Eating behavioral predictors of dietary intake and metabolic health in women with overweight and obesity

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Abstract

Background: In the United States, the majority of adults are overweight or obese, which predisposes them to develop metabolic disorders. In addition, sustained weight loss remains a challenge for most people with overweight or obesity. As a result, there is an urgent need to identify behaviors that are readily modifiable for weight management. Emerging data suggest that changes in eating behavior, such as altering eating timing and food cravings, have the potential to decrease energy intake and body weight. Studies examining the direct association of these eating behaviors with both dietary intake and metabolic indices warrant further investigation.

Objective: The overall objective of this dissertation was to examine the association of eating behavior with dietary intake, diet quality and metabolic health in women with overweight or obesity.

Aim 1: To determine the association of eating timing with dietary intake, diet quality and metabolic health.

Aim 2: To determine the association of food cravings with dietary intake, diet quality and metabolic health.

Methods: This is a secondary data analysis of baseline data from women with overweight or obesity who participated in a weight loss and maintenance trial. Outcomes were obtained using anthropometric and blood measures, questionnaires, and 24-hour diet recall interviews. Eating timing was explored by examining 1) the daily eating interval, defined as the time between first and last eating occasion; 2) time restricted eating (TRE), which refers to the restriction of daily eating interval to ≤11 hours; 3) early energy eaters, defined as consumption of ≥60% of energy during the first half of time awake; and 4) late night eaters, defined as eating within 2 hours of bedtime. A measure of food cravings was determined from the total score of the Food Cravings Questionnaire-Trait. Regression analyses were used to determine the associations of eating timing and food cravings with dietary intake, diet quality and metabolic health.

Results: The 229 women included in the analysis had a mean age of 40.9 ± 0.7 years and body mass index (BMI) of 34.7 ± 6.4 kg/m^2. *Eating timing:* daily eating interval was positively associated with energy intake ($P = 0.01$), glycemic load ($P < 0.01$), eating frequency ($P < 0.01$) and waist circumference ($P = 0.02$). TRE was associated with lower energy intake ($P = 0.045$), glycemic load ($P = 0.03$) and eating frequency ($P < 0.01$). Being an early energy eater was associated with higher carbohydrate intake ($P = 0.02$). Late night eating was associated with higher energy intake ($P < 0.01$), glycemic load ($P < 0.01$) and eating frequency ($P = 0.03$). *Food cravings:* food cravings were positively associated with eating frequency ($P = 0.03$), daily eating interval ($P<0.05$), body mass index ($P = 0.03$) and waist circumference ($P = 0.01$). Higher food cravings was also associated with lower diet quality ($P<0.05$) and lowered odds of having a TRE pattern ($P = 0.02$) compared to non-TRE pattern.

Conclusion: The results identify eating timing and food cravings as potential mechanistic targets for improving dietary intake, diet quality and body composition in weight management programs.

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i. Introduction

Long-term imbalance of energy intake and expenditure results in excess weight gain and increased risk of metabolic dysfunction, the prevalence of which is widespread in the United States.[1,2] Losing weight can significantly improve metabolic health.[3-6] However, weight loss and weight loss maintenance has proven difficult.[7] Intensive multifactorial behavioral interventions are recommended for the successful management of a healthy body weight.[8] Promising behavioral factors that may influence energy imbalance and bodyweight status are therefore highly sought after, and include eating timing and food cravings.[9-11]

The timing of food consumption is emerging as a behavior that contributes to weight status.[12] Consuming energy earlier in the day and limiting intake at night has been linked to better energy balance and lower bodyweight.[13] In addition, restricting the daily eating interval, defined as the time between first and last eating occasion, has resulted in a reduction in energy intake and weight loss.[14,15] Beginning the restricted daily eating interval earlier in the day may also confer additional benefits including improved insulin sensitivity, blood pressure, and oxidative stress.[16] The current literature suggests that factors associated with eating timing may be a promising behavioral target that facilitates weight loss. However, no study has explored eating timing, defined as both 1) when food is consumed and 2) the daily eating interval. In addition, no study has examined these factors with respect to both dietary intake and metabolic health.

Managing food cravings also shows promise in weight management. Food cravings, the desire for food that influences choice, are positively associated with body mass index (BMI) and individuals with obesity report experiencing more cravings compared to those with a normal weight.[17] Foods craved the most tend to have lower nutrient quality.[10]Although a reduction in food cravings has been demonstrated during weight loss interventions,[18-23] there is limited data to suggest how food cravings affect eating, dietary choices and contribute to metabolic health, particularly pertaining to cardiometabolic risk.

Current recommendations for weight management include targeting behavioral aspects of eating. Research suggests both eating timing and food cravings are promising targets that can be modified. To our knowledge, no study has examined the association between behavioral aspects of eating, including timing and food cravings, on both dietary intake and metabolic health in adults with overweight and obesity.

ii. Statement of Hypothesis to be Tested

The overall objective of this dissertation is to determine how behavioral aspects of eating influence dietary intake and metabolic health in women with overweight and obesity. We tested our objective through the following specific aims:

> **Specific aim 1**: Determine the relationship of eating timing with dietary intake and metabolic health measures.
>
> > **Approach:** The main independent variables for eating timing were 1) the daily eating interval, defined as the time between first and last eating occasion; 2) time restricted eating (TRE), which refers to the restriction of daily eating interval to ≤11 hours; 3) early energy eaters, defined as consumption of ≥60% of energy during the first half of time awake; and 4) late night eaters, defined as eating within 2 hours of bedtime. Dietary intake dependent variables included total energy intake, percentage of energy from carbohydrate, fats, proteins, alcohol, and added sugar, fiber (g/1000 kcals), glycemic load, diet quality, diet diversity, energy density, and eating frequency. Body composition (body mass index, body fat, and waist circumference) and cardiometabolic risk (low density lipoprotein cholesterol, high density lipoprotein cholesterol, total cholesterol: high density lipoprotein cholesterol, triglycerides, glucose, glycated hemoglobin, insulin, c-reactive protein, systolic blood pressure, and diastolic blood pressure) were considered indicators of metabolic health.
> >
> > **Hypothesis:** Individuals with a shorter or restricted daily eating interval and those eating earlier in the day and not eating late at night will have healthier dietary intake and more favorable metabolic health.
>
> **Specific aim 2**: Determine the association of food cravings with dietary intake and metabolic health measures.

> **Approach:** Food cravings was determined from the total score of the Food Craving Questionnaire - Trait.[24] Dietary composition (total energy intake, percentage of energy from carbohydrate, fats, proteins, alcohol, and added sugar, fiber, glycemic load, diet quality, diet diversity, and energy density) and eating patterns (eating frequency, daily eating interval, TRE, early energy eaters, and late night eaters) dependent variables were used to describe dietary intake. Body composition (body mass index, body fat, and waist circumference) and cardiometabolic risk (low density lipoprotein cholesterol, high density lipoprotein cholesterol, total cholesterol: high density lipoprotein cholesterol, triglycerides, glucose, glycated hemoglobin, insulin, c-reactive protein, systolic blood pressure, and diastolic blood pressure) dependent variables were used to determine metabolic health.
>
> **Hypothesis:** Individuals with higher food cravings will have less healthy dietary composition and eating patterns as well as less favorable metabolic health compared to those with lower food cravings.

This work provides a new understanding of the association between behavioral aspects of eating and dietary intake and metabolic health. Our results provide support for the design of future interventions that the optimize modification of eating timing and management of food cravings. Targeting these behaviors can potentially maximize the benefits of weight loss interventions on health, and contribute to customizing lifestyle recommendations for individuals with overweight or obesity.

iii. Review of Literature

I. Overweight and obesity

A prolonged imbalance of energy intake and expenditure results in weight gain and leads to overweight and obesity,[1,2] defined as having a body mass index (BMI) ≥ 25 kg/m^2 and ≥ 30 kg/m^2, respectively.[25] The number of United States adults with obesity has increased from 1960 to 2012,[26] with over 70% classified as overweight or obese, and obesity affecting approximately 40% of adults in 2015-2016.[26]

a. Impact on cardiometabolic risk

Overweight and obesity are associated with many adverse health outcomes, including an increased risk of mortality and cardiovascular disease (CVD).[27,28] A series of metabolic changes accompany excess body weight, including alterations in biomarkers associated with CVD such as circulating insulin, inflammatory factors, and vascular-associated factors.[29-31] As weight is a modifiable risk factor for CVD, losing five to 10% of one's body weight can significantly reduce the risk of CVD. [3-5,25]

b. Behavioral factors and their role in dietary management of excess body weight

The industrialization of the food system and ensuing changes in the American diet has accompanied the rise in overweight and obesity in the US over the past several decades.[32,33] The US food system has increased the portion sizes,[34-36] production, and marketing of processed appetizing foods that are inexpensive and energy dense.[32,37] These foods contribute substantial energy to the American diet, and the average energy intake of American adults has increased since the 1970's.[33] Behavioral factors that influence adherence to unhealthy dietary patterns can lead to low energy expenditure and high energy intake.[38,39] On the other hand, behavior modification to promote healthy lifestyle changes has shown success in the treatment of overweight and obesity.[39,40] For instance, modifying an individual's daily eating interval, defined as the time between first and last daily eating occasion, has shown promise in reducing excess weight. A common approach to the modifying daily eating interval is time restricted eating (TRE), a type of intermittent fasting that involves restriction of the daily eating interval and the extension of the fasting period.[14-16] Further research is needed to better understand the effect of meal timing on the obesity paradigm and identify the individual aspects of eating timing that are important targets for weight loss interventions.

Another modifiable behavioral factor is food cravings, which have also been clearly implicated in weight management. Current research has primarily focused on the plasticity of food cravings in response to an intervention.[18-22,41] Food cravings can be successfully manipulated in order to promote weight loss in adults with overweight and obesity.[41] However, there has been no comprehensive examination of the association of food cravings with both dietary intake and metabolic health indices. Further investigation is therefore warranted to examine how promising behavioral factors, including eating timing and food cravings, are related to both dietary intake and cardiometabolic health.

II. Eating timing

a. Early and late eating

Until recently, nutrition research has primarily focused on individual foods and nutrients rather than overall dietary or eating patterns. The emergence of eating pattern research has demonstrated that the time of food intake impacts health. Breakfast is a common focus in meal timing research given that it is the first meal of the day and therefore often represents early eating. In addition, nearly 20% of adults skip breakfast,[42] and skipping breakfast has been inversely associated with diet quality[43] and has also been shown to negatively affect anthropometric measures, including higher BMI, larger waist circumference, and poorer glycemic control.[44,45] Research also indicates that both skipping breakfast and eating late at night may result in adverse changes in metabolic health indices and higher energy intake.[43-49] Conversely, eating earlier in the day is linked to greater satiety[50,51] and regulation of circadian rhythms that control metabolic pathways.[50,52] Although many observational studies indicate breakfast is advantageous to metabolic health, randomized trials report inconsistent results.[53] However, studies that do not restrict the definition of early eaters to be synonymous with breakfast eaters show promising results. Finally, randomized trials that promoting food consumption earlier in the day demonstrate more favorable changes in weight and cardiometabolic health in adults with overweight or obesity.[54-56]

Conversely, adverse effects on weight and overall metabolic health have been observed with high energy consumption at night.[46-49,57] One study showed that both BMI and waist circumference were significantly higher among participants who ate dinner within three hours of bedtime.[46] In addition, data from the National Health and Nutrition Examination Survey determined that for every 10% increase in the proportion of energy consumed at night, there was a 3% increase in c-reactive protein, a marker of systemic inflammation. Higher levels of markers of inflammation are believed to be associated with metabolic conditions such as diabetes, obesity, and some cancers.[49] However, the few randomized trials conducted in this area demonstrate little direct evidence that eating late at night has adverse effects on cardiometabolic health.[58-60]

The potential negative impact of eating timing on health outcomes is concerning. This is particularly true as Americans not only consume 45% of their daily energy during dinner and evening snack,[61] but are also shifting away from the classic consumption of three main meals per day to more irregular eating patterns.[2,62] These irregular eating patterns are linked to adverse health outcomes. Shift work, particularly night shifts, promotes irregular eating patterns and therefore has been frequently studied to examine the effects of irregular eating and lifestyle patterns. For instance, women with more than five years of night shifts had a higher risk of all-cause and cardiovascular disease mortality compared to those who never worked night shifts.[63] In addition, night shift workers have higher cardiometabolic risk compared to non-night shift workers.[64-66] Although differences in energy intake among night shift versus non-night shift workers have not been observed,[67] food consumption during a night shift results in an increase in glucose response and work performance impairment.[68-70] It is clear that eating times are important to cardiometabolic health and may also impact dietary intake.

b. Circadian rhythm

Humans and most other living species have evolved to respond to the daily cycles of their environment, and these adaptions are called circadian rhythms. Circadian rhythms are affected by eating times, and may be a mechanism by which meal times contribute to health. Circadian rhythms can be physiological and behavioral. They are mediated internally via *'clocks'*, as well as by external factors, including the light/dark cycle, physical and social activity, and food availability.[71] Circadian rhythms are controlled centrally by the suprachiasmatic nucleus of the hypothalamus, which is referred to as the *'master clock*'. There are also *'peripheral clocks'* in cells, organs, and organ systems that regulate circadian rhythms. Each individual has their own behavioral and biological circadian rhythm preference, or *chronotype*, relative to the light-dark cycle, resulting in preferences for the morning, evening, or otherwise neutral.[72,73]

Circadian rhythm misalignment occurs when our rhythms are not aligned with our environment. Misalignment could be due to our sleep/wake cycle not corresponding to the biological night, our feeding schedule not matching our sleep/wake cycle, or our peripheral clocks being out of sync with our central clock.[74] Individuals with chronic misalignment include shift workers, those with jet lag or often evening chronotypes, as well as frequent eating with the absence of a defined fasting period.[74,75] Circadian rhythm misalignment is common in our current environment as a result of artificial lighting that extends the light period and also leads to longer daily eating intervals and shorter fasting intervals. These circadian misalignments have detrimental effects on health and increase the risk of chronic disease and poor nutritional status.[76 ,77,78] Emerging research supports the idea that modifying eating times might promote circadian rhythm alignment and therefore improve metabolic health and influence dietary intake.[71,79]

c. Eating interval

There is strong evidence to support the benefits associated with fasting, defined as the voluntary abstinence from food for a specified interval of time.[80] Reducing energy intake for a shorter daily eating interval, the time between the first and last eating occasion, leads to longer fasting intervals and thus more robust circadian rhythms that are needed to confer health benefits.[71] Intermittent fasting (IF) has shown metabolic benefits and increases markers of longevity.[71,81,82] There are different methods of IF (**Table 1**), including alternate day fasts (ADFs), periodic fasting mimicking diets (FMDs), and time restricted eating (TRE). Despite the proposed health benefits associated with IF, there is an extreme burden associated with caloric restriction. Long-term adherence to ADFs and FMDs is therefore a significant challenge.[71,83] On the other hand, TRE allows for ad libitum energy intake within a restricted period of time. TRE has been defined in multiple ways, and includes fasting intervals of 12 to 21 hours- with TRE ranging from 4-12 hours in the day.[14,84] TRE has been demonstrated as an acceptable form of fasting that confers strong health benefits.[15,71,84-86]

Table 1: Methods of intermittent fasting

Fasting method	**Definition**
Intermittent fasting (IF)	Restriction of energy intake over a defined eating interval[80,81]
Alternate day fasting (ADF)	Fast days with reduced or no energy intake, alternating with feast days of ad libitum energy intake[81]
Fasting mimicking diet (FMD)	Low protein, low sugar, and a relatively high fat content containing 10 to 50% of calorie needs for 2 to 7 days every 15 to 365 days [71,87]
Time restricted eating (TRE)	Daily restriction of the eating interval and extension of the fasting period[14,15,71]

i. Dietary intake

Dietary intake may also be affected by the daily eating interval. Americans tend to eat the majority of their calories later in the day and for an extended daily eating interval that lasts more than 12 hours, leading to rampant circadian misalignment.[14,88] Research indicates that the risk for chronic disease is influenced not only by food choices, but also by the timing of meals.[79,89]

Studies evaluating the effects of daily eating interval on dietary composition among adults with overweight and obesity have primarily focused on energy consumed during TRE. Unlike other options for IF, TRE does not require caloric restriction despite the fact that it often leads to decreased energy intake. Adopting a 10 to 11 hour eating interval per day from a ≥14 hour eating interval resulted in a 20% reduction in energy intake and sustained weight loss in eight individuals with overweight.[14] A non-significant trend was also observed with reduction of energy and macronutrient intake consumed before and after Ramadan fast in 82 adults with overweight.[90] However, skipping breakfast to extend the nighttime fast interval did not increase lunchtime energy intake nor did it affect overall daily energy intake.[91] At present, the effects of daily eating interval on energy intake in adults with overweight or obesity is inconclusive, and there has been no in-depth analysis of the relationship of daily eating interval on other dietary factors. No studies have examined the relationship of other determinants of eating patterns, such as eating frequency, with daily eating interval.

ii. Metabolic health

Metabolic benefits associated with TRE have mostly been observed in animal models and show that TRE is effective for normalizing body weight, particularly among younger rodents.[92] In most studies, TRE rodents lose significantly more weight compared to controls[84] and there are consistent benefits of TRE are seen with regard to cardiovascular risk factors, including lower levels of cholesterol, triglycerides, and markers of inflammation, as well as higher insulin sensitivity.[80,84,92] Studies also indicate that rodents are resilient to occasional deviations from TRE. For instance, mice undergoing TRE five days per week and ad libitum feeding on the remaining days had comparable cardiometabolic changes to mice on constant TRE.[92] It is hypothesized that a robust restricted daily eating interval and an extended fasting cycle may improve metabolic health through changes in the physiology and metabolic activity of different organs.[71] For instance, in rodents, TRE promotes gluconeogenesis, increased production of nucleotides, and redirects cholesterol to bile acid formation.[71] It also promotes brown adipose tissue formation that subsequently increases metabolic rate.[93] In the white adipose tissue, TRE decreases inflammation through reducing macrophage infiltration.[71] Although the effects of TRE on metabolic health have been evaluated in rodents, more research is required to determine the impact the daily eating interval on markers of metabolic health in at-risk populations.

