Compliance to a Prescribed Eating Frequency Protocol

Tracey Tran

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Marian Neuhouser

Adam Drewnowski

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Abstract

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Chair of the Supervisory Committee:

Marian Neuhouser

Nutritional Sciences

Background: Participant compliance is an important measure of study success in randomized control trials (RCTs.) However, there is a lack of literature studying participant compliance in dietary interventions, specifically eating frequency (EF) interventions. EF pattern has begun to spark interest in the field of nutrition, and calls for increased participant compliance research to ensure success of current and future EF protocols. The Frequency of Eating and Satiety Hormone Study (theFRESHstudy) is an ongoing EF RCT that provides opportune conditions to measure participant compliance to a prescribed EF protocol.

Objective: The purpose of this study is to examine participant compliance to a prescribed EF protocol in theFRESHstudy.

Design/Methods: Participants (n=30) completed two 21-day, isocaloric intervention phases in a randomly assigned order. In one treatment arm, participants ate with a low EF pattern (three eating occasions per day.) In the other arm, participants ate with a high EF pattern (six eating occasions per day.) Participants prepared and consumed their own foods using a structured meal plan and calorie (kcal) intake level provided by the study dietitian. During each intervention

phase, participants completed an online daily checklist where they reported food group choice, physical activity, sleep, appetite, and extra eating occasions (EEOs.) EEOs and food group choice for each eating occasion were the variables used to measure participant compliance. Data for EEOs and food group choice were extracted from the database, anonymized by subject ID, and transferred to a spreadsheet. Data were then reorganized with new variables to perform statistical analyses. Paired T-tests and chi-squared tests were completed using formula functions programmed within the data spreadsheet.

Results: There was minimal noncompliance in terms of EEOs (<1 EEO per person/day) and no significant differences by EF treatment arm ($p=0.44$.) Starch and fat food group choices were the primary sources of EEOs. The observed number of undereating and overeating occasions for food group choices in each treatment arm was significant ($p<0.05$.)

Conclusion: Participant compliance to theFRESHstudy protocol did not differ between low and high EF treatment arms. Continued research is warranted to analyze participant compliance to future EF nutrition interventions.

Keywords: eating frequency, compliance, eating occasion, food choice

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Tracey Tran

Chair of the Supervisory Committee:
Marian Neuhouser, PhD, RD
Nutritional Sciences

Introduction

Eating Frequency Research

According to the National Health and Nutrition Examination Survey (NHANES), the United States has experienced a shift from low eating frequency (EF) to high EF in the past four decades (Dashti and Mogensen, 2016). Low EF refers to consumption of three or fewer meals per day and high EF refers to intake of six to ten meals per day. This transition may be related to an assumption that a high EF pattern could enhance compliance to energy restriction, leading to decreased appetite and consequent weight loss (Cameron et al., 2010; Raynor et al., 2015). The shift may also be attributed to increased breakfast skipping and decreased family meals, both of which are correlated with increased snacking occasions (Jones, 2018; Leech et al., 2015; Murakami and Livingstone, 2016). Upon closer examination, there is little evidence aside from anecdote and observational studies suggesting that high EF is associated with weight regulation or improved health outcomes within a healthy, adult ($\geq$ 18 years) population (Dashti and Mogensen, 2016; Ohkawara et al., 2013; Raynor et al., 2015). Recent research suggests that high EF may be correlated to unwarranted weight gain, sleep apnea, later meal times, and disordered eating (Dashti and Mogensen, 2016; Perrigue et al., 2015). In contrast, there is also literature that suggests a low EF pattern is correlated with adverse health events, such as obesity, hypercholesterolemia, decreased glucose tolerance, and ischemic heart disease (Dashti and Mogensen, 2016; Hutchison & Hilbronn, 2016). In order to disentangle these inconsistencies, increased experimental research is needed to analyze the physical, clinical, and biochemical impacts of each EF pattern.

