 kg/m^2), smaller sample size (n=8), and equal duration (2 weeks) (LeCheminant et al., 2013). Hence, we cannot attribute the deviation from the literature to methodology aside from daily weighing. Daily weighing is an appropriate explanation for the deviation in results because it is an effective tool for weight management (Pacanowski, Bertz, & Levitsky, 2014). Daily self-weighing plus visual feedback (as utilized in the present study) results in a significant difference in weight loss (Pacanowski & Levitsky, 2015). Consequently, it is likely that daily weighing with visual feedback initiated the weight loss rather than other factors.

Chowdhury et al. (2016) did not report weight loss with TRF and observed an increase in body mass of 0.2 kg over six weeks. In this protocol, obese participants (BMI = 31.9 kg/m^2) participated in either an extended nightly fast until 12:00 (TRF) or a breakfast group that consumed a $\geq$ 700 kcal breakfast before 11:00. The TRF group gained an average of 0.2 kg, but the breakfast group gained 0.6 kg, which was significant. This exact protocol using normal weight adults (BMI 22.8 kg/m^2) elicited contrary results; TRF caused a weight loss of 0.4 kg over six weeks (Betts et al., 2014). These studies suggest that BMI affects ability to regulate energy balance. Lean individuals did not compensate for skipping breakfast during TRF and experienced weight loss. Obese individuals did compensate and gained weight with TRF. However, BMI cannot effusively explain the compensation to TRF. The present study population was overweight (BMI = 27.4 kg/m^2) but so was that of Gill and Panda (2015) that experienced significant weight loss of 3.27 kg over 16 weeks. BMI may play a role in body weight regulation and response to TRF, but it is not the sole explanation for weight change during TRF.

Physical activity

There was a significant decrease in PA following TRF, which mirrors findings from other TRF studies. Chowdhury et al. (2016) attributed the weight gain in TRF participants to a decrease in PA measured by Actiheart (CamNTech), a chest-mounted accelerometer and heart rate monitor. Similarly, Betts et al. (2014) observed a decrease in PA in the TRF cohort. Whether the decrease in PA was intentional or not, data consistently reflects a decrease in PA during TRF. Gill and Panda (2015) reported participants "felt more energetic" during TRF but did not measure PA (p. 796). Participants likely rearranged their eating occasions to accommodate the fasting window, which may have caused them to eat during time of scheduled PA. Additionally, participants may have unintentionally decreased PA as a result of weight loss, and research consistently shows a decrease in PA with weight loss (Henslement, 2016).

Sleep

There is scant and conflicting data regarding the effects of TRF on sleep. One pilot study found that an 8-hour TRF window did not alter sleep quality or duration in obese subjects after

12 weeks (Gabel et al., 2018). Conversely, Gill and Panda (2015) found an increase in self-reported sleep quality. Based on available data at the time of the study, we hypothesized that TRF would shift bedtime earlier, but not affect wake time and therefore increase sleep duration and quality. In a controlled randomized trial, participants who went to bed 90 minutes later than a CON group consumed an average of 136 ± 160 kcal more between 19:00-07:00 (Nedeltcheva et al., 2009). Eliminating evening snacking in the TRF condition could stimulate an earlier bedtime if participants used the time they typically spent eating to prepare for bed. Alternatively, going to bed may have been an avoidance tactic to elude hunger or eradicate the temptation to snack. The most likely explanation for the change in sleep pattern is due to the seasonal change in sunset. As the study progressed, participants went to bed later.

Despite sleeping for the same duration, participants reported statistically significant improvement in sleep quality, similar to findings from Gill and Panda (2015). Gabel et al (2018) found no significant change in sleep quality, however participants reported high sleep quality at baseline, which may explain why there was no reported improvement.

The most plausible explanation for the increase in sleep quality in the present study is the reduction of getting out of bed during the night. During TRF, there was a significant reduction in the number of times participants rose from bed at night. This is likely due to the abstinence from beverage intake, specifically alcohol, which has a diuretic effect. Many participants anecdotally described refraining from drinking wine or beer in the evenings; thus, they would not feel the need to use the bathroom during the night. Staying in bed may explain the improvement in sleep quality. If participants did not get out of bed, they may have less interrupted sleep, resulting in better sleep quality. TRF may be an effective strategy to improve sleep quality and reduce getting out of bed during the night.

Calorie intake

TRF had a modest effect on eating and drinking timing. There was no change in time of first meal consumption because the study protocol specified the eating period had to begin between 5:00 and 8:00. The average wake time was just before 7:00; therefore, participants could eat as soon as they rose in the morning. The only other TRF study that investigated first meal consumption was Gill and Panda (2015) who found that average first calorie consumption was 78 minutes after rising in the morning. There was no change in the time of day participants consumed the most food, which was approximately 17:00. This finding is similar to Gill and Panda (2015) who reported 37.5% of calorie intake occurred after 18:00. Betts et al. (2014) reached a similar conclusion, stating "overall daily eating patterns were unaffected [by TRF]" (p. 542). Likewise, Moro et al. (2016) noted no significant difference in nutrient distribution between the CON and TRF groups, but participants did change the time span between meals. Participants in the present study also changed the time span between meals resulting in a significantly earlier last calorie consumption during TRF. These results indicate participants ate the most food at dinner during TRF but ate dinner earlier.

Limitations and Contributions

Some limitations of the present study may influence interpretation of the data. First, the sample consisted of self-selected individuals interested in participating in a health-related study; behavior may differ from a less health-conscious population. The study population was rather homogenous and consisted of primarily Caucasian women. Generalizations about how TRF may influence individuals in diverse populations are limited. The most apparent limitation of the study is the use of daily weighing to capture changes in body weight. The researcher successfully examined fluctuations in body weight over time, but there was no phase for weight stabilization prior to starting the intervention. Similarly, there was no washout period between the CON and TRF phase so any effects of one condition may have carried over into the subsequent phase. Participants who began in the TRF phase likely retained a heightened awareness of eating behaviors after the first two weeks. Therefore, it is impossible to differentiate the degree to which TRF caused weight loss versus daily weighing and the fact that participants were more cognizant of their eating behaviors and PA. It is likely that daily weighing and participation in the study influenced weight loss during TRF.

The researcher tried to keep participant contact to a minimum to reduce the effect of observation and only emailed participants once to remind them when to switch conditions. Despite these efforts, participants knew the researcher was observing them, which may have influenced weight loss over the course of the study. The intervention was short-term circa the summer solstice; therefore, it is unknown how seasonal variation affected outcomes or long-term feasibility of TRF. Participants lost an insignificant amount of weight for the duration of the study, but it is unknown how this protocol would affect an individual who is weight stable over a longer period. Certain variables (e.g., PA and sleep) may influence weight loss more than TRF. Lastly, all data, except body weight, was self-reported. There may have been a response bias for variables such has night time eating or snacking.

Despite these limitations, the present study has many strengths. This study is the largest, most diverse study to experimentally examine the influence of TRF on body weight, sleep, PA, and calorie consumption behaviors in free-living adults. Moreover the present study is the first study to include a method that ensured participants were not eating outside of the eating phase without admission to a metabolic unit for observation. Allowing participants to remain in their usual environment likely minimized behavior change relative to constant monitoring in a metabolic unit. Finally, this was the first TRF study in non-obese adults to include multiple sleep measurements.

Conclusion

Due to the obesity epidemic, it is pertinent to find a method to control or decrease weight and prevent further weight gain. For the past 60 years, the U.S. government provided guidelines regarding *what* and *how* much to eat to no avail. If individuals are averse to changing *what* they eat, perhaps they are willing to change *when* they eat to indirectly alter the quantity they consume. There was no difference in weight loss between TRF and CON phases of the study despite a significant decrease in PA during TRF. The decrease in PA may be counterproductive to weight management or weight loss efforts and have other negative health consequences known to be associated with low physical activity. Therefore further research is warranted before making recommendations for TRF. Nevertheless, TRF may be a feasible lifestyle to improve sleep quality and reduce the frequency of getting out of bed during the night.

CHAPTER 4: PARTICIPANT EXPERIENCE OF TIME RESTRICTED FEEDING

Abstract

Time restricted feeding (TRF) is an eating pattern in which calories are consumed only during a specific period of time, typically eight to twelve hours per day. A growing body of evidence suggests TRF may be an effective weight management strategy, however quantitative studies fail to capture participant experiences with TRF and assess the acceptability of such an eating pattern. This qualitative study explored TRF as an eating pattern from the individual perspective.

Twenty-one participants (mean age 47.2 years, 80% female, mean BMI 27.0 kg/m^2) who completed a randomized, cross-over trial study of TRF voluntarily participated in a follow-up, individual, semi-structured interview about their experience of TRF and facilitators and challenges to adhering to a TRF regimen. Interview transcripts were analyzed using the Rapid assessment process (RAP).

Facilitators to TRF adherence included accountability, social support and dietary strategies of redistributing meals/snacks, choosing convenience foods, and eating larger dinners. Challenges were scheduling difficulties, social isolation, inconvenience, hunger, overeating and urgency to eating at the end of the feeding window. The experience of TRF was positive for some participants and resulted in a sense of empowerment over eating, increased awareness of motivations to eat, improved dietary intake and time management. In contrast, others reported unhealthy alterations in their eating and found the experience stressful.