Body composition

Modifying the daily eating interval using TRE may be a promising weight loss strategy in humans, particularly among adults with excess weight. However, most TRE research has examined normal-weight adults and benefits related to body composition are inconclusive.[94-102] Studies examining the effects of TRE on body composition among adults with overweight or obesity demonstrate inconsistent results.[14,90,91] No difference in changes in body weight were observed in two studies of adults with overweight following TRE compared to controls.[16,91] One study defined TRE as skipping breakfast for a prolonged nighttime fast compared to consuming breakfast,[91] while the other defined TRE as a 6 hour early daily eating interval compared to a 12 hour daily eating interval.[16]

Conversely, several studies have demonstrated TRE improves body weight [14,15,90,103] and one showed a reduction in waist circumference.[104] Definitions of TRE in these studies varied widely and included Ramadan fasting,[104] limiting the eating interval to breakfast and lunch,[103]an 8 hour eating interval,[15] or eating at least three hours prior to bedtime and within a ten hour interval.[14] Although several studies report that TRE improves weight, studies reporting null results cannot be overlooked as well as the contribution of the inconsistent definitions for TRE potentially impacting the observed results. Additional research is needed to elucidate the connection between TRE and body composition in individuals with excess body weight, and to determine the ideal eating interval for weight loss and cardiometabolic risk modification.

Cardiometabolic risk

The research evaluating eating interval and cardiometabolic risk has also largely focused on TRE in normal weight individuals, and results are limited, inconsistent and remain inconclusive. Although some of these studies observed no changes in lipid profiles following TRE,[95,96,105] others demonstrate improvement.[98-101] Similar inconsistent results are observed with glucoregulatory factors in normal-weight adults.[96,98,99,101,106] To our knowledge, only one study reported an increase in blood pressure when healthy middle aged adults consumed one meal later in the day compared to three meals throughout the day.[105]

Although studies examining TRE and cardiometabolic risk in adults with overweight or obesity are limited, modifying the daily eating interval is suggested to impact cardiometabolic health. A few studies have shown improvements in cardiometabolic health following TRE,[90] including a decrease in blood pressure,[15,90,107] oxidative stress,[107] total cholesterol,[90] triglyceride,[90] low density lipoprotein cholesterol (LDL) concentrations,[90] and very low density lipoprotein cholesterol (VLDL) concentrations,[90] as well as an increase in high density lipoprotein cholesterol (HDL) concentration.[90] These studies defined TRE as the Ramadan fast,[90] an early 6 hour eating interval,[107] or an 8 hour eating interval.[15] Similarly, improvements in glucoregulatory factors have been observed as a result of TRE.[103,107,108] TRE resulted in lowered glucose response,[108] fasting glucose,[103] insulin,[107] and improved insulin sensitivity.[103,107] The definitions of TRE used in these three studies were 9 hour restriction of daily eating interval,[108] reduction of daily eating interval by only consuming breakfast and lunch compared to six smaller meals spread throughout the day,[103] or a six hour early TRE compared to a 12 hour daily eating interval.[107]

Although results are promising, it remains unclear, largely due to the varied definitions for TRE, whether restricting the daily eating interval contributes to improvements in cardiometabolic health. There is therefore a critical need to elucidate how length of daily eating interval affects cardiometabolic health and further examine its association with multiple measures of cardiometabolic health in adults with excess weight.

Limitation of TRE literature

Current research indicates that eating timing affects dietary intake and metabolic health. However, studies conducted to date have several limitations and few have examined the impact in adults with overweight or obesity. Furthermore, the definition of TRE varies widely from study to study. Researchers have used Ramadan fasting as a form of TRE as it limits the daily eating interval from sunset to sunrise, although these studies may not be the best approach to determine effects of TRE on metabolic health and dietary intake. Ramadan's period of energy intake is opposite to our standard daytime eating schedules, thus disrupting our circadian rhythm. In addition, many studies promote skipping breakfast as a form of TRE,[91] but these studies observed no associated body composition or cardiovascular benefits; in fact, the group skipping breakfast had a slight increase in BMI[91]. Emerging research suggests that the timing of when food is consumed as well as the daily eating interval is important and that more favorable health outcomes are observed with daily eating intervals that are in the earlier part of the day than in the latter half of the day.

d. Eating timing conclusion

Given the inconsistent results of eating timing studies in adults with overweight or obesity and their varying definitions of TRE, more research is needed to not only examine the effects of TRE on metabolic health and dietary intake, but to clarify the effects of multiple measures of eating timing. To our knowledge there have been no studies that have examined how different measures of eating timing influence both dietary intake and metabolic health.

II. Food cravings

Food cravings are defined as the desire for food that influences choice. Most people experience cravings during their life,[91,109-112] with 97% of women and 68% of men experiencing food cravings,[19,113-115] with three to four foods typically craved per week.[114,116] Consuming craved foods results in greater activation of reward centers of the brain,[117,118] thereby presenting a motivation to eat that is different from hunger. Only certain foods can alleviate food cravings whereas any food can alleviate hunger.[19,113] As a strong desire to eat is frequently associated with food cravings, these cravings often lead to consumption of the craved food or a similar food and are subsequently linked to overeating.[114,115,119] Although food cravings have been evaluated for their association with body weight, few studies have comprehensively examined the link between food cravings, dietary intake, and metabolic health.

a. Dietary intake

Dietary composition

Over the past 30 years, there have been advances in understanding food cravings in adults. Food cravings influence dietary intake and adults with food cravings are more likely to eat away from home, overeat, deviate from their diet, have binge eating episodes, try to lose weight, and drop out of weight loss treatment.[119-126] Cross-sectional studies report that that food cravings are positively correlated with energy in adults with obesity[20] as well as in adults of normal weight.[91,116,127] Among overweight women, foods craved were higher in energy density and fat, while lower in protein and fiber, compared to their habitual diet both before and after weight loss.[21] Among 32 adults with obesity Kahathuduwa et al. 2018,[128] observed that cravings for high fat and fast foods were negatively correlated with stimulation of regions of the brain that regulate executive control of ingestion. The authors also showed that changes in cravings for sweets and fast foods following a three week calorically restricted diet were negatively correlated with regions of the brain that regulate executive control of ingestion, motor readiness to ingest, food reward, internally focused attention, and visual object recognition.[128] These findings suggest that the decrease in food cravings seen in obesity is reflective of neurophysiologic changes, which control dietary intake, that occur during caloric restriction. Furthermore, research has demonstrated that there is a decrease in food cravings during calorie restriction with different macronutrient content over a six to 24 month period.[18,19] It is therefore important to understand not only how food cravings and energy are related, but also how other dietary composition indices, including diet quality and diet diversity, are related to food cravings.

Eating pattern

There is limited data on food cravings and eating patterns. Food cravings are linked to disordered eating behavior,[129,130] and disordered eating often disrupts eating patterns. However, to our knowledge, only one study has indirectly examined the association between food cravings and eating patterns using a study in chronotypes. Meule et al.,[131] observed that chronotype was associated with eating patterns but not with food cravings. Evening chronotypes were more likely to skip breakfast and have greater inter-meal intervals compared to morning chronotypes. There was no difference between chronotypes and overall cravings. More research is needed to explore how cravings affect eating patterns such as eating frequency, particularly as these patterns are an important attribute of a healthy diet.[40]

b. Metabolic health

Body composition

Food cravings are related to weight and BMI.[10,17,133-137] Intake of greater portions of craved foods are associated with higher lifetime BMI[21] and higher BMIs are associated with cravings for high fat, fast food fats, and sweet food.[134,135] Weight loss studies have demonstrated that calorie restriction can influence food cravings. For instance, one cross-sectional analysis of a weight loss program reported that individuals who were dieting to lose weight had fewer and less intense cravings, as well as a higher ability to resist, them compared to those maintaining their weight.[138] Cravings may therefore be conditioned by intervention and longitudinal studies that promote restriction of craved foods reveal favorable reductions in body weight and food cravings.[18-22] Although there is evidence demonstrating the link between body weight and food cravings, more research is needed to understand the effects of food cravings on body composition outcomes beyond weight and BMI among adults with overweight and obesity.

Cardiometabolic risk

Research indicates that food cravings are associated with body weight, and that excess weight is linked with metabolic dysfunction. However, research evaluating the effect of food cravings on cardiometabolic risk is more limited. Only a few studies have examined the effects of food cravings on glucose homeostasis. No difference in food cravings, as a trait, was observed between adults with and without type 2 diabetes and individuals with type 2 diabetes had greater cravings for carbohydrates and low-fat foods compared to controls without diabetes in a matched control study of 210 adults. The carbohydrate craving score was also positively associated with glycated hemoglobin in these diabetic adults.[139] In addition, among 339 community dwelling adults without chronic medical conditions, food cravings were positively associated with insulin resistance but not with insulin levels; food craving measurements were obtained after six months follow-up, and no significant association between baseline insulin and food cravings was observed after adjusting for baseline BMI and food craving measurements.[140] To our knowledge, no studies have examined the relationship between food cravings and blood lipids, blood pressure, or inflammatory markers. Additional research is required to examine how food cravings influence metabolic health, particularly in adults with overweight and obesity. Information from such studies will help in understanding how food cravings contribute to cardiometabolic disease risk.

c. Food craving conclusion

Food cravings are linked to body weight outcomes, yet there has been limited research examining the relationship between cravings and other indicators of metabolic health. There also seems to be a link between food cravings and dietary intake, although the extent to which cravings influence specific nutrients and eating patterns remains understudied. Further, more research examining the association between food cravings and a comprehensive array of both metabolic health and dietary outcomes in adults with overweight or obesity, is needed.

IV. Overall Conclusions

There has been increasing focus on the behavioral aspects of eating that contribute to weight management. Eating timing and food cravings are promising modifiable factors that could be targeted in order to achieve a favorable energy balance and improve metabolic health outcomes.

Emerging research clearly demonstrates the impact of eating timing on the energy consumption and the importance of this area of study. Studies conducted thus far have primarily focused on restricting the daily eating interval through TRE. However, there is inconsistency in defining TRE as it pertains to the eating interval, and there has been no consensus on the ideal daily eating interval for optimal dietary intake and metabolic health. Furthermore, consuming most of one’s energy earlier in the day and not eating late at night shows promise in supporting healthier dietary intake and metabolic health, although the evidence is still inconclusive. Data supporting an association between eating timing with dietary composition is extremely limited and does not extend beyond the assessment of energy intake. There has been no study that also examines the association between eating timing with both dietary intake and metabolic health.

However, there is research that supports the impact of modifying food cravings on energy intake and body composition. Food cravings have been linked to higher energy intake and lower body weight. Interventions have demonstrated that food cravings can be reduced and result in lower energy intake and improved body weight. Despite the breadth of research related to this topic, there is limited focus on how food cravings affect eating patterns and cardiometabolic risk indices

The objective of the proposed research is to examine the association between eating behaviors, including timing and food cravings, on dietary intake and metabolic health.

iv. Methods

I. Study design

This is a secondary data analysis using baseline data from the Healthy Families Healthy Forces (HF2) study funded by the Department of Defense. This parent study was a one to two-year weight loss and maintenance trial in beneficiaries of military personnel. Participants were randomly assigned to one of two safe and sustainable weight loss programs. The intervention consisted of hour-long group classes held weekly for 4 months and then monthly. Measurements were collected at baseline, before participants were randomized to their intervention group intervention, at 6 months, 12 months, and 18-24 months. This study has been reviewed and approved by the Tufts Medical Center and Tufts University Health Sciences (TUHS) and U.S. Army Institute of Environmental Medicine (USARIEM) Institutional Review Board (IR B). The TUHS and USARIEM IRBs are regulated by Federal guidelines established by the US Department of Health and Human Services and the Food and Drug Administration. All study staff were certified in human subject research participation and designated staff completed ongoing mandatory training. Any changes to the protocol or approved documentations were submitted to IRB per their regulations.

II. Participant characteristics

Participants enrolled in the HF2 study were eligible for inclusion in this analysis. Recruitment for the HF2 study occurred at approved military installations in the greater Boston, Connecticut, upstate New York, central Colorado, and northeast Tennessee/south-west Kentucky areas. Individuals were eligible for inclusion in this study if they were 18 years of age or older, had a military identification card indicating they are a dependent of a military personnel, English speaking, and had a BMI of ≥ 25 kg/m^2 at time of screening. Adults were ineligible for the study if they had recent weight loss, a health condition that influences nutrient absorption or weight loss, were very active, were pregnant or planning to become pregnant, or were enrolled in a concurrent nutrition or weight loss program. Enrollment of 239 adult beneficiaries and obtainment of baseline measurements (N=238) ended January 2018. The sample size used in this secondary data analysis includes 229 female participants who attended baseline outcomes measurements and completed at least one dietary recall.

III. Screening

Screening for eligibility occurred in two parts: pre-screening and screening. Pre-screening was conducted via a short questionnaire verifying participants' self-reported eligibility. Prospective participants were invited to prescreen over the phone or in-person by study team members. Prior to the pre-screening, individuals provided verbal consent to administer the questionnaire. All responses to pre-screening questions have been kept protected, secured, and confidential. If the individual passed the eligibility requirements, they were invited to the in-person screening session. The in-person screening consisted of written consent followed by verification of height and weight to determine eligibility using a measured BMI ≥ 25 kg/m^2. If the individual was eligible and wished to participate after screening, they read and signed the main consent form and were enrolled in the study.

IV. Measurements

This analysis uses baseline HF2 data collected by trained study staff. At baseline visits, participants were instructed to arrive fasted in light clothing and refrain from exercising for 24 hours prior to measurements. Fasting was defined as no food or liquid, besides water, after midnight prior to the measurement day.

a. Questionnaires

Questionnaires were completed online or in-person by participants using StudyTrax, a secure database system, or administered by trained study staff over the phone. Participants were given a username and sent a verification email by the StudyTrax system that prompted them to create a unique password to access the questionnaires. Participants were allowed to skip questions they were not comfortable answering and were informed if they skipped a question that was part of a subscale, failure to respond would prohibit the generation of a composite score.

Demographic and lifestyle: Demographic variables, including age, sex, race, ethnicity, education, and income were obtained from questionnaires. Health history was also obtained and included menopause status as well as lipid, blood pressure, and glycemic medication usage. Lifestyle factors, including whether a participant was engaging in physical activity, were also obtained from questionnaires.