Our results suggest there is a variety of responses to TRF and it may elicit detrimental eating behaviors that predispose some individuals to binge eating. TRF may not be suitable for everyone and careful consideration should be used before recommending it as a weight management method.

Introduction

Aberrant feeding-fasting cycles contribute to circadian rhythm disruption, and increase the risk for chronic diseases such as metabolic disorder, diabetes, cardiovascular disease, and cancer (Manoogian, E., & Panda, S., 2016). Time-restricted feeding (TRF) is an eating pattern in which consumption of food is limited to a particular time frame, without intentional caloric restriction or changes in dietary quality. TRF supports robust metabolic cycles and protects against nutritional challenges, such as a high-fat diet (61% dietary fat), as well as high-fructose and high-sucrose diets, that predispose to obesity and dysmetabolism. (Zarrinpar, A., Chaix, A., & Panda, S., 2015). More specifically, the limited human data available suggest that TRF may reduce body weight, improve insulin sensitivity, reduce blood glucose, lower blood pressure, improve lipid profiles, and reduce markers of inflammation and oxidative stress, although the data are not consistent (Melkani G., & Panda, S., 2017; Antoni R., et al 2017; Bhutani et al., 2013; Biston et al., 1996; Heran et al., 2008; Johnson et al., 2007, Tinsley, G. et al 2017; Byrne, N. et al, 2018; Sutton et al, 2018; Gabel, K. et al 2018).

Quantitative studies demonstrate the effectiveness of TRF as a weight management method but fail to address more in-depth areas of inquiry of participant experience with TRF (Carlson et al., 2007, Gill and Panda, 2015, Moro et al., 2016, Stote et al., 2007, Tinsley et al., 2017, Gabel, K. et al 2018; Sutton et al., 2018). Most recently, Gabel and colleagues conducted a pilot TRF trial in 23 obese subjects that limited eating to 8 hours per day for 12 weeks (Gabel et al., 2018). They found significant ($p < 0.05$) weight loss ($-2.6\% \pm 0.5$) but no alterations in sleep quality. Similarly, Sutton et al. investigated the timing of food consumption during TRF and found that TRF can improve health even in the absence of weight loss (Sutton et al., 2018). Consuming all calories before 15:00 resulted in increased insulin sensitivity and lowered the desire to eat in the evening, which may facilitate weight loss. Although still limited, the growing body of evidence suggests TRF is effective for weight loss and may confer additional health benefits, however the efficacy and practicality remains unknown and is of great interest to health care practitioners who may recommend TRF as a weight management strategy.

Moreover, recent studies have demonstrated that the timing of feeding in the general population is diverse, suggesting further research is necessary to identify those who have poor feeding patterns and selectively recommend behavioral changes in these individuals to improve their health (Zarrinpar, A., Chaix, A., & Panda, S., 2015). Understanding the experience of TRF and the facilitators and barriers to compliance in community settings could provide perspective on the potential for TRF as a short- or long-term dietary strategy. These perspectives and insights are missing from quantitative methods. Numerical data solidifies and elucidates the potential health benefits and potential risks of TRF. Yet, it is important to consider the acceptability and feasibility of TRF as a lifestyle because if a dietary intervention is not pragmatic it is unlikely to yield desired outcomes. The purpose of the present study was to investigate adults' subjective experiences with TRF as a lifestyle to assess its acceptability as a dietary intervention.

Methods

Design

A qualitative study was conducted among adults who completed a four-week randomized cross-over design study of TRF. Sixty adults (mean age 46.6 + 10 years-old; 86% Caucasian;

88% women; mean BMI 27.3 kg/m^2) completed the randomized, cross-over design study. Half of the participants were randomly assigned to two weeks of a control condition followed by two weeks of TRF. The other half received the treatments in reversed order. During the TRF phase, participants ate and drank *ad libitum* within a 12-hour period of their choice between 05:00 and 20:00. Throughout the study, participants weighed themselves daily, upon rising in the morning and after the last evening feeding, using a provided wireless scale (Withings body Wi-Fi scale, Nokia model WB-S05_03) that transmitted body weight to researchers. Participants did not receive instructions on changing dietary intake quality or quantity during the TRF or control phases. Dietary intake and physical activity were not directly measured. Paired *t*-tests were used within-subjects to compare TRF to control data for weight.

Sample

Participants for the TRF randomized cross-over study were recruited via an advertisement on an email list serve to college employees at a single university in April 2017. Eighty-nine people responded to the advertisement. Inclusion criteria stipulated that participants be at least 18 years old, own a device with Wi-Fi or Bluetooth capabilities, be able to complete the TRF study between June and July 2017, and speak English. Exclusionary criteria included a diagnosis of diabetes, eating disorder, binge eating, cancer, pregnancy or intention to become pregnant in the next six months, or use of the following medications: corticosteroids, antidepressants, antipsychotic, or mood stabilizing medications. Ten people were ineligible due to medication use and one person had binge eating disorder. Sixty-eight adults provided written, online consent and completed the pre-study online questionnaire regarding demographics, eating behaviors, physical activity, and sleep. A total of 60 participants completed the randomized trial.

Participants for the qualitative study were recruited in August 2017 from this sample of adults who completed the TRF study (n=60). Individuals received email invitations to participate in a semi-structured individual interview regarding his or her experience with TRF. Twenty-one participants (21/60 = 35%) responded to the email and were scheduled for individual interviews. All participants provided written consent to participate and be audio recorded.

The researcher used convenience sampling, versus purposive sampling, due to the small sample population (n = 60). A goal of 15 interviews was established a priori. Day's (1999) concept of theoretical sufficiency was used as a guide to achieve *concept* saturation rather than *content* saturation (Guest G., Bunce A., Johnson L., 2006). Concept saturation means the researcher has reached a point in which more data will not lead to additional information. No additional data can be found to develop new properties of categories and the relationships between the categories are disentangled (Seale, 1999 p. 87-105).

Interview Guide

The researcher developed an interview guide for the semi-structured individual interviews *a priori*. It included the following open-ended questions/prompts to elicit participants' experience with the TRF phase of the study: (a) please tell me about your experience with TRF; (b) what were some facilitators and what did you find helpful; and (c) what were some barriers to TRF (i.e., what did you find challenging)?

Interviews

Individual semi-structured qualitative interviews were conducted by the PI between August and September, 2017. All interviews were audio-recorded. Each participant received $10 as compensation.

The research team included the PI and two research assistants. One research assistant had preliminary qualitative education and experience; the other did not have any prior qualitative data analysis experience. The PI trained the research assistants to ensure that both had the necessary skills to complete coding. Furthermore, the PI had education and experience with qualitative data analysis. Beebe (2001) recommends having a diversity of perspectives from both insiders and outsiders to the phenomenon to reduce the risk of biased interpretation. Given the diversity of educational backgrounds and experience, the research team had adequate qualifications to analyze the data.

Analysis

Two research assistances transcribed 21 recordings verbatim with all identifying information removed to protect participant privacy. The PI listened to audio recordings several times while reading transcripts before proceeding with coding.

The present study utilized the rapid assessment process (RAP) (Beebe, 2001) to explore participants' experiences with TRF as a lifestyle for two weeks. RAP is an "intensive, team-based qualitative inquiry using triangulation, interpretive data analysis and additional data collection to quickly develop a preliminary understanding of a situation from the insider's perspective" (Beebe, 2001, p. xv). It has no specific research techniques but uses triangulation and iterative analysis. For this study we used multiple coders and the different perspectives of the coders for triangulation. RAP includes a matrix to summarize data, which is a valuable way of displaying, interpreting, evaluating, and disseminating research findings (Averill, 2002). Using RAP as an analytic strategy strengthens and enriches conclusions regarding subjective experiences of TRF.

RAP is appropriate to inform future research and clinical practice given the short duration of the study, qualitative data analysis experience of the research team, and timeline for analysis. The triangulation of data analysis provided an opportunity to systematically analyze participants' responses to the open-ended questions. Moreover, RAP provided an immediate, accessible, and precise reference to specific differences of opinion among participants. RAP was a more direct way of analyzing the data compared to an open coding method.

The researcher created an interview summary template based on the neutral domains established by each question in the interview guide. The researcher and assistants analyzed three interviews at a time using the template and then discussed any necessary revisions or additions to the summary template before coding the next three interviews. This provided an opportunity for iterative review of the data.

Each researcher independently analyzed each transcript by capturing key words and phrases in each domain: experiences, facilitators, and barriers. The researcher entered key words and phrases into the interview summary template for each participant. Therefore, each interview had three summary templates, one from each coder. The PI and two research assistants coded all transcripts for a total of 63 summary templates. They then compiled data into a matrix. From the matrix, the PI organized data into themes and categories within the domains looking for relationships and patterns to address the objective of the study: to better understand participants' experiences of TRF.

Strauss and Corbin (1998: p. 136) suggest that saturation should be concerned with reaching the point where further data collection becomes 'counter-productive', and where new material does not necessarily add anything to the overall story or theory. It was estimated that content saturation would be reached after approximately 15 interviews. Content saturation was reached for the domains expectations and experience after 14 interviews while it took only 12 interviews to reach content saturation for facilitators and ten interviews for challenges. Subsequent interviews confirmed the themes established by earlier interviews.

The PI attempted to reduce bias by having two research assistants independently code the transcripts in addition to her own data reduction to ensure that major biases did not influence data analysis. Triangulation was used as a technique to ensure that the account of TRF was rich, robust, comprehensive, and well-developed. Moreover, a single perspective can never adequately shed light on a phenomenon and using multiple perspectives can help facilitate deeper understanding and minimize bias (Patton, 1999).

The Cornell University IRB for Human Participants approved all research materials, protocols, and procedures prior to the commencement of the study. The research was designed to minimize any risk to participants. For example, the PI did not use any names and asked participants to use his or her participant ID number for any identification during the interview. Moreover, all transcripts were de-identified and uploaded to a secure data cloud approved by IRB that requires a two-step login. After all recordings had been uploaded and transcribed they were deleted.

Results

TRF Randomized Cross-over Study

There was no significant difference in weight change between the TRF phase (-0 .93 $\pm$ 0.23 lbs) and control phase (-0.35 $\pm$ 0.27 lbs) t (59) = -0.94 lbs/D, p = 0.11 and no significant interaction effect between the order of intervention and weight, λ = .564, F (27, 36) = 1.032, p = 0.46. There was a significant effect for weight over time, differences over time, λ = .410, F (27, 36) = 1.920, $p < .05$. The effect for time was large, $\eta^2 = .59$. Yet, there were no differences between the groups in weight loss (effect for treatment, F (1, 62) = .052, p = .821). TRF before the control phase did not lose more weight than the control phase before TRF group, but both groups lost weight as the study progressed.

Qualitative Study

Twenty-one (4 male, 17 female) individuals volunteered and participated in the individual interviews. All participants who expressed interest scheduled an interview. Participant characteristics appear in Table 12. Overall, there was no significant differences in age or BMI between individuals who participated in interviews versus those who chose not to participate. Significantly more minorities (p = 0.05) and men (p = 0.02) chose to be interviewed compared to the portion of the population who were not interviewed. There was no significant difference (p = 0.35) in college education between those who interviewed and those who chose not to interview.

Table 12

Characteristics of Study Participants

Characteristic	**TRF Randomized Trial (n=60)**	**Interview Study Population (n=21)**	**TRF Population Not Interviewed (n=39)**	**P-value comparing interviewed to not-interviewed**
Age (years), (mean +/- SE)	46.4 ± 10.09	47.19 ± 2.45	45.15 ± 1.76	0.38
Gender **Female, count (%)**	53 (88%)	17 (80%)	36 (92%)	0.02
Race **Caucasian, count (%)**	52 (87%)	17 (80%)	34 (87%)	0.05
Percent with a college education	73.3	80.9	71.7	0.35
BMI (kg/m^2), mean +/-SE	27.35 ± 5.56	26.96 ± 1.34	27.64 ± 0.85	0.66
Weight change during TRF, mean +/- SE	-0.93 ± 0.23	-0.94± 0.45	-0.92± 0.27	0.96
Adherence to TRF	46 (77%)_	17 (81%)	29 (74%)	0.79

Adherence to the TRF regimen was based on evening weight measurements taken within 60 minutes of the end of the feeding phase. There was no significant (p = 0.79) difference in adherence between participants who interviewed (81%) and those who did not interview (74%). Likewise, there was no significant difference (p = 0.96) in weight loss between groups. The interviewed group lost an average of -0.94$\pm$ 0.45 lbs while the TRF participants who were not interviewed lost an average of -0.92$\pm$ 0.27lbs.

Themes

Within each of the four domains: expectations, facilitators, challenges, and experiences with TRF, several themes emerged. Refer to Table 13 for a comprehensive list.

Table 13: Summary of Domains and Corresponding Themes for Time-Restricted Feeding Condition in Participants in a Randomized Trial of Time Restricted Feeding

Domain	Themes
Expectations	Weight loss
	Improve health
	Provide structure & routine
	Type of diet
Facilitators	Setting alarms
	Accountability
	- Daily weighing
	- Awareness of monitoring
	Short duration
	Social support
	Dietary Strategies:
	- Substituting beverages for food
	- Choosing convenience foods
	- Redistributing meals/snacks
	- Planning meals/snacks
	- Eating larger dinners
	- Being satiated
Challenges	Eating related challenges
	- Physical hunger
	- Urgency to eat within time restriction
	- Eating based on time restriction vs hunger
	- Overeating
	Scheduling difficulties
	Social events/social isolation
	Inconvenience

Experience of TRF	Enjoyment Empowerment: able to control eating Increased awareness of motivations to eat Improvement of time management Stressful

Expectations

Participants had varying expectations prior to beginning the TRF protocol. Many were hopeful it would cause weight loss or other physical health benefits "I wanted to pursue that kind of a weight loss program given my time constraints." One participant disclosed, "I wanted to see if it changed my sleeping habits." These responses were particularly interesting, as the study was not advertised as a weight loss program or as a program to improve sleep or health. Participants also hoped it would afford additional structure or help them establish a routine in their daily life. They anticipated the time restriction would improve their diet. Some participants considered TRF as "just another diet like gluten-free or paleo" and predicted little difficulty adhering to TRF "It was harder than I expected it to be." Others expected TRF to be challenging, "I thought it would be hard but didn't think it would be that hard."

Facilitators

Participants mentioned multiple strategies that facilitated adherence to TRF, ranging from using alarms to social support, and dietary strategies. There was no difference in adherence between the study population who was interviewed and those who were not (p =0.79). To eat within the allotted 12 hours, participants reported setting alarms on their phone to remind them to eat or begin preparing a meal so they could finish within the feeding window.

For others, the accountability created by participating in a study increased adherence. People explained that being monitored in the research study motivated them to eat only within the allotted time. One woman stated, "just knowing someone's watching me was enough, I didn't want to screw up." Or, "feeling like if I didn't do it [adhere to the protocol], I was messing something up." The daily weighing monitoring also provided incentive for compliance, as evidenced by the comment "the thing that really made me stick to it was the [required] weigh-in".

The short duration of the study was another factor that aided in compliance. Several participants mentioned how they were able to follow the protocol because it was only two weeks long "I didn't feel like I needed anything to help me, but that might be because it was just 2 weeks." This implies that compliance may be lower during a longer period of TRF.

Several participants discussed the importance of social support from friends and family. One woman said, "my partner kind've was just like don't eat that, it's past your time." Another women said her husband would start dinner for her so she could eat as soon as she got home from work and not go past her feeding time. Social support from family also occurred in the form of helping with chores or other tasks to accommodate an altered eating schedule. Social support from friends was perceived as understanding and withholding judgement. "Given my circle of friends who I normally socialize with, I […] said 'I'm just participating in a research study and these are the rules of the research study'".

Dietary strategies were identified as another facilitator and were grouped under the subthemes of substituting beverages for food, choosing convenience foods, redistributing meals/snack, planning meals/snacks, and eating larger dinners and being satiated.

Substituting non-caloric beverages for food helped participants maintain fasting during social events. People felt awkward at evening events with food and alcoholic beverages because they could not partake in them. To relieve the discomfort, people drank water or non-caloric tea, which were permitted throughout the study, to feel less awkward and more included in the event.

The most common dietary strategy was redistributing meals and snacks. Most participants reported moving the time of meals and snacks rather than eliminating them. They did not eat less food; they simply ate it at different times. “I would just eat my bedtime snack at 7:00 PM”. Beverage intake also shifted to facilitate the time restriction. One woman described waiting an extra 30 minutes for her coffee in the morning. A male participant described moving his evening glass of wine to 19:00 rather than 21:00. Drinking and eating earlier, within the feeding time, helped avoid the temptation to eat during the fasting time.

Other forms of planning helped many participants. “Sitting down and consciously setting a schedule” was helpful. Another participant noted, “planning ahead, looking at my schedule, seeing what hours I would be working the next day and from there, figuring out what time [to eat]”. Again, planning was engaged to fit all meals and snacks within the feeding window versus eliminating them.

Most participants reported intentionally consuming larger portions of food just prior to the fasting period. People ate more at dinner to compensate for missing their evening snack. One gentleman summarized many participants’ sentiments when he stated, “I would eat more than I usually would just to prepare, because I knew that after eight I would not be eating again”. Other participants condensed their evening snacks and/or beverages with their evening meal rather than eliminating them. “I just had to pack that into a larger dinner”. To accommodate the evening meal some chose to reduce food preparation time by using more convenience foods rather than cooking meals, commonly using phrases like “something quick” to describe a meal.

Participants also expressed that being satiated helped with the evening fast. “If I could get that last decent chunk of calories in by the 8 PM it’s no problem. It’s like, it wasn’t a matter of will, like if I were on a full stomach at 8 PM, not having to a snack would not be a problem.”

Overall, participants communicated concern about being hungry during the fasting phase and thus chose to eat more food at the end of the feeding window to facilitate adherence in the fasting phase.