Food cravings: Food cravings as a "trait" is stable within individuals over time and situations and was ascertained by the Food Craving Questionnaire, trait (FCQ-T) that consists of 39 questions scored on a 6-point scale ranging from *never* to *always* with a total possible score of 234.[24] It contains nine subscales measuring food cravings as (1) intentions to consume food, (2) anticipation of positive reinforcement, (3) relief from negative states, (4) lack of control over eating, (5) preoccupation with food, (6) hunger, (7) emotions, (8) cues that trigger cravings, and (9) guilt (**Table 2**). The greater the total score, the greater the intensity and frequency of food cravings.

Table 2: Description of the FCQ-T factors

FCQ-T subscales	Description
Plan	An intention and planning to consume food
Positive reinforcement	Anticipation of positive reinforcement that may result in eating
Negative reinforcement	Anticipation of relief from negative states and feelings as a result of eating
Lack of control	Possible lack of control over eating if food is eaten
Thoughts	Thoughts or preoccupation with food
Hunger	Craving as a physiologic state (i.e. hunger)
Emotion	Emotions that may be experienced before or during food craving or eating
Environmental	Environmental cues that may trigger food cravings
Guilt	Guilt that may be experienced as a result of cravings and/or giving into them

Adapted from Cepeda-Benito et al. [24]

Timing and physical activity patterns: Data on sleep timing was obtained from the 7 day Stanford Physical Activity Recall (PAR), which was conducted over the phone or in person with respect to the previous seven days.[141] Days in which a participant didn't sleep or got an unrealistic and inconsistent amount of sleep were not included. The median wake and bedtime over the seven day period was calculated and used to determine awake time, early energy eaters and late night eaters. Awake time was calculated as the time between median wake time and bedtime. Early energy eaters and late night eaters are defined as reported below.

b. Dietary intake

Three baseline dietary recalls were collected by phone using the multiple-pass 24-hour recall method and analyzed using Nutrition Data System for Research (NDSR) software version (2014), developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN. Outcome data from NDSR includes daily estimated energy and nutrient intake, as well as time of eating, food type, food group, diet quality, and volume of food. Implausible reported energy intake were excluded from all analysis of dietary data using the Goldberg cutoff as described in the statistical analysis section.[142] Dietary intake data used in this analysis was an average of the dietary recalls collected at baseline; 94% of the sample had three, 5% had two, and 1% only had one baseline dietary recall.

Dietary composition: Dietary composition variables included total energy intake, percent energy from each macronutrient, fiber, and glycemic load. A diet diversity score was determined by giving a score of one to each food group (grains, vegetables, fruit, meats/protein, and dairy) that was consumed in a day for a total score of 5.[143,144] Diet quality was determined using the Healthy Eating Index-2015 that was scored on a scale of 0 to 100 with a higher score indicating better diet quality.[145] Energy density was determined by dividing food calories consumed by weight of foods (kcals/g) consumed and included only items that were designated as food and not liquids .[146] Food added into beverages was considered a beverage and excluded from the energy density calculation while beverages added into food was considered a food and included in the energy density calculation. For example, sugar added into coffee was considered a liquid and therefore excluded whereas milk added into cereal was considered a food and therefore included in our energy density calculations.

Eating patterns: Eating occasions were defined as meals containing ≥ 20 calories. Eating frequency was determined by the total number of daily eating occasions. Eating timing definitions (**Table 3**) were determined using the meal time information from 24-hour dietary recalls and the sleep and wake time information from the 7 day Stanford PARs.

Daily eating interval was a continuous variable defined as the hours between the first and last eating occasion (hours/day) averaged over the collected 24-hour dietary recalls.

Time restricted eating (TRE) was binary variable defined as those with a daily eating interval of 11 hours or less. Non-TRE pattern was defined as a daily eating interval greater than 11 hours.

The 11hr window to define TRE was set *a priori* before the analysis was conducted and was based on the distribution of eating intervals in our sample and took into consideration the published windows of restriction i.e. 8-12 hours in other studies of TRE.[84,89]

Early energy eaters were defined as those who were consuming 60% or more of their daily energy intake within the first half of their median awake time. Non-early energy eaters were those participants with less than 60% of their energy consumed during the first half of their time awake.

Late night eaters were classified as participants who ate within 2 hours before bedtime. Non-late night eaters were those participants who did not eat within 2 hours before bedtime.

Table 3: Eating timing definitions

Eating timing variables	
Daily eating interval (hours/d)	Total time period of daily eating, captured from midnight -the start of day to midnight –the end of day, and calculated as the time between the first and last eating occasion of the day (hours/day). Mean daily eating interval was obtained from the average over the collected 24-hour dietary recall days.
Time Restricted Eating (TRE)	A daily eating interval of ≤11 hours. • Defining TRE using a 11 hour window was established *a priori* based on the eating interval distribution of our sample and considering that it was within the published 8-12 hours eating interval restriction definitions used in TRE studies
Non-TRE	Participants who had a daily eating interval > 11 hours
Early energy eaters	Eating ≥ 60% of energy during the first half of awake time
Non-early energy consumers	Eating <60% of energy during the first half of their time awake
Late night eaters	Participants who ate within 2 hours of median bedtime
Non-late night eaters	Those who did not eat within 2 hours of bedtime

c. Anthropometric and cardiometabolic health

Body composition: Fasting weight, height, body composition, and waist circumference were obtained at outcome measurement events. Weight was measured in duplicate to ± 0.1 kg using a calibrated scale (Escali BFBW200 Digital, Minneapolis, MN) which also provided data on body composition assessed by the bioelectrical impedance method. Height was taken in duplicate to ±0.1 cm. Body mass index (BMI) was calculated as weight in kg divided by height in square meters (kg/m^2). Waist circumference was measured in duplicate to ± 0.3 cm at the same time as weight according to standard procedures.[147]

Cardiometabolic risk: Fasting systolic and diastolic blood pressure was taken in triplicate to obtain readings within 5 mm/Hg of each other following 5 minutes of rest. Phlebotomists drew 30 ml of blood during the outcome measurement event. Blood samples were processed on site and frozen for transport to Tufts University for analysis.

HDL, triglycerides, and glucose concentrations were measured on an automated chemistry analyzer. LDL concentrations were calculated using the Friedewald formula unless triglyceride concentrations exceed 400 mg/dL at which point LDL was measured directly.[148] Insulin was measured using a radioimmunoassay. Glycated hemoglobin was measured by Tosoh G7 high performance liquid chromatogaphy assay. C-reactive protein concentrations was measured on a chemiluminescent immunometric analyzer (Siemens, Immulite 1000). Metabolic syndrome was calculated as defined by the National Cholesterol Education Program Adult Treatment Panel III.[149]

V. Power calculation

This dissertation aims to determine the associations of eating timing (aim 1) and food cravings (aim 2) with dietary intake and metabolic health outcomes; the primary outcome for dietary intake is energy and for metabolic health is BMI. However preliminary data on these relationships are scarce. This is a secondary data analysis and is restricted to the sample size of the collected data; N=146 for plausible energy reporters and N= 229 for all participants. Post hoc power analyses were conducted with G*Power 3.1 software using a type I error rate of 0.05.[150]

For aim one, differences in daily energy and BMI between TRE and non-TRE in adults with overweight and obesity were based of the pilot study by Gabel et al., 2018,[15] who found a 350 kcal lower daily energy intake and 1 unit lower BMI in TRE group (N=23) following 8 weeks of intervention compared to control group (N=23). Given our available sample size of plausible reports (N=52 with TRE and N=94 with non-TRE) and all participants (N=98 with TRE and N=131 with non-TRE) we had a 0.77 and 0.94 power, respectively, to determine an effect between TRE and daily energy as well as 0.46 and 0.59 power, respectively, to determine an effect between TRE and BMI. For this post-hoc power calculation, we used the only which examined TRE in adults with overweight or obesity with a control group that had both energy and BMI measures.[15] However, there are limitations to using this study for our power calculations. The major limitation being the difference in study design and definitions of TRE; Gabel et al.,[15] conducted an intervention study that defined TRE as an 8 hour or less restriction of daily eating interval whereas this dissertation is a cross-sectional analysis defining TRE as 11 hour or less restriction of daily eating interval. These differences may affect the magnitude of change possible for us to observe and therefore influence post-hoc power; it is conceivable that the shorter daily eating interval of Gabel et al.,[15] TRE and the fact that it was an intervention would create a greater observed change then this cross sectional analysis with TRE defined as 11 hour or less restricted daily eating interval would see and thus overestimate our power calculations.

For aim two, the effect of food cravings on daily energy and BMI were examined. To our knowledge, no studies have compared the cross-sectional association of food cravings on BMI or daily calories using the FCQ-T. However, one study examined the cross sectional correlation (r=0.21) of food cravings and energy intake in adults with excess weight.[20] Using their data, we had a power of 0.72 to examine the association of food cravings and daily energy intake for plausible energy reporters and 0.90 to examine the association of food cravings and daily energy intake for all participants. Additionally, two studies have used the Food Craving Inventory[123] to examine the cross-sectional correlation (r=0.15 and r=0.18) of food cravings and BMI.[20,136] Using their data, we had a power of 0.44-0.59 to examine the association of food cravings and BMI in plausible energy reporters as well as a power of 0.62-0.78 to examine the association of food cravings and BMI in all participants. Again, there are limitations given that the FCI and FCQ-T measures different food cravings; FCI measures cravings for specific foods while the FCQ-T measures the frequency and intensity of food cravings as a trait. Additionally, we are basing this post-hoc power calculations off of correlations whereas we will be running adjusted regressions.

VI. Data analysis

Data was checked for entry error, range checks, and implausibility. Descriptive statistics were reported as mean ± standard error for continuous variables and as a percent for categorical variables. Differences in descriptive continuous variables were determined via independent t-tests for continuous normally distributed variables and Wilcoxon rank-sum test for non-normally distributed variables. Differences in descriptive categorical variables were determined using Chi squared test. Regression analysis was used to determine the associations of eating timing (aim 1) and food cravings (aim 2) on dietary intake and metabolic health. The threshold for statistical significance was set at a $P < 0.05$. All analyses were performed using Stata statistical software version 15.1 (Stata Corp, College Station, TX).

a. Metabolic health

Body composition and cardiometabolic risk factors were examined for their association with each eating behavior. Body composition was determined by BMI, waist circumference, and body fat percentage. Cardiometabolic risk was determined by LDL, HDL, total cholesterol:HDL, triglycerides, glucose, glycated hemoglobin, insulin, systolic blood pressure, diastolic blood pressure, c-reactive protein, and metabolic syndrome.

b. Dietary intake

Dietary composition and eating patterns were examined for their association with each eating behavior. Dietary composition was determined by energy, percent energy from macronutrients (carbohydrate, fat, protein, alcohol, and added sugar), dietary fiber (grams per 1,000 calories), glycemic load, diet quality, energy density, and diet diversity. Eating patterns were determined by daily eating interval, TRE, early energy eaters, late night eaters, and eating frequency.

c. Covariates

Covariates for all models included age, income, and physical activity. Models with the independent variables of daily eating interval, TRE, early energy eaters, and late night eaters included time awake as a covariate. Menopause status was not included as a covariate in all models as it was found to not be a confounder; age and menopause status was not a significant predictor nor did it change the regression coefficient by greater than

10%. Models with the dependent variables LDL, HDL, total cholesterol:HDL, and triglycerides also included lipid medication as a covariate. Models with the dependent variables systolic blood pressure and diastolic blood pressure additionally included blood pressure medication as a covariate. Models with glucose and glycated hemoglobin additionally included glycemic medication as a covariate. Models with c-reactive protein the dependent variable also included BMI as a covariate. Total energy intake was additionally included as a covariate in models of dietary dependent variables that did not inherently adjust for energy intake within the definition of the variable. These included diet diversity, glycemic load, eating frequency, eating interval, TRE, early eaters, and bedtime eaters.

d. Analytic models

All regression models were applied with and without transformations or categorizations. When no difference in results was observed, we present models without transformation or categorization. The assumptions for linear regression were assessed Violations to the assumptions were addressed through transformation, categorization, or quantile as appropriate. Substantial influential points were identified and a robust linear regression was applied. Logistic regression models were used for binary dependent variables, and were applied with and without influential points with no difference in results. No influential points were therefore removed. Implausible dietary intake was determined by the Goldberg cutoff.[151-154] In order to address the issue of underreporting which could confound the association of eating timing and food cravings with dietary intake and metabolic health outcomes, models were applied with and without implausible energy reporters. All models presented exclude implausible energy reporters and were similar to models with all participants unless otherwise specified.

v. Chapter I:

Eating Timing: Associations with Dietary Intake and Metabolic Health

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Key words: *time restricted eating, eating timing, eating interval, dietary intake, metabolic health*

Author contributions statement:

SKD, SBR, AB, and CHG were involved in the larger study design. SBR, SKD, AT, AB, CHG, AH, EM and AK, were involved in study implementation and data collection. AT, SKD, AHL, and CHG designed this secondary data analysis, and manuscript preparation. AT performed the statistical analysis with the guidance of SKD. All authors reviewed and approved the manuscript.

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organizations and trade names in this report do not constitute an official Department of the Army endorsement of approval of the products or services of these organizations.

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RESEARCH SNAPSHOT

Research question

Is there an association between eating timing and dietary intake and metabolic health?

Key findings

In women with overweight and obesity, we found that a shorter daily eating interval, time restricted eating, and not eating before bedtime was associated with lower energy intake, glycemic load, and eating frequency. A shorter daily eating interval was also associated with a lower waist circumference. There was no significant association between eating timing and cardiometabolic risk factors in this group of women with excess weight.

ABSTRACT

Background. Emerging research indicates that eating timing may impact dietary intake and metabolic health. However, studies to date have not examined the association of multiple measures of eating timing on both dietary intake and metabolic health in adults with overweight and obesity.

Objective. To examine the association of multiple measures of eating timing on dietary intake (dietary composition, diet quality, and eating frequency) and metabolic health (body composition and cardiometabolic risk).

Design. Cross-sectional analysis of baseline data from a weight loss and maintenance intervention in adult beneficiaries of active duty and retired military personnel.

Participants/setting. Participants were women with overweight or obesity (BMI: 33.5±0.4 kg/m^2, age: 41.8±0.9 years).

Main outcome measures. Eating timing variables examined included daily eating interval (time between first and last eating occasion), time restricted eating (TRE, ≤11 hours daily eating interval), early energy eaters (eating ≥60% of energy during the first half of time awake), and late night eaters (eating within 2 hours of bed).

Statistical analysis. The main analysis was limited to those reporting plausible energy intake (64% of total sample, N=146). Linear, quantile or logistic regression models were used to determine the association of eating timing with measures of dietary intake and metabolic health.

Results. In individuals reporting plausible energy intake, each additional one hour in daily eating interval was associated with 53 kcal higher energy intake, higher glycemic load, eating frequency, and waist circumference ($P<0.05$ for all). Significant associations were observed for: TRE and a lower energy intake, glycemic load, and eating frequency; early energy eating and higher carbohydrate intake; late night eating and a higher energy intake, glycemic load, and eating frequency.

Conclusions. These findings support the mechanistic targeting of eating timing in behavioral interventions aimed at improving dietary intake and body composition.

INTRODUCTION

Overweight, and obesity are associated with poor dietary intake and metabolic health, and affect more than 1.9 billion people worldwide.[1] Americans have shifted from the classic consumption of three meals per day[2,3] to consuming an average of 45% of their daily energy from dinner and evening snacking[4] with around 60% of American adults living in urban areas regularly snacking at night.[5] It has been suggested that this eating pattern contributes to misalignment in circadian rhythms and disruption of metabolic processes resulting in excess energy intake and impaired metabolic health.[6,7] However, dietary interventions for weight control have traditionally focused on calorie restriction and manipulating macronutrient composition and only more recently considered the impact of meal timing on energy balance.[8-11]

Eating timing studies conducted thus far suggest that adults with overweight or obesity who shift to consuming their dietary energy earlier in the day have favorable changes in weight and cardiometabolic health.[11-15] Eating late in the evening has been associated with greater energy intake and negatively associated with metabolic health.[16-20] An emerging area of eating timing research involves manipulation of the total daily eating interval defined as the time between first and last daily eating occasion, and examining its impact on metabolic health. The available data indicates that limiting the daily eating interval results in beneficial alterations in circadian rhythms and improved metabolic health parameters associated with obesity and cardiovascular disease.[8,21,22] Time restricted eating (TRE), defined as limiting energy intake within a specific daily eating interval of typically 8-12 hours has been shown to decrease energy intake and improve metabolic health.[10,23] However, there are no studies examining the effect of multiple measures of eating timing on both dietary intake and indices of metabolic health in adults with overweight or obesity.

The aim of this analysis was to evaluate the associations between measures of eating timing, dietary intake (diet composition, dietary quality, and eating frequency), and metabolic health (body composition and cardiometabolic risk) in adult women with overweight and obesity. Specifically, we examined the association of the following eating timing variables: daily eating interval (defined as the time between first and last eating occasion); time restricted eating (TRE, defined as ≤ 11 hours daily eating interval); early energy eaters (defined as eating ≥ 60% of energy during the first half of time awake); and late night eaters (defined as eating within 2 hours of bed), with dietary intake, body composition, and cardiometabolic risk factors. We tested the hypotheses that a shorter daily eating interval, having a TRE pattern, being an early eater, and not being a late night eater will be associated with more favorable dietary intake and metabolic health.

METHODS

Study Design: This is a secondary cross-sectional analysis of baseline data from the Healthy Families Healthy Forces study (trial # NCT02348853), a weight loss and maintenance study in beneficiaries of active duty or retired military personnel. All participants provided written informed consent. The study was approved by the Institutional Review Boards at Tufts University and the U.S. Army Medical Research, and Material Command (USAMRMC), as well as the USAMRMC Human Research Protection Office.

Healthy Families Healthy Forces study participants (N=239) were eligible to participate if they had a body mass index (BMI) ≥ 25 kg/m^2, spoke English, had no health conditions that influenced body composition or nutrient absorption, were not enrolled in a concurrent nutrition program, and had complete baseline dietary assessment and anthropometric measurements (N=229). Obtainment of baseline measurements ended January 2018. Demographic and lifestyle information including age, race, ethnicity, education level, income, engagement in physical activity, employment status, and menopause status were collected using questionnaires.

Dietary Intake

Baseline dietary intake was estimated using three 24-hour dietary recalls, collected by phone by trained staff. Dietary intake data were collected and analyzed using Nutrition Data System for Research software.[24] Output data were used to calculate average baseline energy, nutrient, and food group intake. Dietary composition variables examined included: total daily energy (kcals), percent energy from macronutrients and added sugar, as well as total fiber (g/1000 kcals). Diet quality measures included glycemic load, energy density, diet quality, and dietary diversity. Energy density was defined as the average daily energy divided by weight (kcals/g) for food only.[25] Diet quality was estimated using the Healthy Eating Index-2015, which scores from 0 to 100, with higher scores indicating higher diet quality.[26] Dietary diversity was assessed using an aggregate score based on the daily consumption of five food groups (grains, animal- and plant-based protein sources, fruit, vegetables, and dairy), where 1 point or 0 was assigned for the presence or absence of each food group with total scores ranging from 0 to 5.[27,28] In addition, eating frequency was determined by summing the total number of daily eating occasions. An eating occasion was defined as consuming 20 or more kcals.

Eating Timing

Eating timing variables were calculated using data from the 24-hour dietary recalls, and wake, and sleep time information was obtained from the Stanford Seven–Day Physical Activity Recall.[29] Both instruments were administered at the same time. Total awake time was defined as the time between the median wake time, and median time in bed. These data were used as a covariate in the analyses.

Daily eating interval was defined as the total time period of daily eating, calculated as the time between the first and last eating occasion in a 24 hour period (hours/day), and presented as an average for 24-hour dietary recalls.

TRE was defined as participants with a daily eating interval ≤ 11 hours. The definition for having a TRE pattern using an 11 hour interval was established *a priori* based on the daily eating interval distribution of our sample. The interval falls within the range used in previously published studies (8-12 hours).[10,30] A non-TRE pattern was defined as a daily eating interval > 11 hours.

Early energy eaters were classified as those who consumed ≥ 60% of their energy during the first half of awake time. Non-early energy eaters were defined as those who consumed < 60% of their energy during the first half of their time awake.

Late night eaters were classified as participants who ate within 2 hours of median bed time. Non-late night eaters were defined as participants who did not eat within 2 hours of bed.

Metabolic Health

Body composition: Fasting weight, height, body fat, and waist circumference measures were obtained in duplicate by trained staff. Weight was measured to ± 0.1kg using a calibrated digital scale (Escali BFBW200 Digital, Minneapolis, MN) that included an assessment for body fat percent via bioelectrical impedance. Height was measured to ± 0.1cm using an upright stadiometer (Model 213, Seca). Body mass index (BMI) was calculated as kg/m^2. Waist circumference was measured to ± 0.3 cm using standard procedures.[31]

Cardiometabolic risk: Systolic and diastolic blood pressure were measured in triplicate (within 5 mmHg) following 5 minutes of rest. Fasting blood samples were collected by trained phlebotomists. Plasma and serum were processed and samples were separated into aliquots. Frozen samples were transported to the Human Nutrition Research Center on Aging at Tufts University for subsequent analysis. Measures included plasma cholesterol, high density lipoprotein cholesterol (HDL), total cholesterol, triglyceride, and blood glucose from serum concentrations were measured using an automated chemistry analyzer (Beckman Coulter AU480). Low density lipoprotein cholesterol (LDL) concentration was calculated using the Friedewald formula.[32] Insulin and C-reactive protein concentrations were measured on a chemiluminescent immunometric analyzer (Siemens, Immulite 200xPi). Glycated hemoglobin was measured on an automated Chemistry analyzer (Roche Cobas MIRA), using an immunoturbidmetric assay (Pointe Scientific, Canton MI). Metabolic syndrome was defined as having the presence of at least three of the following: high waist circumference (>35 inches), high blood pressure (>130/85 mmHg), high triglycerides concentrations (150 mg/dl), high glucose concentrations (>100 mg/dl), and low HDL concentrations (<50 mg/dl).[33,34]

Criteria for Plausible Energy Reporters

To address the issue of underreporting which could alter findings, the Goldberg cut off was used to determine plausible energy reporters.[35-37] Plausible energy reporters were defined by assessing the agreement between energy intake and energy expenditure. Energy intake was estimated using the ratio of reported energy intake to predicted basal metabolic rate. Energy expenditure was estimated using a Physical Activity Level of 1.55. Under-reporters were classified as those reporting energy intake below the lower standard deviation cutoff limit of energy expenditure. Over-reporters were classified as those reporting energy intake above the upper limit standard deviation cutoff limit of energy expenditure.

Statistical Analysis

Descriptive statistics were calculated for the total sample and by TRE status. Continuous variables are reported as means ± standard error, and as a percentage for categorical variables. Differences between TRE pattern groups were determined by independent samples t-tests (for continuous variables that were normally distributed), the Wilcoxon rank-sum test (for continuous variables that were not normally distributed), and the Chi-square test (for categorical variables).

Robust linear regression models were used to examine the association between eating timing and dietary intake, and indices of metabolic health in plausible energy reporters and the total sample. Logistic regression was used to evaluate the separate associations of eating timing and metabolic syndrome. The assumptions for all regression models were evaluated and violations were addressed through transformation or the use of quantile regression. All models were adjusted for age, income, physical activity, and awake time. Lipid medications were adjusted for in models using LDL, HDL, and triglyceride concentrations, as the dependent outcome. Glycemic medications were adjusted for in models using glucose and glycated hemoglobin as the outcome. Hypertension medications were adjusted for in models using systolic and diastolic blood pressure as the outcome. BMI was included as a covariate in models evaluating c-reactive protein as the outcome. For models with the dependent variables of diet diversity, glycemic load, and eating frequency an additional adjustment for total energy intake was used, and results were similar to the unadjusted models (shown) unless otherwise specified.

The threshold for statistical significance was set as a *P* value less than 0.05. All analyses were performed with Stata statistical software version 15.1 (Stata Corp, College Station, TX).

RESULTS

The mean age of the women (N=229) was 40.9 ± 0.7 years (**Table 1**). The majority of participants were non-Hispanic white (77%), with a household income of over $40,000/year (83%), physically inactive (62%), pre-menopausal (72%), and approximately 50% were employed and had a college degree or higher. Thirty six percent of the sample (N=83) was deemed as reporting implausible dietary intake as determined by the Goldberg cutoff. [35-37] All of the implausible reporters under-reported. Participants reporting plausible dietary intakes (N= 146) were older (*P*=0.04), had a lower BMI (*P*<0.01), and reported lower physical activity (*P*=0.02) compared to those under-reporting their energy intake (**Table 1**). Data for the remaining results are presented for plausible reporters only, determined by the Goldberg cutoff [35-37] and results from the total sample are discussed where the findings were different from plausible reporters (**Tables 4 and 6**).

Eating Timing and Dietary Intake

The mean ± standard error energy intake was 2210 ± 40 kcals/day for the plausible energy reporters (**Table 2**). On average, 46.7 ± 0.5% energy was from carbohydrates (14.7 ± 0.5% of which was from added sugar), 36.6 ± 0.4% energy from fat, 15.3 ± 0.3% energy from protein, and 1.5 ± 0.3% energy from alcohol. The average daily eating interval was 11.6 ± 0.1 hours and 35.6% of the sample had a TRE pattern, 38.4% were early energy eaters, and 37.8% were late night eaters. Participants with non-TRE patterns consumed significantly more fiber (*P*=0.02) and had a greater eating frequency (*P*<0.01) compared to those with TRE patterns.

Findings in plausible energy reporters*:* For every additional hour in the daily eating interval, on average, energy intake per day was 53 calories higher (*P*=0.01), glycemic load was 6 units higher (*P*<0.01), and eating frequency was 0.3 greater eating occasions (*P*<0.01), (**Table 3**). Conversely, having a TRE pattern was associated with energy intake per day that was 140 calories lower (*P*=0.045), a 15 unit lower glycemic load (*P*=0.03), and an eating frequency that was 1.0 fewer in eating occasions (*P*<0.01), compared to participants who had a non-TRE pattern. Being classified as an early energy eater was associated with a 2.4% higher energy intake from carbohydrate (*P*=0.02) compared to participants who were not classified as early energy eaters. Being classified as a late night eater was associated with energy intake per day that was 235 calories higher (*P*<0.01), a 22 unit higher glycemic load (*P*<0.01), and an eating frequency with 0.05 greater eating occasions (*P*=0.03), compared to participants who were not classified as late night eaters.

After adjusting for energy intake, TRE pattern and being a late night eater were no longer significantly associated with glycemic load (β =-0.27 95% CI: -0.66, 0.13, *P*=0.18; β =0.34, 95% CI: -0.09, 0.7, *P*=0.12, respectively), and being a late night eater was no longer significantly associated with eating frequency (β=0.46 95% CI: -0.20, 0.94, *P*=0.06). There were no significant associations between eating timing and fat, protein, added sugar, alcohol, and fiber intake as well as diet diversity, and diet quality.

Findings in the total sample: Our findings in the total sample remain consistent with plausible energy reporter models, in that total daily energy, glycemic load, and eating frequency were also positively associated with daily eating interval, negatively associated with having a TRE pattern, and positively associated with being classified as a late night eater (**Table 4**). Also consistent with plausible energy reporters, the associations between both TRE pattern and late night eaters with glycemic load were no longer significant after adjusting for energy in the total sample.

Our findings in the total sample that differed from the findings in the plausible energy reporter models were that carbohydrate intake was no longer significantly associated with being classified as an early energy eater (β=-2.6, 95% CI: -4.2, -0.3, *P*=0.03; PS: Model P=0.25) (**Table 4**). Fiber became negatively associated with having a TRE pattern (β=-0.8, 95% CI: -1.6, -0.02, *P*=0.045) in the total sample. Additionally, eating frequency became positively associated with being classified as an early energy eater (β=0.37, 95% CI: 0.002, 0.73, *P*=0.049), an association that remained significant after adjusting for energy intake (β=0.40, 95% CI: 0.05, 0.75, *P*=0.02).

Eating Timing and Indices of Metabolic Health

As shown in (**Table 2**) participants with plausible energy intake had a (mean ± standard error) BMI of 33.5 ± 0.4 kg/m^2 (27.4% with overweight, and 72.6% with obesity), percentage body fat of 40.5 ± 0.7%, waist circumference of 96.4 ± 0.9 cm and mean cardiometabolic risk factors were within accepted optimal ranges.

For every additional one hour in daily eating interval, on average, waist circumference was about 1.3 cm higher (*P*=0.02), (**Table 5**). Body composition and cardiometabolic risk factor findings were not significant in models with the total sample (**Table 6**).

DISCUSSION

In this cross-sectional analysis of women with overweight or obesity we found that a one hour shorter daily eating interval, or having a TRE pattern (eating within an 11 hour daily eating interval), or not eating within 2 hours of bed time was associated with 53, 140 and 235 calories respectively per day lower energy intake. A one hour shorter daily eating interval was also associated with a smaller waist circumference. In addition, a shorter daily eating interval, having a TRE pattern, and not eating two hours before bed were associated with a lower glycemic load and eating frequency. Combined, these results strongly support the inclusion of eating timing modification as mechanistic targets in lifestyle and behavior change programs aimed at reducing energy intake and improving body composition.

An important advantage to actively targeting eating timing in behavioral interventions involves the concomitant lowering of energy intake without the emphasis on actual reduction in total calories. Our findings using multiple measures of eating timing, including the daily eating interval, TRE pattern, early energy eaters, and late night eaters, support the hypothesis that energy intake is lower in participants with shorter eating intervals. Previous studies examining one aspect of eating timing have shown that eating less at night, i.e. after 5pm, was associated with lower energy intake.[38,39] In a separate study, reducing food intake from ≥14 hour per day to 10 to 11 hour per day resulted in a 20% reduction in energy intake and weight loss of 3.3 kg of which was sustained at one year.[23] Our findings therefore strengthen the emerging research in this area, and lend support for the inclusion of eating timing in behavioral interventions for weight management.

A strength of our dietary analysis was that we examined the association of eating timing with and without adjusting for energy intake in models with dependent variables that did not inherently adjust for energy within their definition. These include glycemic load, diet diversity, and eating frequency. The energy adjusted approach was used to discern the true contribution from the dietary variable *vs*. the potential contribution from total energy intake. Our findings did demonstrate that total energy consumed mitigates or eliminates the significance of some of the observed associations between glycemic load and eating timing as well as eating frequency, suggesting that adjustment for energy may be warranted in future analyses examining such associations. [40]

We found no significant association between eating timing and BMI except for daily eating interval which was positively related to waist circumference, a key measure of abdominal obesity. Our findings are aligned with the inconsistent observations with some[23,41-47] but not all studies[8,30,47-51] demonstrating reductions in body weight and cardiometabolic risk factors with TRE. A likely contributor to the disparate findings with regards to eating timing and metabolic health is the use of varying definitions of TRE among the published studies, with some studies using TRE windows of 8-12 for the restricted period, others using Ramadan fasting as a definition for TRE, and yet others using breakfast skipping as a means of TRE. Ramadan's period of energy intake is not representative of our daily eating intervals and involves a large meal closer to bedtime with the potential for disrupting circadian rhythms with impact on metabolic health. An additional reason we may not have observed any associations with eating timing and cardiometabolic risk may be due to the fact that the majority of our participants were relatively young, and did not present with elevated cardiometabolic risk factors based on current cut-points for values defined as being within the optimal range. Research suggests that an individual could still be at risk, despite having values within the clinically normal range, and therefore may warrant intervention prior to full blown cardiometabolic disease.[52,53] This may be particularly relevant in younger individuals with overweight and obesity, as excess weight combined with subclinical metabolic risk factors may accelerate cardiometabolic risk with advancing age.[54,55]

A major strength of this study was the examination of both dietary and metabolic variables in the same study. An additional strength is that we used a well establish method, the Goldberg cut off, to adjust for implausible energy intake reporting. This minimizes the potential impact of confounding by dietary misreporting. Of note, in these analyses, excluding data from those reporting implausible intake of energy did not alter the significance of observed associations when all participants were included. Limitations of this secondary analysis pertain to the constraints of available baseline data collected from a weight loss and maintenance intervention, and the cross-sectional nature of the analyses which preclude us from being able to infer causality.