Challenges

Eating-related challenges such as hunger and psychological challenges such as difficulty socializing at evening events made compliance with TRF more difficult. Participants described feeling “really hungry the first few days” but then “got used to it”. Nearly all participants reported hunger in the morning prior to breakfast. As one woman explained the challenge of waiting “Those 30 minutes were really hard”. In contrast, only two participants (2/21) said they went to bed hungry in the evenings.

Participants felt a sense of urgency or lack of time to eat and ate quickly to finish before the time restriction. “I got to eat…I scarfed it down”. Another participant remarked, “quick, I gotta finish my glass of wine before eight o’clock! So I was like chugging the glass of wine.” This was evident in social settings as well. One woman began to eat before everyone else at a party and explained, “I have to eat to be done by 7:15! And I would eat really fast”.

In some instances, participants found themselves eating when not physiologically hungry and feeling the need to overeat to prepare for the fasting period. Participants expressed eating because of the time of day rather than hunger. “There was some pressure when I was not hungry to eat”. Furthermore, one stated “It was hard to get the last meal in on time”. Eating before the time restriction felt like a necessity whether the participant felt physically hungry or not.

> Oh quick, I’ve got to have something because it’s going to be eight PM soon!” And it made no sense, like “but you’re not hungry, you never eat after eight PM. What are you doing?” But just because I couldn’t, I wanted it.

Several participants reported eating more foods and overeating during TRF.

> It did feel almost like there was a little rebel streak in me that was like “Oh my goodness, I can’t eat past eight PM?” So that was [a] small thought […] early on I guess, for a couple of days, but then I just didn’t think about that anymore.

Participants were dissociating eating from their physiologic feelings of hunger and satiety.

Another barrier was scheduling difficulties. Work, family commitments, and social engagements made TRF more challenging. TRF shifted meal times which conflicted with other activities and forced individuals to rearrange their schedule. Participants often moved meal times, which required additional planning and preparation.

In some instances TRF was challenging because it “got in the way of socializing”. They noticed how prevalent food and beverages were at evening social events and not participating was isolating. Some abstained from social events all together because being unable to eat “feels like I would be setting myself apart in this kind of way”. One women explained, “it was hard to get people to go out earlier [for dinner] so we ended up not going out”. Many participants felt isolated at events because they could not eat with others. “I had to sit by and watch everyone else eat”. Finally, there was a fear of social labeling associated with not partaking in food and beverages at social events. “It might be like, Kelly is the one who can’t eat after 7:45”.

A final challenge was the inconvenience and logistics of bringing additional food to work for those consuming larger meals to compensate for TRF. One man walked three miles to get to work in the morning and carrying his breakfast “got heavy”. Another woman expressed the inconvenience of having to pack additional food and dinner to bring to work so she could eat within the feeding window.

Experience with TRF

Healthy eating and diet plans are often associated with a sense of sacrifice and denial. In contrast, many participants reported very positive experiences with TRF noting the ease of following the regimen, enjoyment of the regimen and the empowerment it provided. TRF was described as “easy“, “not difficult”, “went well”, “easier than I thought” while others indicated it was an enjoyable experience, using words such as “fun”, “good”, and “enjoyed it”. TRF also provided a sense of empowerment. People felt “good” about adhering to the time restriction protocol. One participant explained that TRF provided discipline, commitment, motivation, and structure. “If this had been a week ago, I wouldn’t have been able to respond to [tolerate] this hunger. I lived, I survived. I did it then, I should be able to do it now”. Some felt satisfaction in not eating in the evening. “I wish I didn’t have it [ice cream] after I ate it, so I actually felt pretty good. I’m like, ‘See, you can do this’”. TRF helped participants gain confidence in their ability to control their eating.

Following a TRF regimen elucidated participants’ motivations to eat and raised awareness of eating in response to hunger, behavioral cues, and emotions. Some participants used hunger as a feedback mechanism to gauge previous intake and dictate how much they should consume at that moment, stating things like, “hunger in the morning meant I must not have overeaten yesterday”. Many participants were more conscious of what, when, and where they were eating. “Life is busy and I think sometimes I just eat when I can and I don’t think about it…this [TRF] made me stop and listen, like, ‘Am I really hungry’”. People talked about eating when they were awake, available, or not busy. “Eating my ice cream on Saturday night is more of a habit than enjoyment”. Others increased their awareness of external eating, such as eating in response to a specific location. One woman said, “For me, every time I walk through the kitchen I think, ‘Oh, what can I have?’”. Another participant noticed “pretty much every time I’m at my desk I’m eating something.” These reports of increased awareness of eating cues was in stark contrast to the participants that noted TRF reinforced eating when not hungry or when satiated.

Another motivation to eat elucidated by the TRF experience was emotional hunger, eating for relaxation as opposed to eating for physiologic reasons. Participants noticed they associated certain foods and beverages with relaxation, such as coffee in the morning and wine in the evening. “Eating is not just about hunger obviously, it’s about a lot of things. It’s part of the routine, it’s part of making space for this period of relaxation and disengagement”. Eating was noted as a way to take a break, “It’s not like hunger usually drives it [eating], it’s more wanting that break and so I just probably gave myself space to do that without the food I guess”.

Along with these cognitive effects of TRF, participants reported behavioral changes and evidence of improved diet quality. The evening fast helped to eliminate foods consumed after the evening meal. One woman stated ”I liked the structure of it […] I didn’t have to think, ‘Well it’s ten o’clock at night and I’m laying [sic] in bed watching TV and I really want a snack.’ I mean it eliminated those urges.” While others acknowledged the improvement in the nutritional content of their diet, “It was probably good for me because none of it is nutrition [sic] after a certain time. It’s not like I’m snacking on carrot sticks at nine o’clock at night. These examples contrast with the reports of participants that overate before the onset of the fast, highlighting the individual effect of TRF.

Outside of the impact of TRF on eating, adhering to the TRF regimen helped with time management. Participants were more conscious of the time. One participant noted improved planning skills after having to plan meals to fit within the feeding time. Others felt TRF helped them go to bed earlier, which they perceived as positive.

Despite these reported positive aspects of TRF, stress was noted as a predominant emotion. Some participants described their experience with TRF as *hectic, stressful*, and *hard*. "It weighed on me psychologically," one woman said. She felt pressure; "it [TRF] was always on my mind". Another participant stated, "there was quite a bit of worrying in the whole thing, just trying to eat between those two times." Participants felt relieved when the TRF phase was over. "Wow that's like a load off! I can eat whatever I want now". While many participants found it stressful throughout the two weeks, others found it initially stressful and then adjusted over time and as stated by a participant "got used to it".

Discussion

This study addressed a gap in the literature by exploring participants' experiences with TRF during a two-week, 12-hour time restriction on food consumption. We explored four domains: expectations, facilitators, challenges, and experience of TRF. Expectations for participating in TRF included weight loss, improved physical & mental wellbeing, and increased structure and routine. The most common facilitators to compliance were accountability, social support, planning and redistributing meals/snacks, and eating larger dinners. The challenges of TRF were physical hunger, scheduling difficulties, social events/social isolation, rapid eating to fit food in the feeding window, and overeating in anticipation of fasting. The experience of a 12 hour fasting regimen was positive for some, creating feelings of empowerment over eating and increased awareness of motivations to eat while others found the experience stressful. The data suggest there is a wide variety of responses to TRF and it may not be advantageous for everyone.

Participants' expectations about TRF revealed a sense of hope that TRF would provide structure and facilitate a routine for their eating habits, while others described an expectation of weight loss. Yancy et al. (2015) noted the importance of a sense of hope when beginning a diet; however, data showed that choosing a diet (such as participating in a TRF study) provides a sense of hope, but it does not result in more weight loss compared to an assigned diet (Yancy et al., 2015). For some in this study, TRF did improve time management. In terms of weight loss, our 2-week TRF did not result in a significant weight change. Body weight decreased in both the TRF (-0.92 $\pm$ 0.23 lb) and control (-0.35 $\pm$ 0.27 lb) phases of the four-week study and there was no significant difference in weight loss between participants who interviewed and those who did not (p = 0.96). This result is similar to other short-term TRF studies who found a significant weight loss of ~3% body weight over 12 weeks of TRF (Gabel et al., 2018). Other forms of IF appear to result in greater weight loss, approximately 4-6% body weight over 12 weeks, which is likely due to a greater calorie deficit (Bhutani et al., 2013; Klempel et al., 2013; Hoddy et al., 2014). No calorie intake data was collected so we do not know how TRF affected total calorie intake either directly or indirectly. However, many participants described moving evening calories to the feeding window suggesting no reduction in caloric intake; yet, they expected to still see weight loss.