Conclusions

Effective and feasible strategies for prevention and reduction of excess weight are urgently needed. Our findings support the mechanistic targeting of eating timing variables as modifiable factors to improving dietary intake and body composition. Additional research to identify optimal eating timing that supports favorable dietary intake, metabolic health and weight loss in a sustainable manner, will facilitate intervention at the community and clinical levels.

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Table 1: Demographics of total sample, plausible energy reporters, and under-reporters

	Total sample	***N***	**Plausible energy reporters**	***N***	**Under-reporters**	***N***	**P value**
Age, years	40.9 ± 0.7	*229*	41.8 ± 0.9	*146*	39.3 ± 1.2	*83*	**0.04**
Race		*223*					
White	77.1		78.5	*113*	74.4	*59*	0.52
Black	14.4		14.6	*21*	13.9	*11*	
Other [a]	8.5		6.9	*10*	11.4	*9*	
Ethnicity		*222*					0.82
Hispanic or Latino	9.5		90.2	*129*	91.1	*72*	
Not Hispanic or Latino	90.5		9.8	*14*	8.9	*7*	
Annual family income		*221*					0.32
< $40,000	17.2		14.7	*21*	21.8	*17*	
$40,000 - $79,999	41.6		41.3	*59*	42.3	*33*	
≥ $80,000	41.2		44.1	*63*	35.9	*28*	
Education		*222*					0.22
Less than a college degree	48.2		45.1	*65*	53.9	*42*	
College degree or higher	51.8		54.9	*79*	46.2	*36*	
BMI	34.7 ± 0.4	*229*	33.5 ± 0.4	*146*	36.8 ± 0.8	*83*	**<0.01**
Employed	48.4	*221*	52.1	*74*	41.8	*33*	0.14
Physical activity	38.2	*220*	32.4	*46*	48.7	*38*	**0.02**
Post-menopausal	27.6	*214*	29.5	*41*	24	*18*	0.39

Continuous variables are displayed as mean ± standard error and differences between plausible and under reporters are determined by independent T-test or Wilcoxon Rank test

Categorical variables are displayed as %, and differences between plausible, and under reporters are determined by Chi square tests

a. Includes multiracial

Table 2: Description of dietary intake, and metabolic health by TRE pattern in plausible energy reporters

	Plausible energy reporters	***N***	**Non-TRE**	***N***	**TRE**	***N***	**P value**
Dietary intake							
Total daily energy (kcals)	2210 ± 40	*146*	2253 ± 60	*94*	2133 ± 60	*52*	0.12
Carbohydrates (% kcals)	46.7 ± 0.5	*146*	46.8 ± 0.7	*94*	46.5 ± 0.8	*52*	0.81
Protein (% kcals)	15.3 ± 0.2	*146*	15.1 ± 0.3	*94*	15.6 ± 0.4	*52*	0.29
Fat (% kcals)	36.6 ± 0.4	*146*	36.8 ± 0.6	*94*	36.1 ± 0.6	*52*	0.44
Alcohol (% kcals)	1.5 ± 0.3	*146*	1.4 ± 0.3	*94*	1.9 ± 0.6	*52*	0.78
Added sugar (% kcals)	14.7 ± 0.5	*146*	14.8± 0.7	*94*	14.4 ± 0.9	*52*	0.57
Fiber (g/1000 kcals)	9.1 ± 0.2	*146*	9.5 ± 0.3	*94*	8.4 ± 0.4	*52*	**0.02**
Glycemic load	148.8 ±3.5	*146*	152.4 ± 4.7	*94*	142.3 ± 5.2	*52*	0.10
Diet quality [i]	52.0 ± 1.0	*146*	52.0 ± 1.4	*94*	52.0 ± 1.5	*52*	0.99
Diet diversity [ii]	4.53 ± 0.04	*146*	4.56 ± 0.04	*94*	4.47 ± 0.06	*52*	0.23
Energy density (kcals/g) [iii]	2.07 ± 0.03	*146*	2.08 ± 0.05	*94*	2.05 ± 0.06	*52*	0.76
Eating frequency [iv]	5.3 ±0.1	*146*	5.6 ± 0.1	*94*	4.7 ± 0.1	*52*	**<0.01**
Metabolic Health							
BMI (kg/m^2)	33.5 ± 0.4	*146*	33.6 ± 0.6	*94*	33.3 ± 0.7	*52*	0.65
Body fat (%)	40.5 ± 0.7	*146*	40.6 ± 0.8	*94*	40.2 ± 1.0	*51*	0.73
Waist circumference (cm)	96.4 ± 0.9	*145*	97.8 ± 1.1	*94*	93.9 ± 1.5	*52*	**0.04**
LDL (mg/dL)	118 ± 3	*139*	119 ± 4	*89*	118 ± 4	*50*	0.98
HDL (mg/dL)	56 ± 1	*139*	57 ± 2	*89*	56 ± 2	*60*	0.97
Total cholesterol:HDL	3.6 ± 0.1	*139*	3.6 ± 0.1	*89*	3.6 ± 0.1	*50*	0.70
Triglyceride (mg/dL)	123 ± 5	*139*	121 ± 6	*89*	126 ± 9	*50*	0.54
Glucose (mg/dL)	98 ± 1	*139*	98 ± 1	*89*	98 ± 2	*50*	0.58
Glycated hemoglobin (%)	5.4 ± 0.0	*138*	5.4 ± 0.1	*89*	5.5 ± 0.1	*49*	0.33
Insulin (uIU/mL)	15.6 ± 1.4	*139*	15.6 ± 2.1	*89*	15.5 ± 1.4	*50*	0.73
C reactive protein (mg/L)	10.5 ± 1.3	*139*	11.5 ± 1.8	*89*	8.8 ± 1.6	*50*	0.73
Systolic blood pressure (mmHg)	114 ± 1	*146*	114 ± 1	*94*	114 ± 1	*52*	0.38
Diastolic blood pressure (mmHg)	77 ± 1	*146*	77 ± 1	*94*	77 ± 2	*52*	0.48
Metabolic syndrome (%)	38.3	*141*	37.4	*91*	35.5	*50*	0.76

Significance is set as P value less than 0.05, bolded P values indicate significant P values

Continuous variables displayed as mean ± standard error and differences are determined by independent T-test or Wilcoxon Rank test

Categorical variables displayed as %, and differences are determined by Chi square tests

i. Diet quality was measured using the Healthy Eating Index – 2015

ii. Diet diversity was determined by the average number of food groups consumed per day

iii. Energy density was calculated using food only

iv. Eating frequency was defined as the number of eating occasions per day

Table 3: Regressions predicting dietary intake by eating timing in plausible energy reporters

Independent variables	Daily eating interval *(N=130)*		TRE *(N=130)*		Early energy eaters *(N=130)*		Late night eaters *(N=130)*	
	Estimate (95% CI)	***P* value**	**Estimate (95% CI)**	***P* value**	**Estimate (95% CI)**	***P* value**	**Estimate (95% CI)**	***P* value**
Dependent variables								
Total daily energy (kcals) [a]	53 (15, 91)	**0.01**	-140 (-285, 5)	**0.045**	-46 (-194, 102)	0.54	235 (85, 386)	**<0.01**
Carbohydrates (% kcals) [a]	0.20 (-0.37, 0.77)	0.48	-0.64 (-2.78, 1.51)	0.56	2.40 (0.31, 4.49)	**0.03**	-0.06 (-2.34, 2.22)	0.96
Fat (% kcals) [a]	0.17 (-0.28, 0.62)	0.46	-1.13 (-2.83, 0.57)	0.19	-1.05 (-2.75, 0.65)	0.23	0.15 (-1.67, 1.97)	0.87
Protein (% kcals) [a]	-0.16 (-0.45, 0.14)	0.30	0.87 (-0.25, 1.99)	0.13	-0.60 (-1.73, 0.52)	0.29	-0.56 (-1.75, 0.63)	0.35
Alcohol (% kcals) [b]	0.002 (-0.15, 0.15)	0.98	0.001 (-0.57,0.57)	1.00	-0.02 (-0.65, 0.61)	0.95	-0.001 (-0.60, 0.60)	1.00
Added sugar (% kcals) [a]	0.45 (-0.17, 1.08)	0.15	-1.91 (-4.26, 0.44)	0.11	0.72 (-1.67, 3.12)	0.55	0.49 (-2.06, 3.04)	0.70
Fiber (g/1,000 kcals) [a]	0.11 (-0.13, 0.35)	0.37	-0.64 (-1.54, 0.27)	0.17	0.33 (-0.60, 1.26)	0.48	-0.09 (-1.07, 0.89)	0.86
Glycemic load [a]	6.13 (2.54, 9.72)	**<0.01**	-15.36 (-29.05, -1.67)	**0.03**	6.57 (-7.64, 20.78)	0.36	22.23 (8.05, 36.41)	**<0.01**
Diet quality [a, i]	-0.35 (-1.58, 0.88)	0.57	2.53 (-2.13, 7.18)	0.29	1.54 (-3.15, 6.23)	0.52	-0.86 (-5.85, 4.12)	0.73
Diet diversity [b, ii]	0.008 (-0.04, 0.06)	0.76	-0.13 (-0.33, 0.07)	0.19	0.01 (-0.18, 0.21)	0.89	0.13 (-0.08, 0.34)	0.21
Energy density (g/kcals) [a, iii]	0.02 (-0.03, 0.06)	0.51	-0.09 (-0.26, 0.08)	0.31	-0.05 (-0.22, 0.12)	0.56	0.08 (-0.10, 0.26)	0.40
Eating frequency [a, iv]	0.31 (0.21, 0.42)	**<0.01**	-0.95 (-1.36, -0.05)	**<0.01**	0.31 (-0.14, 0.75)	0.17	0.53 (0.06, 1.00)	**0.03**

Significance set as P value less than 0.05, bolded P values indicate both significant model, and dependent variable P values

Covariates: age, income, physical activity, awake time

a. Data determined by robust linear regression, estimate reported as β (95% CI)

b. Data determined by quantile regression, and reported as β (95% CI)

i. Diet quality was measured using the Healthy Eating Index – 2015

ii. Diet diversity was determined by the average number of food groups consumed per day

iii. Energy density was calculated using food only

iv. Eating frequency was defined as the number of eating occasions per day

Table 4: Regressions predicting dietary intake by eating timing in the total sample

Independent Variables	Daily eating time *(N=202)*		TRE *(N=202)*		Early energy eaters *(N=202)*		Late eaters *(N=202)*	
	Estimate (95% CI)	***P* value**	**Estimate (95% CI)**	***P* value**	**Estimate (95% CI)**	***P* value**	**Estimate (95% CI)**	***P* value**
Dependent Variables								
Energy (kcals) [a]	81 (42, 119)	**<0.01**	-278 (-424, -131)	**<0.01**	-40 (-199, 119)	0.62	364 (206, 522)	**<0.01**
Carbohydrates (% kcals)[a]	0.61 (0.09, 1.14)	0.02	-2.26 (-4.24, -0.28)	0.03	2.42 (0.35, 4.49)	0.02	0.58 (-1.64, 2.80)	0.61
Fat (% kcals) [a]	-0.08 (-0.50, 0.34)	0.69	0.24 (-1.35, 1.83)	0.77	-0.60 (-2.25, 1.05)	0.47	-0.20 (-0.97, 1.55)	0.82
Protein (% kcals) [a]	-0.36 (10.64, -0.08)	0.01	1.41 (0.35, 2.47)	0.01	-0.76 (-1.87, 0.39)	0.18	-1.34 (-2.52, -0.17)	0.03
Alcohol (% kcals) [b]	0.002 (-0.06, 0.07)	0.96	-0.001 (-0.25, 0.25)	0.99	-0.01 (-0.27, 0.25)	0.93	0.01 (-0.25, 0.28)	0.92
Added sugar (% kcals) [a]	0.01 (0.002, 0.01)	0.01	-0.021 (-0.04, -0.002)	0.03	0.01 (-0.01, 0.03)	0.46	0.01 (-0.01, 0.03)	0.44
Fiber (g/1,000 kcals) [a]	0.1 (-0.1, 0.3)	0.35	-0.8 (-1.6, -0.02)	**0.045**	0.5 (-0.4, 1.3)	0.28	-0.3 (-1.1, 0.6)	0.58
Glycemic load [a]	8.2 (4.9, 11.4)	**<0.01**	-25.9 (-37.4, -12.6)	**<0.01**	2.5 (-10.9, 15.9)	0.72	30.1 (-16.7, 43.4)	**<0.01**
Diet quality [a ,i]	-0.3 (-1.3, 0.6)	0.48	0.3 (-3.3, 4.0)	0.86	1.7 (-2.1, 5.5)	0.37	0.1 (-3.9, 4.2)	0.96
Diet diversity [b, ii]	0.002 (-0.05, 0.05)	0.94	-0.12 (-0.30 0.06)	0.18	-0.10 (-0.29, 0.08)	0.55	0.09 (-0.11, 0.29)	0.40
Energy density (g/kcals)[a, iii]	0.01 (-0.03, 0.04)	0.76	0.02 (-0.12, 0.15)	0.82	-0.07 (-0.21, 0.07)	0.33	0.10 (-0.06, 0.25)	0.21
Eating frequency [a, iv]	0.30 (0.22, 0.38)	**<0.01**	-1.01 (-1.32, -0.69)	**<0.01**	0.37 (0.002, 0.73)	**0.049**	0.57 (0.18, 0.96)	**<0.01**

Significance set as P value less than 0.05, bolded P values indicate both significant model, and dependent variable P values

Covariates: age, income, physical activity, awake time

a. Data determined by robust linear regression, estimate reported as β (95% CI)

b. Data determined by quantile regression, and reported as β (95% CI)

i. Diet quality was measured using the Healthy Eating Index – 2015.

ii. Diet diversity was determined by the average number of food groups consumed per day

iii. Energy density was calculated using food only

iv. Eating frequency was defined as the number of eating occasions per day

Table 5: Regressions predicting metabolic health by eating timing in plausible energy reporters

Independent Variable	Daily eating interval		TRE		Early energy eaters		Late night eaters		
	Estimate (95% CI)	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	***N***
Dependent Variables									
Body composition									
BMI (kg/m^2) [a]	0.49 (-0.03, 1.0)	0.07	-0.99 (-3.00, 1.02)	0.33	1.35 (-0.65, 3.36)	0.18	1.06 (-1.06, 3.19)	0.33	*130*
Body fat (%) [a]	0.42 (-0.35, 1.19)	0.28	-1.30 (-4.23, 1.64)	0.38	2.17 (-0.75, 5.09)	0.15	0.20 (-2.94, 3.34)	0.9	*130*
Waist circumference (cm)[a]	1.28 (0.21, 2.34)	**0.02**	-3.30 (-7.37, 0.77)	0.11	1.59 (-2.47, 5.65)	0.44	4.00 (-0.25, 8.24)	0.07	*130*
Cardiometabolic risk									
LDL (mg/dL) [a]	0.12 (-2.75, 2.99)	0.93	6.48 (-4.31, 17.28)	0.24	2.32 (-8.61, 13.08)	0.68	-0.30 (-11.99, 11.39)	0.96	*126*
HDL (mg/dL) [a]	-0.60 (-1.88, 0.67)	0.36	2.23 (-2.62, 7.08)	0.36	2.37 (-2.52, 7.26)	0.34	1.75 (-3.52, 7.02)	0.51	*126*
Total cholesterol:HDL [a]	0.04 (-0.04, 0.12)	0.33	0.02 (-0.28, 0.33)	0.88	-0.10 (-0.41, 0.20)	0.51	-0.06 (-0.39, 0.27)	0.71	*126*
Triglycerides (mg/dL) [a]	1.36 (-3.50, 6.21)	0.58	1.65 (-16.60, 19.89)	0.86	-8.49 (-26.64, 9.66)	0.36	8.68 (-10.91, 28.27)	0.38	*126*
Glucose (mg/dL) [b]	0.07 (-1.13, 1.28)	0.90	-0.69 (-5.27, 3.89)	0.77	-1.99 (-6.23, 2.26)	0.36	-0.69 (-5.04, 3.67)	0.75	*126*
Glycated hemoglobin (%) [a]	-0.004 (-0.06, 0.05)	0.86	0.08 (-0.11, 0.27)	0.38	-0.03 (-0.22, 0.16)	0.76	-0.04 (-0.25, 0.16)	0.67	*125*
Insulin (uIU/mL) [a]	-0.09 (-0.74, 0.56)	0.78	-0.64 (-3.11, 1.84)	0.61	0.69 (-1.81, 3.19)	0.59	-1.33 (-4.01, 1.35)	0.33	*126*
C reactive protein (mg/L) [a]	-0.20 (-0.79, 0.38)	0.50	-0.29 (-2.47, 1.88)	0.79	-1.18 (-3.36, 1.00)	0.29	-1.40 (-3.78, 0.99)	0.25	*126*
Systolic blood pressure (mmHg) [a]	0.38 (-0.89, 1.64)	0.56	-1.46 (-6.27, 3.34)	0.55	2.08 (-2.74, 6.89)	0.4	-1.35 (-6.54, 3.84)	0.61	*130*
Diastolic blood pressure (mmHg) [a]	0.19 (-0.88, 1.25)	0.73	-1.29 (-5.31, 2.73)	0.53	1.17 (-2.87, 5.22)	0.57	-3.40 (-7.66, 0.85)	0.12	*130*
Metabolic syndrome [c]	1.01 (0.82, 1.25)	0.94	1.12 (0.50, 2.52)	0.78	0.45 (0.19, 1.07)	0.07	0.68 (0.28, 1.63)	0.38	*127*

Covariates: age, income, physical activity, awake time

a. Data determined by robust linear regression, estimate reported as β (95% CI)

b. Data determined by quantile regression, and reported as β (95% CI)

c. Data determined by logistic regression, and reported as odds ratio (95% CI)

Table 6: Regressions predicting metabolic health by eating timing in the total sample

Independent Variable	Daily eating interval		TRE		Early energy eaters		Late night eaters		
	Estimate (95% CI)	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**N**
Dependent Variables									
Body composition									
BMI (kg/m^2) [a]	0.21 (-0.24, 0.66)	0.35	-0.51 (-2.21, 1.19)	0.55	0.14 (-1.64, 1.91)	0.88	0.15 (-1,73, 2.02)	0.88	202
Body fat (%) [a]	0.22 (-0.45, 0.89)	0.52	-0.89 (-3.43, 1.65)	0.49	0.57 (-2.08, 3.21)	0.67	-1.24 (-4.05, 1.57)	0.39	201
Waist circumference (cm)[a]	0.76 (-0.16, 1.66)	0.10	-2.14 (-5.63, 1.35)	0.23	0.83 (-2.83, 4.49)	0.65	1.04 (-2.84, 4.91)	0.6	202
Cardiometabolic risk									
LDL (mg/dL) [a]	0.59 (-1.86, 3.05)	0.63	2.09 (-7.37, 11.56)	0.66	2.85 (-6.95, 12.66)	0.57	-0.52 (-11.19, 10.15)	0.92	191
HDL (mg/dL) [a]	-0.30 (-1.24, 0.64)	0.53	1.50 (-2.11, 5.10)	0.41	2.56 (-1.18, 6.30)	0.18	0.53 (-3.56, 4.63)	0.8	191
Triglycerides (mg/dL) [a]	1.31 (-2.31, 4.92)	0.48	-1.72 (-15.58, 12.13)	0.81	-2.06 (-16.47, 12.34)	0.78	8.07 (-7.55, 23.69)	0.31	191
Glucose (mg/dL) [b]	0.58 (-0.40, 1.56)	0.24	-0.18 (-3.85, 3.49)	0.92	-1.42 (-5.14, 2.30)	0.45	-1.66 (-5.64, 2.33)	0.41	191
Glycated hemoglobin (%)[a]	0.02 (-0.02, 0.05)	0.44	0.04 (-0.11, 0.18)	0.62	0.003 (-0.15, 0.16)	0.97	-0.04 (-0.20, 0.12)	0.65	191
Insulin (uIU/mL) [a]	-0.33 (-0.99, 0.33)	0.32	0.76 (-1.74, 3.26)	0.55	-0.34 (-2.97, 2.30)	0.8	-2.23 (-4.97, 0.52)	0.11	192
C reactive protein (mg/L)[a]	0.13 (-0.33, 0.58)	0.59	-0.60 (-2.36, 1.16)	0.5	-1.25 (-3.05, 0.56)	0.18	-1.18 (-3.13, 0.77)	0.24	192
Systolic blood pressure (mmHg) [a]	-0.21 (-1.10, 0.69)	0.65	-0.19 (-3.60, 3.23)	0.92	0.60 (-2.94, 4.14)	0.74	0.63 (-3.12, 4.38)	0.74	202
Diastolic blood pressure (mmHg) [a]	-0.21 (-0.95, 0.53)	0.57	-0.76 (-3.57, 2.06)	0.6	0.03 (-2.90, 2.96)	0.98	-0.98 (-4.09, 2.12)	0.53	202
Metabolic syndrome [c]	1.04 (0.88, 1.22)	0.68	1.08 (0.58, 2.04)	0.8	0.69 (0.35, 1.36)	0.28	0.70 (0.34, 1.42)	0.32	192

Covariates: age, income, physical activity, awake time

a. Data determined by robust linear regression, estimate reported as β (95% CI)

b. Data determined by quantile regression, and reported as β (95% CI)

c. Data determined by logistic regression, and reported as odds ratio (95% CI

vi. Chapter II:

Food Cravings: Associations with Dietary Intake and Metabolic Health

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KEY WORDS Food cravings; dietary intake; eating patterns; metabolic health; TRE; body composition

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ABSTRACT

Food cravings are a desire for specific foods which, if uncontrolled may lead to excess energy intake and weight gain. However, information on the relation between food cravings, dietary intake, and indices of metabolic health is limited. This study used baseline data from females (n=229; aged 40.9 ± 0.7 years; BMI 34.7 ± 6.4 kg/m^2) who were dependents of active duty and retired military personnel, and enrolled in the Healthy Families Healthy Forces weight loss and maintenance study. Measures obtained included food cravings using the Food Craving Questionnaire-Trait (which provides a habitual and stable measure of food cravings), dietary composition and eating patterns from three 24-hour dietary recalls and the Stanford 7-day Physical Activity Recall, body composition from anthropometric measures, cardiometabolic risk factors from blood measures, and demographic information from questionnaires. Linear, quantile, or logistic regression models were used to examine the association of total food craving scores on dietary intake, and indices of metabolic health. In individuals reporting plausible energy intake (n=146; 2210 ± kcals/day) higher food craving scores were associated with a lower diet quality ($P<0.05$), higher eating frequency ($P=0.02$), longer daily eating interval ($P<0.05$), and a lower likelihood of following a time restricted eating pattern ($P=0.02$). Food cravings were also positively associated with BMI ($P=0.03$) and waist circumference ($P=0.01$), but not with measures of cardiometabolic risk (LDL, HDL, total cholesterol:HDL, triglycerides, glucose, glycated hemoglobin, insulin and C-reactive protein concentrations, blood pressure, metabolic syndrome). Our findings of significant associations of food cravings with lower diet quality, poor eating patterns, and unfavorable body composition strongly support efforts of targeting cravings in behavioral programs for weight management.

INTRODUCTION

The association of excess body weight with increased risk of chronic disease has heightened the focus on targeting behaviors to promote adherence to sustainable weight loss and a healthy lifestyle (Hales, Fryar, Carroll, Freedman, & Ogden, 2018). One such behavior is food cravings. This widely prevalent behavior has been reported to occur by 97% of women and 68% of men at least once in their lifetime (Weingarten & Elston, 1990; Yanovski, 2003). Craved foods are usually palatable, energy dense and collectively contribute to higher energy intake, disordered eating, and metabolic dysregulation (Buscemi, Rybak, Berlin, Murphy, & Raynor, 2017; A. M. Chao, Grilo, & Sinha, 2016; Gilhooly et al., 2007; Hill, Weaver, & Blundell, 1991; Hormes, Orloff, & Timko, 2014; Massicotte, Deschenes, & Jackson, 2019; McCuen-Wurst, Ruggieri, & Allison, 2018; Richard, Meule, Reichenberger, & Blechert, 2017; Zarrinpar, Chaix, & Panda, 2016). When craved foods are consumed, the reward centers of the brain undergo greater activation compared to when non-craved foods are consumed (Rolls & McCabe, 2007; Ulrich, Steigleder, & Gron, 2016). Food cravings therefore present a motivation to eat, independent of hunger, and are linked to excess energy intake and a higher lifetime body mass index (BMI) (Gilhooly et al., 2007; Hill & Heaton-Brown, 1994; Siwik & Senf, 2006; Weingarten & Elston, 1991).

Food cravings may be conditioned by interventions (Anton et al., 2012; Batra et al., 2013; Buscemi et al., 2017; Gilhooly et al., 2007; Martin, O'Neil, & Pawlow, 2006; Martin et al., 2011). Longitudinal studies promoting restriction of craved foods have resulted in reduced body weight and food cravings (Anton et al., 2012; Batra et al., 2013; Buscemi et al., 2017; Gilhooly et al., 2007; Martin et al., 2006; Martin et al., 2011). In a 6-month worksite weight loss intervention, we have previously demonstrated a significant reduction in food cravings-trait, and a correlation between higher baseline food cravings and lower reduction in body weight (Batra et al., 2013). In the same study we observed an activation in the regions of the brain which control rewards and cravings. A craving for low calorie foods *vs*. high calorie foods was greater following the weight loss intervention compared to baseline values prior to participation in the program (Deckersbach et al., 2014). Although relationship between body weight and food cravings (Anton et al., 2012; Batra et al., 2013; Buscemi et al., 2017; Gilhooly et al., 2007; Martin et al., 2006; Martin et al., 2011), and separately, the association between excess body weight and increased cardiometabolic risk, has been demonstrated, little data are available evaluating the direct effect of food cravings on cardiometabolic risk. In addition, while a link between food cravings and energy intake has been demonstrated, the association of food cravings and eating patterns has not yet been examined.

Our aim was to examine the association of food cravings with dietary intake, eating patterns, body composition, and indices of cardiometabolic health in women with overweight and obesity using cross-sectional data. We tested the hypothesis that greater food cravings are associated with greater energy intake, and less favorable dietary pattern and metabolic health measures.

MATERIALS AND METHODS

Study characteristics

Data were obtained from baseline information collected from 239 participants enrolled in the Healthy Families Healthy Forces weight loss and maintenance trial in adult beneficiaries of active duty and retired military personnel. To be eligible, participants had a BMI of ≥25 kg/m^2 at screening, no health conditions that influenced nutrient absorption or weight loss, were not pregnant or planning to become pregnant, were not concurrently enrolled in other nutrition programs, and were English speaking. Two hundred and twenty nine females with baseline outcome measurements and at least one dietary recall were included for this secondary data analysis. From the total cohort, four males were excluded due to the small sample size, one female was excluded for not completing any baseline measurements, and five females were excluded for missing dietary data. The main analysis was limited to the 146 participants who met the additional criterion of reporting plausible energy intake, as defined by the Goldberg cut off (Black, 2000; Goldberg et al., 1991; Rhee et al., 2015). The study was approved by both the Tufts Medical Center and Tufts University Health Sciences Institutional Review Boards and U.S. Army Institute of Environmental Medicine Institutional Review Board.

Measurements

Demographics: Demographic variables including age, sex, race, ethnicity, education, and income were obtained using online questionnaires completed by participants remotely or in-person. Health history included menopause status as well as medication use for lipid, blood pressure and glycemic control, physical activity, and employment status.

Food cravings: Food cravings were ascertained by the Food Craving Questionnaire -Trait (FCQ-T) which consists of 39 questions scored on a 6-point scale ranging from *never* to *always* with a total possible score of 234 (Cepeda-Benito, Gleaves, Williams, & Erath, 2000). The FCQ-T is a robust and validated questionnaire that captures stable total food cravings, not situational cravings or cravings specific to foods or food groups. Higher total FCQ-T scores indicate more intense and frequent food cravings, although these cannot be quantified separately. High food cravers were classified as those participants with a FCQ-T score of ≥113, which was the median score in our sample.

Dietary intake: Three baseline dietary recalls were collected by phone using the multiple-pass 24-hour recall method and analyzed using Nutrition Data System for Research software (2014), developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN. *Dietary composition* data from Nutrition Data System for Research includes daily total calories (kcals), percent of calories from macronutrients, fiber (g/1000 kcals), and glycemic load. Diet diversity was scored by awarding one point for each food group consumed (grains, vegetables, fruit, meats/protein, and dairy), resulting in a total maximum score of 5 (Kant & Graubard, 2005; Kant, Schatzkin, Harris, Ziegler, & Block, 1993). Diet quality was determined using the Healthy Eating Index-2015, scored on a scale of 0 to 100 with a higher score indicating better diet quality (Reedy et al., 2018). Energy density was determined by dividing calories consumed by weight (kcals/g) for food, but not beverages (Vernarelli, Mitchell, Rolls, & Hartman, 2013).

Eating patterns were calculated using the Nutrition Data System for Research 24-hour dietary recall and the Stanford 7-day Physical Activity Recall data (Richardson, Ainsworth, Jacobs, & Leon, 2001), which was captured over the phone or in person. Eating occasions were defined as any episode at which 20 or more calories were consumed and included solid or liquid foods. Eating frequency was defined as the total number of daily eating occasions. Daily eating interval was defined as the number of hours between the first and last eating occasion. Time restricted eating (TRE) pattern was defined as those participants who had a daily eating interval of 11 hours or less. The median wake time, time in bed, and time awake were calculated using the Stanford 7-day Physical Activity Recall, and was used to define early energy eaters and late night eaters. Participants were designated as early energy eaters if they consumed ≥ 60% of their daily calories within the first half of their time awake. Late night eaters were defined as those participants who ate within 2 hours of median bedtime.

Metabolic health: *Body composition* was assessed using fasting weight, height, body fat percentage, and waist circumference measures. Weight was measured in duplicate to ± 0.1 kg using a calibrated scale. Percentage body fat was estimated using the same scale by bioelectrical impedance. Height was obtained in duplicate to ± 0.1 cm and was used to calculate BMI as kg/m^2. Waist circumference was measured in duplicate to ± 0.3 cm using standard procedures (WHO, 2008).

Cardiometabolic risk was assessed using blood pressure and fasting blood measurements. Systolic and diastolic blood pressure were taken in triplicate to obtain readings within 5 mm/Hg of each other following 5 minutes of rest. A fasting blood sample was obtained from trained phlebotomists. High density lipoprotein cholesterol (HDL), total cholesterol, triglyceride and glucose concentrations were measured on an automated chemistry analyzer (Beckman Coulter AU480). Low density lipoprotein cholesterol (LDL) concentrations were calculated using the Friedewald formula unless triglyceride concentrations exceeded 400 mg/dL (Friedewald, Levy, & Fredrickson, 1972). When that was the case LDL concentrations was measured directly measured on an automated chemistry analyzer (Beckman Coulter AU480). Insulin and C-reactive protein concentrations were measured on a chemiluminescent immunometric analyzer (Siemens, Immulite 200xPi). Glycated hemoglobin was measured on an automated Chemistry analyzer (Roche Cobas MIRA), using an immunoturbidmetric assay (Pointe Scientific, Canton MI). Metabolic syndrome was calculated as defined by the National Cholesterol Education Program Adult Treatment Panel III: high waist circumference (>88.9 cm), high blood pressure (>130/85 mmHg), high triglyceride concentrations (150 mg/dl), high glucose concentrations (>100 mg/dl), and low HDL concentrations (<50 mg/dl) (Grundy et al., 2005).

Data analysis

Descriptive statistics were calculated for the total sample and categorized by plausible energy reporters or under-reporters as well as high or low food craver status, with continuous variables reported as a weighted mean ± standard error, and categorical variables presented as percentages. Differences between high and low food cravers were determined by independent samples t-tests for continuous variables that were normally distributed, the Wilcoxon rank-sum test for continuous variables that were not normally distributed, and the Chi-square test for categorical variables.