Social support was cited as both a facilitator and barrier to compliance with TRF, with most participants discussing the importance of family members or friends in facilitating eating within the feeding window. Gender may play a role in the degree and type of social support. The study population who was interviewed was comprised of more males relative to the TRF study population. It is possible that men did not experience as great a shift in social support for dietary practices relative to women. Social support is especially helpful for women who are trying to change their diets while, for men, the most important factor is motivation (Kelsey et al., 1996). Perhaps the men in the study already had a great deal of support from family and/or friends so the change in level of support was smaller and therefore less noticeable. Family was more often helpful; whereas, friends were both facilitators and barriers to following the TRF regimen. This finding is consistent with the interference of TRF with engagement in social events. The role of social support in adherence to weight management behaviors is not fully understood. Social support for adherence with dietary regimens has been shown to be a facilitator as well as a barrier (Gonzalez L., Asencio J., de las Nieves, C.; 2017). The distinction, may be in the type of support that is provided, as suggested by the results of the MedWeight study, which compared people who maintained or regained weight after losing ten percent or more of their body weight. Individuals that maintained their weight loss received compliments and active participation, whereas those who regained their weight received verbal instructions and encouragements (Karfopoulou, et al., 2016). In our study, participants reported active participation from family members, such as meal prepping or picking up children from activities as well as verbal encouragement, and these enabled participants to adhere to TRF. Friends however provided primarily verbal feedback, without actions, and could be a facilitator or barrier depending on context and the individual. There were no evident patterns to determine characteristics of whether a friend would be a facilitator or barrier. This is the first study to report social support and barriers to TRF. Based on other studies, such as Karfopoulou, et al., it is likely that participants who received greater social support had greater adherence, and potentially greater weight loss, compared to those who had social barriers (Karfopoulou, et al., 2016) although this was not directly assessed in our study.

The study population that was interviewed consisted of more men and minorities compared to those who were not interviewed. Another TRF study also included many minorities, but not as many men. Gabel et al. consisted of primarily African Americans and women, including only three men in the study (Gabel et al., 2018). The wide variation in demographics in our sample may have contributed to the breadth of experiences reported with TRF.

TRF elicited undesirable eating behaviors among multiple participants. Many participants ate right before the time restriction and therefore ate quickly and felt rushed. This sense of urgency resulted in stress and possible overeating. It is generally advisable to eat slowly rather than faster to improve satiety and aid digestion (Angelopoulos et al., 2014). Rapid eating is also one of the characteristic features of binge eating behavior. Many participants chose convenience foods over more healthful choices that would take more time to prepare and eat. Greater consumption of convenience foods may be detrimental to health as they are not as nutrient dense and often times higher in sodium, fat, and more calorie dense. Some interviewees ate when they were not hungry because they knew they could not eat later. This phenomenon contradicts the positive message of mindful eating frequently included in general weight management advice (Warren et al., 2017). Therefore, TRF may inadvertently promote ignoring hunger ques and consuming unnecessary calories due to predicted hunger. As such, participants also engaged in overeating to avoid forecasted hunger after the overnight fast. Eating quickly, eating when not hungry, and overeating are all unfavorable eating behaviors consistent with binge eating behaviors (Bak-Sosnowska M., 2017). Although persons with binge eating disorder (BED) were excluded from this study, it appears that TRF may encourage unhealthy eating behaviors that could contribute to binge eating. No nutrient intake data was collected, but future research may want to include measures of diet quality, such as the healthy eating index to track any changes in nutrient intake during TRF. There is little research on TRF and BED however Agras and Telch (2013) found that a 14-hour period of caloric deprivation increased the occurrence of binge eating in 60 obese women and also led participants to eat significantly more during a buffet

(Agras and Telch, 2013). These findings are consistent with our findings of greater intake during the evening meal.

TRF was very socially challenging and isolating for some individuals. Many participants avoided social events or expressed feeling awkward not eating or drinking at social gatherings. Socializing is an important component of mental and physical health. People with a higher BMI tend to feel more socially disconnected than people with a lower BMI (Jaremka et al., 2017). If an individual is overweight, adopting TRF as a lifestyle may exacerbate social disconnection and lead to poor health.

The experience of TRF provided participants with insights into their motivations for eating and the multiple functions of food. Participants acknowledged that food was more than nourishment; they ate for reasons other than physical hunger. Food was a justification or a treat, a component of relaxation. This form of emotional regulation is consistent with previous findings (de Zwaan et al., 2006; Meule et al., 2014; Shillito et al., 2018; Vander Wal, 2012). For some, food was a method to reduce stress and negative emotions. Some individuals noted that they ate to alleviate emotional distress through comfort or distraction. These results are supported by an accumulating body of evidence that indicates that stress leads to the consumption of unhealthy, energy-dense, palatable food (Masih, T. et al., 2017). By eliminating forms of *automatic* eating with TRF, participants increased awareness of emotions and eating habits. Therefore, TRF may be beneficial for raising awareness of eating habits and could potentially reduce *mindless* eating, which often occurs during the evening hours (Gill and Panda, 2016; Gabel et al., 2018). Participants were surprised by the amount of evening snacking they did prior to TRF, which seemed automatic and routine rather than satiating a physical hunger.

Although TRF may have reduced mindless eating, it may have induced overeating in response to the restriction phase. The argument of restraint theory is that restraint can cause paradoxical overeating (Wardle & Beinart, 1981; Koch et al., 2018). Participants seemed to anticipate greater hunger in the evening knowing they could not eat past a certain time. This finding supports Lowe's (1982) hypothesis that anticipated deprivation increases food consumption, particularly among restrained eaters. The questionnaire did not include restraint measurements so it is unclear how restraint may have influenced overeating during the restriction phase. A recent study by Gabel, K. et al 2019, showed no change in eating disorder symptoms, including binge behavior and restrictive eating, or changes in the eating behaviors of dietary restraint, uncontrolled eating or emotional eating pre and post a three month TRF period in obese individuals. This data would suggest that participants would not have an increase in overeating behaviors, however the results of Gabel et al are inconsistent with participant statements in our qualitative study describing greater consumption at the evening meal to avoid forecasted hunger (Gabel et al., 2019).

The variety of emotional experience of TRF is as diverse as the participants themselves. Some enjoyed the process and others found it stressful. Dietary recommendations must be specific to the individual and there is no *one size fits all* approach. Several female participants discussed that they felt empowered by adhering to TRF. They felt good about not eating in the evenings, particularly unhealthy foods. TRF provided discipline, commitment, motivation, and structure during this short-term study. The length of the protocol may have contributed to the high rate of adherence and sense of accomplishment or empowerment. On the other hand, TRF caused a great deal of stress and anxiety for other participants. Some found the idea of going without food or having to change schedules caused additional stress and anxiety. TRF may be more appropriate for some individuals and not others.

Limitations

The Primary Investigator considered that her personal role, experience, and knowledge may have influenced the interviews, analysis, and interpretation. The study population was very homogeneous and primarily composed of highly educated, Caucasian, middle-aged women. However, there was a significant difference (p = 0.05) in the proportion of Caucasians in the TRF study compared to the sub-population who were interviewed. More Caucasians chose not to interview compared to minorities, which may have influenced emerging themes of TRF. Likewise, proportionally more men chose to interview (p = 0.02), which may indicate stronger sentiments towards TRF. The researcher recruited participants from a single list serve for the original TRF study, which may explain some of the homogeneity. Generalized conclusions about how other populations might experience TRF are not possible. The researcher used convenience sampling to recruit participants for the interviews due to the small population of the original TRF study. Individuals who responded to the email invitation to participate had better compliance with the TRF and more weight loss than those that did not participate. This suggests that volunteers for the interview may have had stronger feelings (either positive or negative) regarding TRF, which may explain the wide variation in experiences.

The sample size was small (n = 21), however there is no reason to believe the sample size was too small as it met concept saturation as defined by Day (Day, 1999). Indeed after approximately 15 interviews the concepts were well solidified and after consulting with a qualitative research expert, it was deemed that sufficient depth of understanding had been achieved. Additional interviews likely would not have provided new information or modified the concepts established for this sample.

Additionally, the exclusionary criteria did not include restrained/restrictive eating, or emotional eating, it only included eating disorders of anorexia, bulimia, and binge eating. Not knowing the prevalence or severity of restrained eating habits of the study population may limit extrapolation to the general population. It is likely that restrained eaters may react differently to an imposed restriction compared to unrestrained eaters and could have accounted for our observation of overeating in the feeding time period.

The TRF intervention was only two weeks in duration and many participants attributed adherence to the time restriction to the short duration of the study. When asked if they would have participated if it was a two-year study, they responded they would likely decline. Therefore the short intervention may fallaciously inflate adherence and the ability to comply long term.

Implications for Practice

Findings from this study revealed peoples' experiences with TRF and provide insight into the acceptability of TRF as a lifestyle and potential impact on dietary quality and eating behaviors. Themes from the data emphasize the importance of considering a holistic approach to dietary interventions and recommendations that carefully consider social, cognitive and emotional characteristics of individuals. Based on the present findings, individuals who live alone, have a consistent daily schedule, or those who have few social engagements outside the feeding window may find TRF easier to follow compared to individuals with children, a highly variable daily schedule, or many social engagements outside the feeding window. People who struggle with night eating may benefit from TRF because of the simplicity of eliminating night eating after a certain time. TRF also raised awareness of eating habits and motivations to eat (boredom, stress relief, etc.). However, TRF may also promote binge eating type behaviors and not be appropriate for anyone with high levels of anxiety, depression, emotional eating habits, or those with a history of an eating disorder or restrictive eating. Overall, the quality of dietary intake may be improved with TRF or conversely decline as participants consume more convenience foods and overeat.

Recommendations for Future Research

Future TRF research should include measurements of mood (e.g., restraint, depression, anxiety, and eating behaviors such as emotional eating, night eating, and binge eating) to identify characteristics that indicate whether an individual would experience stress and/or unhealthy eating versus feel accomplishment and improved dietary intake with TRF. Moreover, measuring diet quality, such as the Healthy Eating Index, may provide additional insights into how TRF affects food choices. Using a more diverse population would benefit generalizability of the conclusion regarding the feasibility of TRF for different lifestyles. Furthermore, researchers should consider other lifestyle and social factors such as having children or shift work, which may greatly influence the ability to adhere to a TRF schedule.

Conclusion

This research is the first qualitative study of TRF and contributed new insights into experiences of TRF, the challenges and facilitators to a TRF lifestyle, and the resulting consequences. The emergent themes suggest there is a wide variety of responses to TRF and it may not be suitable for all individuals. Future research should focus on identifying characteristics of individuals that may determine whether TRF would be a beneficial or stressful experience and whether it contributes to the improvement or decline of diet quality and eating behaviors.

CHAPTER 5: INVESTIGATING THE EFFECT OF DECREASING PORTION SIZE ON ENERGY INTAKE

Introduction

Increased portion size (PS) greatly affects EI and may be an environmental factor contributing to obesity (Kral et al., 2011; Livingstone et al., 2014; Rolls, 2014). Environmental factors may play a greater role in food consumption than biological forces (Levitsky, 2005). Controlled human experiments consistently demonstrated that serving a larger portion of a single food or beverage leads to increased intake (Diliberti et al., 2004; Flood et al., 2006; Kral et al., 2004; Rolls et al., 2002; Rolls et al., 2007). People may override satiety signals and perception of amount of food they consumed when presented with a larger PS (Rolls et al., 2006). Rolls et al exampled this in a controlled feeding study (Rolls et al., 2006). For two consecutive days for three weeks, subjects ate their main meal in a controlled setting and ate controlled snacks between meals. PS varied for all foods and beverages in a given week (either 100%, 150%, or 200% of baseline intake). In this study, Rolls et al. (2006) found that increased PS had a significant effect on EI in both men and women ($p < 0.001$) resulting in an increase in calorie intake by 16% for the 50% increase in PS and 26% increase for the double portion serving size. Compensation is not evident in studies that examined the effects of increased PS on eating behavior. It is unknown whether reduced PS leads to decreased intake at the same meal. It is unknown at what percentage of the original portion people begin to eat more of other foods to compensate for reduced entrée portions, which could reduce foods waste or overeating.

The purpose of the present study was to investigate the point at which participants increase a compliment food (CF) in response to a blind reduction in PS of a main entrée. The researcher assessed hunger and appetite before each test entrée (BE) and at various points during the meal: after entrée (AE) and after dessert (AD). The researcher examined whether reduced PS of the entrée affects intake of a CF and hypothesized that a reduction of 10%, 15% and 20% of the entrée would not illicit an increase in CF, but a reduction of 25% of the entrée would induce compensation and increase intake of the CF. There is no research to support this hypothesis, it is predicted that visually a quarter less of a portion served would be noticed.

Methods

Experimental Design

The researcher used a crossover design with repeated measures within subjects so each subject served as his or her own control. Once a week for five consecutive weeks, participants reported to the Human Metabolic Research Unit and ate a lunch consisting of macaroni and cheese. The first week, participants served themselves *ad libitum* (i.e., 100% as a baseline amount). For the following four weeks, they consumed 75%, 80%, 85%, or 90% of their baseline intake. All participants reported to the laboratory between 11:00 and 12:30 on the same day of the week for the five weeks for consistency. The researcher counterbalanced the order of the PS across subjects using Latin squares and randomly assigned subjects one of the condition sequences based on the day of the week they participated in the study (see Table 14).

Table 10

Latin Square Assignment of Weekly Entrée Portion

	Monday	Tuesday	Wednesday	Thursday
Ad Lib Week	X	X	X	X
Week 2	90	85	80	75
Week 3	85	80	75	90
Week 4	80	75	90	85
Week 5	75	90	85	75

Subjects

The researcher recruited undergraduates aged 18 to 69 years using an in-class advertisement. Table 15 include subjects' characteristics. Respondents were eligible if they did not have any food allergies, intolerances, or restrictions; did not have a history of an eating disorder; and could attend lunch in the metabolic unit for five consecutive weeks. Height and weight were self-reported. Individuals provided signed informed consent and received compensation in the form of extra credit for the class in which the study was advertised. The Cornell University IRB approved the study protocol.

Table 11

Participant Characteristics

	All Participants (n=52)	Women (n=41)	Men (n=12)
Age (y)	19.71 ± 7.02	20 ± 7.88	18.64 ± 1.21
Height (in)	67.38 ± 6.01	66.46 ± 6.40	70.79 ± 1.92
Weight (lbs)	139.73 ± 27.78	131.95 ± 19.95	168.73 ± 34.22
Body Mass Index (kg/m2)	21.72 ± 3.41	21.23 ± 3.24	23.55 ± 3.56
Ethnicity	1: n=26	1: n=21	1: n=5
	2: n=1	2: n=1	2: n=0
	3: n=3	3: n=3	3: n=0
	5: n=13	5: n=11	5: n=2
	6: n=8	6: n=5	6: n=3
	7: n=1	7: n=0	7: n=1

Note. Ethnicity key: 1= White, 2= Hispanic or Latino, 3= Black or African American, 4= Native American or American Indian, 5= Asian/ Pacific Islander, 6= Mixed Ethnicity, 7= Other.

Procedure

Subjects were asked to maintain the same breakfast intake on the weekday they participated in the study for the five weeks. Prior to lunch, participants completed a validated questionnaire regarding hunger, satiation, desire to eat, and projected intake (Blundell et al., 2010). This was the BE survey. Participants circled answers on a Likert scale from 1 (not at all) to 7 (extremely). After subjects finished the entrée, they completed the same questionnaire assessing their hunger, satiation, desire to eat, and projected intake. This was the AE survey. After completing the AE survey, subjects served themselves as much ice cream as they desired with an unlimited number of servings. The researcher weighed the dish before and after each serving to calculate intake. After finishing the ice cream, participants completed an AD survey (see Figure 33).

			How hungry are you?					
Not at all	1	2	3	4	5	6	7	Extremely
			How full are you?					
Not at all	1	2	3	4	5	6	7	Extremely
			How satiated are you?					
Not at all	1	2	3	4	5	6	7	Extremely
			How strong is your desire to eat?					
Very weak	1	2	3	4	5	6	7	Very strong
			How much do you think you could (or would want to) eat right now?					
Nothing at all	1	2	3	4	5	6	7	A very large amount

Figure 33. Survey participants completed before and after the entrée and dessert each week.

Data Analysis

Ninety-nine participants enrolled in the study and 74 (74.7%) completed all five weeks of the study. The other 25 participants had at least one week of missing data and are not part of the present analysis. The researcher used JMP 13.0 Pro for all statistical analyses. The researcher used analysis of variance for intake data and set significance at $p \leq 0.05$ for all tests. For the purposes of this study, the researcher only analyzed dessert consumption data.

Results

The final sample consisted of 12 males and 62 females with an average BMI of 21.6 kg/m^2 and 19.58 years of age. See Table 15. There was no significant difference in dessert intake between any of the PS served F (3,131) = 1.6147, $p = 0.1892$ (see Figure 30). There was no effect of treatment order on dessert consumption F (63,131) = 0.9015, p = 0.4962 (see Figure 34).

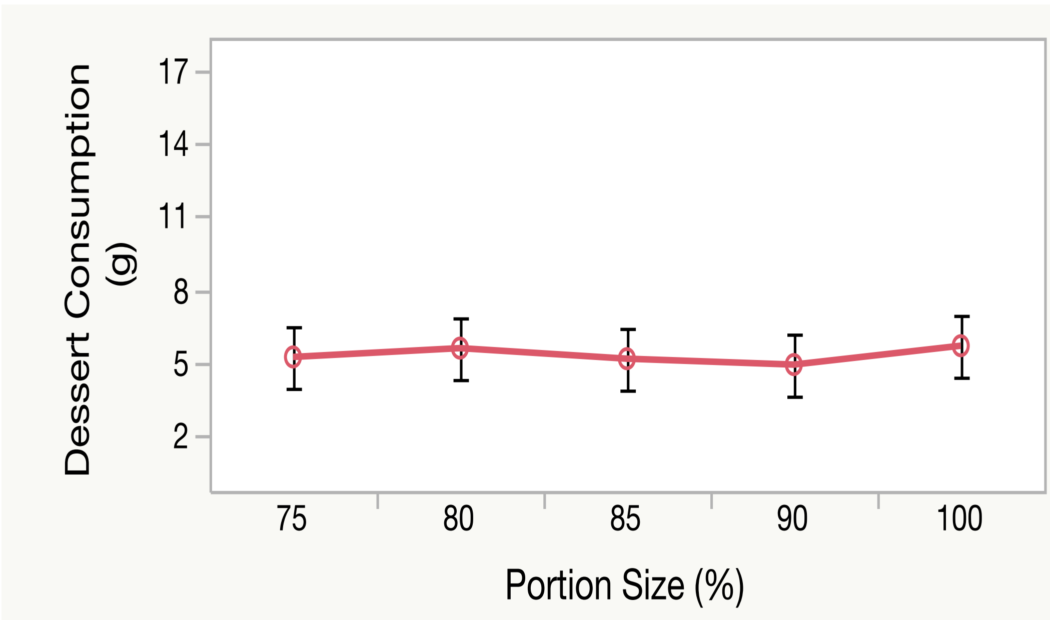

Figure 34. Dessert consumption in g after each portion served. X-axis represents percent of baseline intake served.