Robust linear, logistic, or quantile regression models were used to examine the influence of food cravings on dietary intake and metabolic health. Models were run in the total sample (N=229) and limited to plausible energy intake reporters (N=146) as determined by the Goldberg cutoff (Black, 2000; Goldberg et al., 1991; Rhee et al., 2015). The results are presented for the plausible energy reporters and were similar to models including the total sample (plausible and implausible energy reporters) unless otherwise stated. The assumptions for all regression models were evaluated, and transformations or the use of quantile regression were applied as needed. All models were adjusted for age, income, and physical activity. Medication usage was adjusted for in all models pertaining to metabolic health and body composition. BMI was included as a covariate in models evaluating c-reactive protein as the dependent variable. Total daily energy was included as a covariate in dietary intake models in which the dependent variable did not inherently adjust for energy; this included the dependent variables of diet diversity, glycemic load, eating frequency, daily eating interval, TRE, early energy eaters, and late night eaters. Results were similar to the unadjusted models (shown) unless otherwise specified.

The threshold for statistical significance was set as a *P* value less than 0.05. All analyses were performed with Stata statistical software version 15.1 (Stata Corp, College Station, TX).

RESULTS

Demographics

Data in **Table 1** are presented for the total sample (n=229), plausible reporters (n=146) and under-reporters (n= 83). The primary analysis was restricted to plausible reporter subgroup. The mean age of the total sample was 40.9 ± 0.7 years with the majority being white, non-Hispanic, sedentary, pre-menopausal, and with a family income greater than $40,000 per year. Approximately half of the total sample were also college educated and employed. The mean ± standard error FCQ-T score was 115.6 ± 2.4. Using the Goldberg cutoff for plausible energy intake, we estimated 36% of our sample was comprised of under-reporters (Black, 2000; Goldberg et al., 1991; Rhee et al., 2015). The remaining 64% of participants reporting plausible dietary intake had a lower BMI ($P<0.01$), were older ($P=0.04$), more sedentary ($P=0.02$), and had higher food cravings scores (*P*<0.01) compared to those who were under-reporting energy intake.

Dietary intake of plausible energy reporters

The daily energy intake of plausible energy reporters was 2210 ± 40 kcals (mean ± standard error) with 46.7 ± 0.5% of energy from carbohydrates (14.7 ± 0.5% of which were from added sugar), 36.6 ± 0.4% of energy from fat, and 16.3 ± 0.3% of energy from protein (**Table 2**). Total daily energy (*P*=0.02) and energy density (*P*=0.049) were higher while diet quality was lower (*P*<0.01) in high food cravers compared to the low food cravers. A greater proportion of high food cravers were classified as late night eaters (*P*=0.01) compared to the low food cravers.

Dietary intake associations in plausible energy reporters

Higher food cravings were significantly associated with lower diet quality (*P*=0.048), a higher eating frequency (*P*=0.02), longer daily eating interval (*P*=0.049), and lower odds of having TRE (*P*=0.02) compared to lower food cravings (**Table 3**). When energy was included as a covariate the association between food cravings and eating frequency (β =0.01, 95% CI: -0.001, 0.01, *P*=0.07) and daily eating interval (β =0.01, 95% CI: -0.001, 0.02, *P*=0.09) were no longer significant (data not shown).

Dietary intake associations in total sample

Food cravings were positively associated with daily energy intake (*P*<0.01) and glycemic load (*P*<0.01), but not diet quality *(P*=0.08) (**Table 4**). The finding for glycemic load was no longer significant after adjusting for energy (β =-0.05, 95% CI: -0.14, 0.04, *P*=0.27, data not shown).

Consistent with plausible energy reporters, food cravings of the total sample were significantly associated with eating frequency (*P*<0.01), daily eating interval (*P*=0.02), and TRE pattern (*P*<0.01) in the total sample (**Table 4**). These associations were no longer significant after adjusting for energy (β =0.003, 95% CI: -0.002, 0.008, *P*=0.22; β =0.003, 95% CI: -0.003, 0.1, *P*=0.33, odds ratio =0.99, 95% CI: 0.98, 1.00, *P*=0.08, respectively). Additionally, in the total sample but not in plausible reporters, we observed that food cravings increased the odds of being classified as a late night eater (*P*<0.01), although this association was not significant when adjusted for energy intake (odds ratio =1.01, 95% CI: 1.00, 1.02, *P*=0.18, data not shown).

Metabolic health of plausible energy reporters

Seventy-two percent of plausible reporters were classified as obese. Their mean BMI was 35.5 ± 0.4 kg/m^2, body fat was 40.5 ± 0.7%, and waist circumference was 96.4 ± 0.8 cm (**Table 2**). Thirty-eight percent of plausible reporters were classified as having metabolic syndrome. Their mean serum triglyceride concentration was 123 ± 5 mg/dL, HDL concentration was 56 ± 1 mg/dL, and blood pressure was 114/77 ± 1 mmHg.

Metabolic health associations in plausible energy reporters

Individuals who were high food cravers, defined as above the median FCQ-T score, had a lower LDL (*P*=0.04) and higher C-reactive protein (*P*=0.03), BMI (*P*=0.03) and waist circumference (*P*=0.01) than low food carvers, but not with other measures of cardiometabolic risk (**Table 5**).

Metabolic health associations in the total sample

There were no statistically significant associations between food cravings and measures of metabolic health in models which included the total sample (**Table 6**).

DISCUSSION

Findings from this study indicate that in the subset of plausible energy reporters, higher food cravings were associated with a greater BMI and waist circumference, higher eating frequency, longer daily eating interval, reduced likelihood of having a TRE pattern compared to non-TRE pattern, and a lower diet quality. The associations of higher food cravings with multiple unfavorable outcomes suggest that targeting the reduction of cravings is a promising approach for interventions aimed at weight loss and establishing healthy eating patterns.

Consistent with previous research, we found that higher food cravings were associated with lower diet quality (Kim, Choue, & Lim, 2016). However, our findings also identified no significant association between cravings and energy intake in adults with overweight or obesity. These data are inconsistent with prior reports in which food cravings were positively correlated with energy intake in adults with (Buscemi et al., 2017) and without obesity (Hill et al., 1991). Although, the previous studies did not limit their analysis to plausible energy reporters. Indeed, we also found a positive association between food cravings and energy intake in models that were not constrained to plausible energy reporters, consistent with previously published studies. Of note, we observed a positive association between energy intake and BMI (β =0.003, 95% CI: 0.001, 0.004, P <0.01), which was not significant in the total sample with the under-reporters included (β =0.0.0001, 95% CI: -0.001, 0.002, P =0.88), which underscores the importance of correcting for plausible reporting in future studies to better understand true associations between exposures and outcomes.

A unique component of our study that contributes to its strength is that we addressed implausible energy intake. In our sample, over a third of participants were classified as under-reporters of energy intake. Inclusion of dietary data that is misreported has the high potential for altering the true association between eating behavior and diet or diet and health outcomes. Further, plausible energy reporters had higher cravings in comparison to those with implausible energy reporting (all under-reporters). We cannot rule out the possibility that under-reporters also underreported food cravings. An additional strength was that we examined the association between food cravings and dietary intake, both with and without adjusting for energy for dietary variables that did not inherently adjust for energy within their definition. These include: glycemic load, diet diversity, eating frequency, daily eating interval, TRE, early energy eaters, and late night eaters. Adjusting for total energy intake weakened the associations between food cravings and diet quality and eating patterns, confirming the strong influence of total energy intake. Previous studies examining food cravings and body weight related outcomes have used different tools for capturing food cravings. We used the food cravings "trait" questionnaire, the FCQ-T, which is not only a validated questionnaire with high test- re-test reliability, for both populations with overweight and obesity, but is also a tool that measures the "stable trait" of food cravings that is not influenced by situational factors (Taylor, 2019).

Our finding of a positive association between food cravings and both BMI and waist circumference are consistent with previous studies (Abiles et al., 2010; Avitia, Loya Mendez, Portillo Reyes, Reyes Leal, & Capps Iv, 2018; A. Chao, Grilo, White, & Sinha, 2014; Massicotte et al., 2019; White Marney, Whisenhunt Brooke, Williamson Donald, Greenway Frank, & Netemeyer Richard, 2012) and confirm the negative impact of cravings on BMI and waist circumference.

A limitation of this study is the lack of a positive association between cravings and indices of cardiometabolic risk may, in part, be attributed to the mean values in our study sample falling within ranges considered as clinically optimal; we may have been limited in the heterogeneity required for detecting a statistical significance. Another limitation is the self-reported nature of the dietary intake data. As this was anticipated, we used the well-established 24 hour dietary recall method which was administered by trained personnel, and additionally excluded implausible dietary energy reporters who, in our study sample, were entirely comprised of under-reporters (Subar et al., 2015). In addition, this secondary data analysis was limited to the available data collected for the primary weight loss and maintenance intervention, and the subsequent reduction for plausible reporting which may have limited the sample size needed to detect all possible differences. Further, this secondary data analysis used only baseline data and is descriptive in nature; our findings of associations are observations for which we cannot ascertain a mechanistic role or infer causality.

Conclusions

Modifying eating behavior is an integral part of weight loss programs and our findings suggest that reduction in food cravings may have a positive impact on eating patterns, diet quality, and body composition in women with overweight or obesity. Further research should examine the role of food cravings and dietary intake and metabolic health in both men and women with and without risk factors for cardiometabolic disease.

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Table 1: Demographics of the total sample, plausible energy reporters, and under-reporters

	Total sample	***N***	**Plausible energy reporters**	***N***	**Under-reporters**	***N***	**P value**
Age, years	40.9 ± 0.7	*229*	41.8 ± 0.8	*146*	39.3 ± 1.2	83	**0.04**
Race		*223*					
White	77.1		78.5	*113*	74.4	*59*	0.52
Black	14.4		14.6	*21*	13.9	*11*	
Other [a]	8.5		6.9	*10*	11.4	*9*	
Ethnicity		*222*					0.82
Hispanic or Latino	9.5		9.8	*129*	8.9	*72*	
Not Hispanic or Latino	90.5		90.2	*14*	91.1	*7*	
Annual family income		*221*					0.32
< $40,000	17.2		14.7	*21*	21.8	*17*	
$40,000 - $79,999	41.6		41.3	*59*	42.3	*33*	
≥ $80,000	41.2		44.1	*63*	35.9	*28*	
Education		*222*					0.22
Less than a college degree	48.2		45.1	*65*	53.9	*42*	
College degree or higher	51.8		54.9	*79*	46.2	*36*	
BMI	34.7 ± 0.4	*229*	33.5 ± 0.4	*146*	36.8 ± 0.8	*83*	**<0.01**
Employed	48.4	*221*	52.1	*74*	41.8	*33*	0.14
Physical activity	38.2	*220*	32.4	*46*	48.7	*38*	**0.02**
Post-menopausal	27.6	*214*	29.5	*41*	24.0	*18*	0.39
Food cravings	116 ± 2	*214*	122 ± 3	*137*	104 ± 4	*77*	**<0.01**

Continuous variables are displayed as mean ± standard error and differences between plausible and under reporters are determined by independent T-test or Wilcoxon Rank test.

Categorical variables are displayed as % and differences between plausible and under-reporters are determined by Chi square tests.

a. Includes multiracial

Table 2: Description of dietary intake and metabolic health by food cravings in plausible energy reporters

	Plausible energy reporters	***N***	**Low food cravings**	***N***	**High food cravings**	***N***	**P value**
Dietary intake							
Total daily energy (kcals)	2210 ± 40	146	2120 ± 57	60	2311 ± 58	77	**0.02**
Carbohydrates (% kcals)	46.7 ± 0.5	146	46.4 ± 0.9	60	46.7 ± 0.7	77	0.81
Protein (% kcals)	15.3 ± 0.2	146	15.5 ± 0.4	60	15.0 ± 0.3	77	0.46
Fat (% kcals)	36.6 ± 0.4	146	36.5 ± 0.7	60	36.8 ± 0.6	77	0.37
Alcohol (% kcals)	1.5 ± 0.3	146	1.6 ± 0.4	60	1.6 ± 0.4	77	0.93
Added sugar (% kcals)	14.7 ± 0.5	146	14.2 ± 0.8	60	15.0 ± 0.8	77	0.56
Fiber (g/1000 kcals**)**	9.1 ± 0.2	146	9.6 ± 0.4	60	8.6 ± 0.3	77	0.08
Glycemic load	148.8 ± 3.5	146	141.2 ± 5.0	60	156.4 ± 5.1	77	0.07
Diet quality [i]	52.0 ± 1.0	146	55.3 ± 1.7	60	49.7 ± 1.3	77	**<0.01**
Diet diversity [ii]	4.53 ± 0.04	146	4.58 ± 0.06	60	4.51 ± 0.05	77	0.25
Energy density [iii] (kcals/g)	2.07 ± 0.04	146	2.0 ± 0.06	60	2.15 ± 0.05	77	**0.049**
Eating frequency [iv]	5.26 ± 0.09	146	5.14 ± 0.13	60	5.34 ± 0.14	77	0.36
Daily eating interval [v] (hours)	11.6 ± 0.2	146	11.6 ± 0.2	60	11.7 ± 0.2	77	0.53
TRE [vi]	35.6	146	40.0	60	32.5	77	0.48
Early energy eaters [vii]	38.4	146	40.0	60	39.0	77	0.90
Late night eaters [viii]	37.8	146	25.5	60	47.2	77	**0.01**
Metabolic health							
BMI (kg/m^2)	33.5 ± 0.6	*146*	32.8 ± 0.6	*60*	34.2 ± 0.6	*77*	0.17
Body fat (%)	40.5 ± 0.7	*145*	39.5 ± 0.9	*60*	41.3 ± 1.0	*76*	0.19
Waist circumference (cm)	96.4 ± 0.9	*146*	94.0 ± 1.3	*60*	98.1 ± 1.3	*77*	0.07
LDL (mg/dL)	118 ± 3	*139*	121 ± 4	*56*	115 ± 3	*74*	0.22
HDL (mg/dL)	56 ± 1	*139*	56 ± 2	*56*	56 ± 2	*74*	0.98
Total cholesterol:HDL	3.6 ± 0.1	*139*	3.7 ± 0.1	*56*	3.6 ± 0.1	*74*	0.64
Triglycerides (mg/dL)	123 ± 5	*139*	121 ± 8	*56*	125 ± 7	*74*	0.85
Glucose (mg/dL)	98 ± 1	*139*	98 ± 2	*56*	98 ± 1	*74*	0.48
Glycated hemoglobin (%)	5.4 ± 0.0	*138*	5.5 ± 0.1	*55*	5.4 ± 0.1	*74*	0.05
Insulin (uIU/mL)	15.6 ± 1.4	*139*	17.3 ± 3.3	*56*	14.3 ± 0.9	*74*	0.97
C-reactive protein (mg/L)	10.5 ± 1.3	*139*	8.8 ± 1.7	*56*	11.7 ± 1.9	*74*	**0.049**
Systolic blood pressure (mmHg)	114 ± 1	*146*	116 ± 2	*60*	113 ± 1	*77*	0.15
Diastolic blood pressure (mmHg)	77 ± 1	*146*	78 ± 2	*60*	76 ± 1	*77*	0.24
Metabolic syndrome (%)	38.3	*141*	43.2	*57*	56.8	*75*	0.95

Continuous variables displayed as mean ± standard error and differences determined by independent T-test or Wilcoxon Rank test.