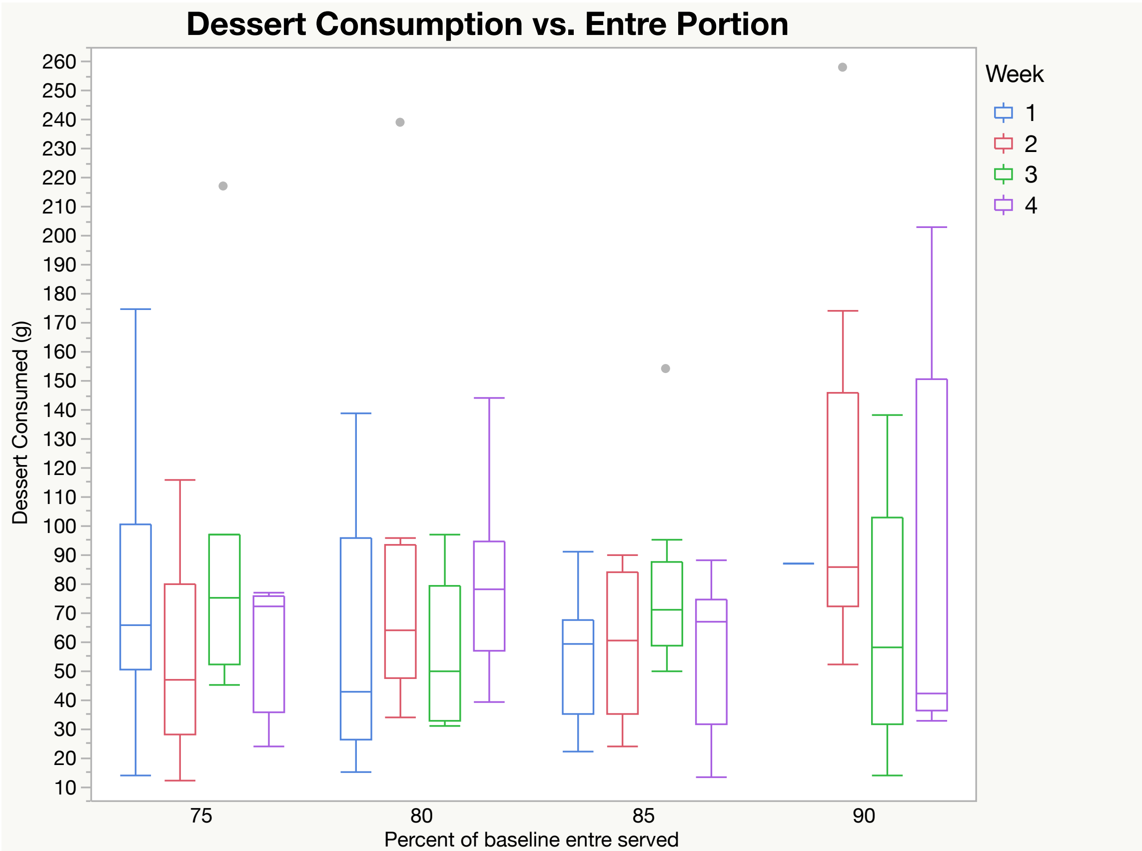

Figure 35. Dessert consumption by week of study. Treatment order was random.

Discussion

The purpose of this study was to examine the effect of decreasing PS of an entrée on dessert intake. The hypothesis was that a reduction in PS by 25% of baseline amount of an entrée would elicit compensatory behavior as evidenced by increased dessert consumption, However, this was not the case. At no point in entrée reduction did participants consume more dessert. The amount of dessert consumed remained constant regardless of the PS served. This is the first study to investigate a blind reduction of PS of food in a single-meal setting. Rolls et al. (2006), among other scholars, demonstrated in numerous studies that large PS leads to increased intake; such findings do not support compensatory behavior to regulate intake in single-meal settings or with chronic exposure to large PS (Burger et al., 2011; Diliberti et al., 2004; Jeffery et al., 2007; Rolls et al., 2002; Rolls et al., 2007). If there is no compensation for increased PS, it is feasible that there would be little to no compensation in response to decreased PS as shown here.

Comparison to other portion reduction studies is challenging due to a lack of past research. Kesman et al. (2011) found that a portion control plate and bowl along with dietary counseling reduced in weight in obese patients. This demonstrates the importance of environmental factors such as PS on EI, and thus, body weight. Caution is necessary when drawing comparisons between Kesman et al. (2011) and the present study for several reasons. Participants in the study by Kesman et al. (2011) consciously tried to reduce PS and lose weight, whereas in the present study, participants were blind to PS. Participants in the Kesman et al. (2011) study were obese compared to normal weight subjects in the present study. Lastly, participants in the present study ate in a communal setting rather than at home.

One way to surreptitiously change PS is to vary the size of dinnerware; reducing plate size can decrease self-served PS by up to 22% (McClain et al., 2013; Wansink et al., 2013). However, when plates become too small, they cease to have this effect and result in refills and reactance (Rolls et al., 2007; Shah et al., 2011). Plate size was controlled in the present study; therefore, plate size did not affect intake.

Limitations and Contributions

There are several limitations to the present study. First, this was a short-term study and results may not translate to long-term effects. The researcher did not control for beverage consumption, which may influence gastric stretching and thus consumption of the entrée and/or dessert. Additionally, the researcher is unaware of intake outside of the meal provided. Participants could have consumed additional food after leaving the lab if they felt hungry or desired other food. The study did not include measurements of participant dietary restraint, disinhibition, or hunger tendency scores. Furthermore, the test meal consisted of only two foods, which is not representative of typical meal patterns that consist of mixed meals. Finally, the study population was very homogenous and is not representative of the general population.

The present study has several strengths and contributes to the literature by providing novel insight into compensatory behavior (or lack thereof) in response to a blind, imposed energetic challenge. The within-subject, randomized controlled design was a strength that reduced the large interindividual variability in response to eating. In addition, participants established their own baseline intake rather than receiving an arbitrary amount as baseline.

Conclusion

There was no significant difference in dessert consumption based on PS. This is the first study that investigated complementary food consumption in a within-meal setting. Results compliment studies of increased PS that show little to no compensation. Further research should investigate whether long-term portion reduction effectively reduces calorie intake and serves as a weight management strategy.

CHAPTER 6: CONCLUSIONS

In conclusion, the research examined in this dissertation focuses on energetic compensation. Chapter one reviewed the extensive body of evidence of human response to imposed energetic challenges and subsequent weight changes. Furthermore, it quantified the imprecision of body weight regulation. Chapter one determined an average "settling zone" in which there is little energetic compensation, and physiological mechanisms do not correct for energy imbalances as evidenced by weight loss in reduced calorie intake studies and weight gain in overfeeding studies. The weighted average change in energy intake across all eight categories of studies was 334 kcal. This is estimated to be the largest error in energy balance that would occur before corrective feeding mechanisms would ensue. Based on the Hall equation, this would equate to approximately 33 lbs in three years, a figure that is supported by epidemiological research and population trends in body weight. Hence, physiological mechanism to regulate body weight (fat) are not nearly as precise as once believed.

Of the three variables to eating (what, when, and how much), the largest research gap lies in when people eat. In an attempt to expand the scant body of evidence on nutrient timing and body weight, a pilot study was conducted among undergraduates to test whether a 12-hour time restriction would cause weight loss. It was hypothesized that by limiting the feeding window to 12 hours, participants would eliminate evening snacks, and hence lose weight. Due to poor adherence, we were unable to draw conclusions regarding the effectiveness of TRF as a weight management tool and sleep aid.

After reviewing the pilot study, a larger TRF study was conducted among free-living adults in the Cornell community. By using an older population, we were able to improve external validity as the study population had lifestyles and routines more similar to the general population relative to undergraduate students. Moreover, we were able to have a larger sample size and include other demographic variables that may affect weight, such as income, education, race, etc. As evidenced by Chapter Three data, TRF did not significantly affect weight change relative to the control period, however it did result in a significant improvement in sleep quality and arousal during the night. To the best of our knowledge, this is only the second study to examine sleep quality during any variation of intermittent fasting. It is also the largest structured TRF study to date, with a final study population of 60 participants. Other novel interactions were discovered in Chapter Three that have not been included in other IF, ADF, or TRF studies. These data may provide insight as to how to best develop weight management strategies and public health recommendations to optimize health.