Categorical variables displayed as % and differences determined by Chi square tests.

i. Diet quality was measured using the Healthy Eating Index – 2015.
ii. Diet diversity was determined by the average number of food groups consumed per day
iii. Energy density was calculated using food only
iv. Eating frequency was defined as the number of eating occasions per day
v. Daily eating interval was defined as the time between the first and last eating occasion of the day

vi. TRE was classified as a daily eating interval > 11 hours
vii. Early energy eaters were classified as consuming ≥ 60% of energy during the first half of awake time
viii. Late night eaters were classified as eating within 2 hours of bed

Table 3: Regressions predicting dietary intake by food cravings in plausible energy reporters

Independent variable	Food cravings *(N=135)*	
	Estimate (95% CI)	**P value**
Dependent variables		
Dietary composition		
Energy (kcals) [a]	1.74 (-0.55, 4.02)	0.13
Carbohydrates (% kcals) [a]	-0.001 (-0.03, 0.03)	0.92
Fat (% kcals) [a]	0.01 (-0.01, 0.04)	0.26
Protein (% kcals) [a]	-0.005 (-0.02, 0.01)	0.52
Alcohol (% kcals) [b]	0.0003 (-0.01, 0.01)	0.95
Added sugar (% kcals) [a]	-0.006 (-0.04, 0.03)	0.71
Fiber (g/1,000 kcals) [a]	0.001 (-0.01, 0.01)	0.92
Glycemic load [a]	0.06 (-0.13, 0.25)	0.55
Diet quality [a, i]	-0.06 (-0.12, -0.001)	**0.048**
Diet diversity [b, ii]	-0.002 (-0.01, 0.001)	0.18
Energy density [a, iii]	0.001 (-0.001, 0.003)	0.24
Eating patterns		
Eating frequency [a, iv]	0.006 (0.001, 0.02)	**0.02**
Daily eating interval (hours) [a, v]	0.009 (-0.0002, 0.02)	**0.049**
TRE [c, vi]	0.987 (0.976, 0.998)	**0.02**
Early energy eaters [c, vii]	0.995 (0.99, 1.01)	0.35
Late night eaters [c, viii]	1.01 (0.999, 1.02)	0.06

Significance set as P value less than 0.05, bolded p values indicate both significant model and dependent variable P values

Covariates: age, income, physical activity

a. Data determined by robust linear regression, estimate reported as β (95% CI)
b. Data determined by quantile regression and reported as β (95% CI)
i. Diet quality was measured using the Healthy Eating Index – 2015.
ii. Diet diversity was determined by the average number of food groups consumed per day
iii. Energy density was calculated using food only
iv. Eating frequency was defined as the number of eating occasions per day
v. Daily eating interval was defined as the time between the first and last eating occasion of the day
vi. TRE was classified as a daily eating interval > 11 hours
vii. Early energy eaters were classified as consuming ≥ 60% of energy during the first half of awake time
viii. Late night eaters were classified as eating within 2 hours of bed

Table 4: Regressions predicting dietary intake by food cravings in the total sample

Independent Variable	Food cravings *(N=213)*	
	Estimate (95% CI)	**P value**
Dependent Variables		
Dietary composition		
Energy (kcals) [a]	4.6 (2.5, 6.7)	**<0.01**
Carbohydrates (% kcals) [a]	-0.01 (-0.03, 0.02)	0.66
Fat (% kcals) [a]	0.02 (-0.01, 0.04)	0.16
Protein (% kcals) [a]	-0.01 (-0.03, 0.003)	0.10
Alcohol (% kcals) [b]	0.0001 (-0.003, 0.004)	0.97
Added sugar (% kcals) [a]	0.002 (-0.02, 0.03)	0.90
Fiber (g/1,000 kcals) [a]	0.0003 (-0.01, 0.01)	0.95
Glycemic load [a]	0.26 (0.08, 0.42)	**<0.01**
Diet quality [a, i]	-0.04 (-0.10, 0.01)	0.08
Diet diversity [b, ii]	0.002 (-0.001, 0.004)	0.24
Energy density [a, iii]	0.002 (-0.0001, 0.004)	0.07
Eating patterns		
Eating frequency [a, iv]	0.01 (0.002, 0.01)	**<0.01**
Daily eating interval (hours) [a, v]	0.01 (0.001, 0.02)	**0.02**
TRE [c, vi]	0.99 (0.98, 0.997)	**<0.01**
Early energy eaters [c, vii]	0.996 (0.99, 1.00)	0.36
Bedtime eaters [c, viii]	1.01 (1.003, 1.02)	**<0.01**

Significance set as P value less than 0.05, bolded p values indicate both significant model and dependent variable P values

Covariates: age, income, physical activity

a. Data determined by robust linear regression, estimate reported as β (95% CI)
b. Data determined by quantile regression and reported as β (95% CI)
c. Data determined by logistic regression and reported as odds ratio (95% CI)
i. Diet quality was measured using the Healthy Eating Index – 2015.
ii. Diet diversity was determined by the average number of food groups consumed per day
iii. Energy density was calculated using food only
iv. Eating frequency was defined as the number of eating occasions per day
v. Daily eating interval was defined as the time between the first and last eating occasion of the day
vi. TRE was classified as a daily eating interval > 11 hours
vii. Early energy eaters were classified as consuming ≥ 60% of energy during the first half of awake time
viii. Late night eaters were classified as eating within 2 hours of bed

Table 5: Regressions predicting metabolic health by food cravings in plausible energy reporters

Independent variable	Food cravings		
	Estimate (95% CI)	**P value**	***N***
Dependent variables			
Body composition			
BMI (kg/m^2) [a]	0.03 (0.003, 0.06)	**0.03**	*135*
Body fat (%) [a]	0.03 (-0.01, 0.07)	0.09	*134*
Waist circumference (cm) [a]	0.07 (0.02, 0.13)	**0.01**	*135*
Cardiometabolic risk			
LDL (mg/dL) [a, i]	0.04 (-0.10, 0.18)	0.59	*128*
HDL (mg/dL) [a, i]	-0.01 (-0.07, 0.06)	0.83	*128*
Total cholesterol:HDL [a, i]	0.001 (-0.003, 0.01)	0.51	*128*
Triglycerides (mg/dL) [a, i]	0.07 (-0.18, 0.33)	0.57	*128*
Glucose (mg/dL) [b, ii]	0.01 (-0.04, 0.06)	0.59	*128*
Glycated hemoglobin (%) [a, ii]	-0.002 (-0.004, 0.001)	0.11	*127*
Insulin (uIU/mL) [a]	0.004 (-0.03, 0.04)	0.83	*128*
C-reactive protein (mg/L) [a,iii]	-0.01 (-0.04, 0.02)	0.63	*128*
Systolic blood pressure (mmHg) [a, iv]	-0.03 (-0.10, 0.03)	0.28	*135*
Diastolic blood pressure (mmHg) [a, iv]	-0.04 (-0.09, 0.01)	0.15	*135*
Metabolic syndrome (%) [c]	1.00 (0.99, 1.01)	0.63	*130*

Significance set as P value less than 0.05, bolded p values indicate both significant model and dependent variable P values

Covariates: age, income, physical activity

a. Data determined by robust linear regression, estimate reported as β (95% CI)
b. Data determined by quantile regression and reported as β (95% CI)
c. Data determined by logistic regression and reported as odds ratio (95% CI)
i. additional covariate of lipid medication
ii. additional covariate of glycemic medication
iii. additional covariate of BMI
iv. additional covariate of blood pressure medication

Table 6: Regressions predicting metabolic health by food cravings in the total sample

Independent Variable	Food cravings		
	Estimate (95% CI)	**P value**	**N**
Dependent Variables			
Body composition			
BMI (kg/m^2) [a]	0.01 (-0.01, 0.04)	0.25	213
Body fat (%) [a]	0.01 (-0.0, 0.05)	0.54	209
Waist circumference (cm) [a]	0.05 (-0.002, 0.10)	0.06	213
Cardiometabolic risk			
LDL (mg/dL) [a, i]	0.05 (-0.09, 0.18)	0.50	199
HDL (mg/dL) [a, i]	-0.03 (-0.08, 0.02)	0.29	199
Total cholesterol:HDL [a, i]	0.003 (-0.0002, 0.006)	0.06	199
Triglycerides (mg/dL) [a, i]	0.16 (-0.03, 0.36)	0.10	199
Glucose (mg/dL) [b, ii]	0.01 (-0.03, 0.06)	0.57	199
Glycated hemoglobin (%) [a, ii]	-0.001 (-0.003, 0.001)	0.56	199
Insulin (uIU/mL) [a]	-0.01 (-0.04, 0.03)	0.70	200
C-reactive protein (mg/L) [a, iii]	0.0003 (-0.02, 0.02)	0.98	200
Systolic blood pressure (mmHg) [a, iv]	-0.02 (-0.07, 0.03)	0.47	213
Diastolic blood pressure (mmHg) [a, iv]	-0.01 (-0.05, 0.03)	0.49	213
Metabolic syndrome (%) [c]	1.005 (0.996, 1.01)	0.28	201

Significance set as P value less than 0.05, bolded p values indicate both significant model and dependent variable P values

Covariates: age, income, physical activity

a. Data determined by robust linear regression, estimate reported as β (95% CI)
b. Data determined by quantile regression and reported as β (95% CI)
c. Data determined by logistic regression and reported as odds ratio (95% CI)
i. additional covariate of lipid medication
ii. additional covariate of glycemic medication
iii. additional covariate of BMI
iv. additional covariate of blood pressure medication

vii. Summary and Discussion

The prevalence of overweight and obesity in the United States has risen in the past 50 years and is now widely recognized as an epidemic, with over 70% of adults faced with this condition.[155,156] This is of particular concern as excess body weight is associated with chronic disease and mortality, costing up to $210 billion dollars a year in healthcare.[157,158] However the accumulation of excess body weight is both preventable and treatable by dietary and lifestyle behavior change.[8,39]

Our lifestyles influence what we consume each day, the cumulative impact of which may result in weight gain if daily energy intake is greater than energy expenditure. Changing behaviors to promote a healthier lifestyle is currently the most promising strategy for weight loss and weight management.[8]

It is therefore imperative to understand how behavioral aspects of eating affect dietary composition, eating patterns, and how these eating behaviors are associated with both body composition and cardiometabolic risk in order to best treat the growing number of adults with excess weight. Emerging research suggests that the timing of food consumption as well as the total daily interval over which eating occurs may influence energy intake and metabolic health,[79,84,89] however no study has examined both these measures of eating timing on other measures of dietary composition in addition to metabolic health indices. Another promising behavioral target are food cravings. Research has demonstrated that food cravings may be conditioned,[18-22] although there has yet to be a study that examines if food cravings are associated with both dietary intake and metabolic health outcomes. We studied the association of eating timing and food cravings on both dietary intake and metabolic health outcomes in women with overweight and obesity.

Eating timing

We hypothesized that a shorter daily eating interval, TRE, eating earlier in the day, and not being a late night eater would be associated with more favorable dietary intake and metabolic health outcomes. Consistent with our hypothesis, a shorter daily eating interval, TRE, and not eating late at night were significantly associated with a lower energy intake, glycemic load, and eating frequency. The only significant association with early energy eaters we observed was that being an early energy eater was significantly associated with a higher carbohydrate intake compared to non-early energy eaters. However, early energy eaters and non-early energy eaters both had mean carbohydrate intake that were within the acceptable macronutrient distribution range (48%, 45% respectively, *P*=0.12), thus considered a healthy amount of carbohydrate intake.[159] We did not observe a significant association between eating timing and other measures of dietary intake. It would be noteworthy to further investigate whether the consumption of food groups and types of foods are affected by our eating timing measures. This is particularly relevant as we consume whole foods, and by only studying nutrients we are potentially missing other components of food that may be important in our understanding of diet and health.[160,161] Examining how eating timing also affects food intake will enhance our understanding of what behaviors to target in intervention aiming to promote a balanced diet, weight management and positive health outcomes.

We observed a significant association between a longer daily eating interval and greater waist circumference. This finding lends support to the inclusion of reducing daily eating interval in lifestyle interventions in order to promote healthy body composition. In our sample, we found that a longer daily eating interval was also associated with greater energy intake and may in part explain the significant positive association between daily eating interval and waist circumference. However, we did not find a significant association between TRE and waist circumference. It is possible that our definition of TRE, daily eating interval ≤11 hours, although within the window for published definitions of TRE [84,89] is not optimal for positively impacting body composition. One study that observed a reduction in waist circumference defined TRE as Ramadan fasting.[104] However, a Ramadan TRE has the daily fasting interval during the day and the eating interval during the night which poses challenges to the circadian clock and human diurnal rhythms which may result in other metabolic dysregulations.[76-78] It is also important to note that intervention studies are better able to determine causation whereas the current study was a cross-sectional analysis of typical dietary intake where there was no manipulation of behaviors and therefore causality cannot be ascertained..

A novel aspect of this analysis was the examination of daily eating interval as a continuous variable as well as TRE as a categorical variable. We found for every one hour reduction in daily eating interval there was a decrease in waist circumference (1.3 cm), daily energy intake (53 kcals), glycemic load (6 units), and eating frequency (0.3 eating occasions). Similar results were observed with TRE, although there was no significant association with waist circumference. These results may help inform effective TRE intervals and suggest that although restricting daily eating interval to 11 hours is associated with a favorable dietary intake, an even shorter eating interval may be needed to observe favorable body composition.

With regards to the distribution of energy intake within the daily eating interval, the limited research conducted on this topic has yet to identify the optimal energy distribution throughout the day for maximal health benefits. We evaluated both early energy eaters and late night eaters and found that not eating late at night was associated with more favorable dietary intake but did not influence metabolic health. In addition, early energy eaters who consumed 60% or more energy in the early half of the day did not appear to have more favorable dietary intake or metabolic health compared to non-early energy eaters. These findings suggest that the last eating occasion of the day may be more influential than the distribution of daily energy intake. More research is needed to elucidate whether there is a threshold beyond which individuals should stop eating (i.e. not eating late at night) or if in fact the distribution energy intake within an individual's daily eating interval matters in relation to the effects on health outcomes.

Food cravings

Research indicates that food cravings account for up to 11% of the variance in dietary behaviors and weight gain.[9,162] We found that food cravings were associated with dietary quality and eating patterns. Greater food cravings were associated with lower diet quality, greater eating frequency, longer daily eating interval, and a lower likelihood of having a TRE eating pattern. It is therefore possible that targeting a reduction in food cravings, may promote healthier diet quality and eating patterns and subsequently successful weight management. Future directions include implementing a weight loss study that focuses on reducing food cravings and measures changes in diet quality and eating patterns in relation to both changes in cravings and weight loss success.

Contrary to the literature, we did not observe a significant association between food cravings and total energy intake. The difference in our findings could be due to the fact that most studies evaluated total energy intake with change in food cravings following an intervention. Of the studies that examined food cravings cross-sectionally, only one study examined this relationship in adults with overweight and obesity, however, the reported correlation was weak ($r=0.21$, $P<0.05$) and the analysis did not adjust for potential confounders.[20] Additionally, food craving studies exploring dietary composition beyond energy intake predominantly do so in the craved foods, but fail to extend the effects of food cravings on the overall diet. A strength of our analysis is our examination of the relationship between food cravings to the typical daily diet, which has a greater effect on health than individual snack foods. Research is needed to further examine whether food cravings are associated with dietary composition and if there are mechanistic factors by which this association may be linked.

With regards to the effect of cravings on metabolic health, as hypothesized, food cravings were associated with less favorable measures of body composition. We observed that greater food cravings were associated with a higher BMI and waist circumference. This is especially interesting as we did not observe a significant association of food cravings with total energy intake. However, we did find that lower food cravings promote healthier eating patterns. This warrants a more in depth study of the specific contributions of cravings and dietary intake on body composition.

Very few studies have examined the association between food cravings and cardiometabolic risk factors and the findings thus far are regarding glycemic control and are not specific to adults with overweight and obesity.[139] We did not observe an association between food cravings and any of the indices of cardiometabolic risk. These findings add to the literature on food cravings and blood lipids, blood pressure, and inflammatory markers as well as glycemic measures in adults with overweight and obesity. As there is limited research in this area, it is important that future studies consider examining the impact of food cravings on cardiometabolic health.

Our study has many strengths including the correction for plausible energy reporting, examining both dietary intake and metabolic health outcomes, explored multiple measures of eating timing, and used a validated questionnaire, FCQ-T, to examine food cravings. However, there were a few limitations. This was a cross-sectional study and therefore causation could not be established. Additionally, our population, did not display elevated cardiometabolic risk despite having overweight or obesity, and therefore may have limited our ability to detect clinically significant differences for the various eating timing measures and food cravings. Future research is necessary to explore whether eating timing and food cravings affect dietary intake and cardiometabolic risk. In particular, it is important to explore the benefits of modifying these eating behaviors in individuals with cardiometabolic risk in order to better determine the impact on metabolic health.

Summary

This was the first analysis of the association between eating timing and food cravings on both dietary intake and metabolic health indices in women with overweight and obesity. Our findings suggest that restricting the daily eating interval, avoiding eating before bed, and reducing food cravings is associated with more favorable dietary intake, eating patterns, and body composition. These important findings indicate that eating timing and food cravings are viable mechanistic targets for behavioral interventions aiming to improve health and promote weight management. Our results provide evidence of the importance of a multifactorial behavior approach to weight management. Further research is imperative to understand how modifying eating timing and food cravings longitudinally influence dietary intake as well as metabolic health, and ultimately to see if these eating behaviors can promote successful weight management.

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