There is very little human research on time restriction and to date, no published qualitative studies addressing the feasibility and acceptability of TRF as a lifestyle to manage weight and improve health. Chapter Four included analysis of 21 individual interviews of participants who successfully completed a four-week TRF study. Three independent coders analyzed the transcripts of the recorded interviews and came to a consensus about recurring themes among TRF participants. Participants had mixed experiences with TRF. Some found it very easy to adhere to and enjoyed the practice and have continued the lifestyle after the study ended. Others found it more challenging and incongruent with their lifestyle and schedule. Positive aspects included improved self-efficacy and overall positive attitude about health and not snacking at night. The largest negative aspect reported by participants was an imposition to socializing and evening engagements. Further research is warranted to explore lifestyle characteristics that may be used to identify individuals that would benefit from TRF.

Finally, Chapter Five was the first study to directly investigate the effects of blind portion reduction on complement foods in a within-meal setting. The entrée was randomly reduced to either 90%, 85%, 80%, or 75% of baseline *ad libitum* intake prior to offering an *ad libitum* dessert. We hypothesized that no compensation would occur at 90%, 85%, or 80% of original entrée portion, but consuming 75% of baseline amount would elicit compensation as evidenced by an increase in dessert. We found no compensation at any portion reduction. Participants consumed the same amount of dessert regardless of the portion size served. These data provide further evidence of weak physiological mechanisms to regulate body weight within a narrow range.

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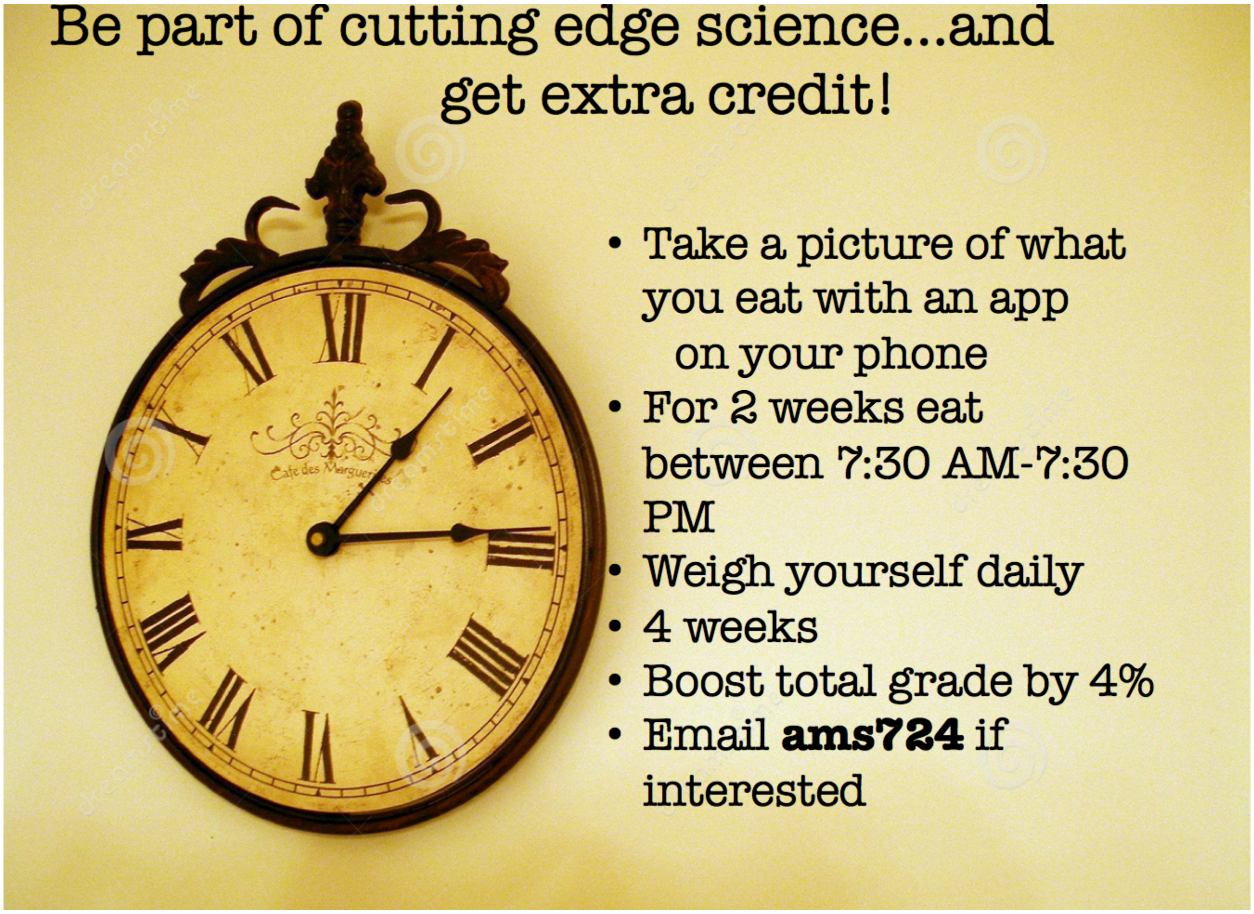
APPENDIX A: ADVERTISEMENT



APPENDIX B: PARTICIPANT PROTOCOL

Fall 2016

Setting up the Scale

If you have not already, set up the scale by following the instructions in the box. You will need to create a Withings account. At a later point, you will need to grant us access to your data, but don't worry about that right now.

Getting the App

The app is not ready to use yet. For the mean time please use the camera on your phone to take before/after pictures of your food/drinks. When the app is available you will receive email instructions on how to download and use the app.

Taking Pictures of your food and drinks

Place your student ID next to your plate/food/beverage. Take a photo of the food before you start eating. After you are finished eating, take an "after" photo. Make sure your student ID is in every picture. Please take photos of all of your food/caloric beverages. (You do not need to photograph water, black coffee, etc.)

Morning

A) Record what time you woke up

B) Weigh yourself after using the bathroom, before you eat or drink anything

C) If you are in the TRF portion of the study, do not eat until 7:30 AM

D) When you eat, take a picture of your meal using the app on your phone (for now please use your phone camera). Make sure your student ID is in the picture (next to your plate or whatever you're eating/drinking).

E) When you finish eating (meal or snack) take a picture of your plate making sure your student ID is in the photo.

Daytime

Eat and drink as you normally would, making sure to take a picture before and after you eat remembering to have your student ID in each photo.

Evening

A) Continue taking pictures of your food (with student ID) before and after you eat.

B) If in the 2-week TRF portion, weigh yourself immediately after your last meal (you should finish by 7:30 PM). Do not eat or drink any caloric beverages until 7:30 AM.

C) Record what time you go to bed.

IF YOU HAVE ANY QUESTIONS PLEASE EMAIL AMS724

If you are compliant and follow all of the instructions, you will have 4 points added to your final NS 1150 grade.

APPENDIX C: RECRUTIMENT ADVERTISEMENT

Can you lose weight without dieting? Let's find out! Participate in a research study examining the effects of eating within 12 hours. For two weeks eat as you normally would and for two weeks eat all of your food within 12 hours of your choice between 5 and 8. For example, you can choose to eat 5 AM- 5 PM or 6 AM-6 PM, etc. Research indicates that eating within 12 hours may lead to weight loss without having to diet. Participants will be asked to record when they wake up and go to bed and weigh themselves daily (you will receive a wireless scale valued at $150, yours to keep after the study ends) and $20 compensation. Email Anna Sewall at ams724@cornell if you are interested in participating.

APPENDIX D: PARTICIPANT INSTRUCTIONS

Thank you for participating in the TRF study. The purpose of this study is to examine the effects of restricting eating to a 12-hour timespan. For this four-week study you will be asked to record your bedtime, when you wake up (wake time), and weigh yourself twice a day. For two of the four weeks, you will be asked to restrict your eating to a 12-hour timespan. For the other two weeks, you may eat whenever you like. You may choose your 12-hours between 5:00-8:00. It does not need to be on the hour either, it could be 6:45 AM-6:45 PM, but you must keep the same 12-hour time span for those two weeks.

You will receive an email instructing you whether you will begin a two-week period by restricting your eating time (TRF phase) or if you can eat freely. You will also receive an email indicating when it is time to switch from control group (eat whenever you please) to the treatment group (12-hour eating window) or vice versa. Participants will not all be in the same group (TRF or control group) at the same time, so if you have friends/colleagues who are in a different group, please don't be alarmed.

Morning

1. Record what time you wake up on the sheet provided. Please make sure to include AM or PM.
2. After using the bathroom, please remove all garments and step on the scale. After the weight stabilizes, it will go through other measurements such as lean tissue, body fat percentage, etc. Record your weight in pounds on the sheet provided.

Evening

1. As soon as you finish your last meal of the day, remove all garments and weigh yourself. After the weight stabilizes, record your weight in pounds and the time you weighed yourself.
2. Record what time you go to bed on the sheet. Please include AM/PM

You will receive an email at the end of the study letting you know when the study is over. We will ask you to fill out a final survey. At this time we will schedule a time for you to turn in your record sheet with wake/bedtimes and weights and collect your payment.

If you have any questions or concerns, please email A'nna Sewall at ams724@cornell.edu.

APPENDIX E: RECRUITMENT SLIDE