The Frequency of Eating and Satiety Hormone Study (theFRESHstudy) is one such intervention that is delving into the complexities of EF. The FRESHstudy is an ongoing

randomized, cross-over clinical trial aimed at comparing the effects of low versus high EF on systemic inflammation, production of adipokine, and appetite/satiety in normal weight, overweight/obese adult males and females (NCT02392897.) Each participant is asked to complete two, 21-day isocaloric phases in a randomly assigned order: one of which is low EF (three eating occasions per day) and the other of which is high EF (six eating occasions per day). Highly structured eating plans are provided, but participants are free-living and are expected to prepare their own foods, maintain usual physical activity, and uphold a stable weight throughout the study. Throughout the duration of each phase, participants are asked to report their daily food intake, "perceived appetite", and "extra eating occasions" via an online system. At baseline and endpoint of each phase, participants are assessed for blood-based inflammatory biomarkers, appetite/satiety, and adipokines.

TheFRESHstudy provides an optimal setting for measuring participant compliance to a specific EF pattern. As the study requires participants to be free-living, the researchers have less control over actual energy intake. Measuring compliance in theFRESHstudy would not only improve upon study outcomes, but would also fill in a gap in current EF compliance research that could further establish a groundwork for future EF intervention trials and clinical recommendations.

Dietary Compliance Research

The success of any randomized control trial is highly dependent upon participant compliance. Evaluation of compliance is an essential component of experimental studies, as making incorrect assumptions about participant adherence to protocol may distort research outcomes. Additionally, increased dietary compliance serves as a foundation for more effective prevention and management of chronic diseases (Desroches et al., 2013). According to the World

Health Organization (WHO), non-adherence rates to disease management are between 50% and 80% (Desroches, et al., 2013). Studies have suggested that adherence to prescribed dietary plan, rather than the dietary plan itself, had a greater impact on desired health outcomes (Desroches et al., 2013). This suggests that there is clinical significance in focusing on compliance for future nutrition interventions.

The literature on dietary compliance, let alone EF compliance, is scarce. Upon conducting a literature search on PubMed, Embase, and Web of Science databases, 82,620 articles and reviews between the years 2007-2017 were retrieved with the search terms, "((eating frequency) OR (meal frequency)) AND ((compliance) OR adherence)), all of which had little to no relevance to this study question. There is a lack of research surrounding dietary compliance, and those that have been published are predominantly focused on dietary patterns rather than on EF. Although the current literature on dietary compliance does not directly apply to EF pattern, it provides loose guidance for the planning of this proposed study.

The published literature identifies three primary measures of compliance to a nutrition protocol: (1) self-reported food assessment, (2) comparison of the consumed diet to the prescribed dietary plan, and (2) objective measures. Self-reported assessment methods include 24-hour recalls, food diaries, food frequency questionnaires (FFQs), and diet history (Desroches et al., 2013; Greenberg et al., 2009). Methods of self-reported adherence and food records of excess food intake are often utilized to compare consumed diet to the prescribed dietary plan. Finally, objective measures include bioassays and measurement of dietary biomarkers, (Desroches et al., 2013).

Self-reported food assessment was the most commonly utilized measure of compliance, as it tends to be direct, inexpensive and simple (Desroches et al., 2013.) Although susceptible to

reporting and social desirability biases, self-report can be statistically controlled by using multiple measures of compliance (Descroches et al., 2013). Dietary biomarkers were less utilized in studies measuring dietary compliance, as the focus tended to be on specific nutrients rather than on overall dietary pattern or eating frequency (Desroches et al., 2013).

Summary of Background

The lack of literature surrounding EF compliance highlights the novelty and significance of this research topic. This study offers innovative insight that may guide future research on EF and satiety, appetite, and other nutrition-related markers. Given the societal trend toward high EF in the U.S. despite its inconclusive health outcomes, it is critical to examine the influence of EF compliance in order to better provide clinical guidance for individuals in a healthy, adult population.

Thesis Hypothesis

The purpose of this study is to examine the impact of EF on participant compliance in the context of theFRESHstudy, and to test the hypothesis that the high EF arm is associated with greater noncompliance. Compliance will be measured using variables of self-reported "extra eating occasions," (per study protocol) and undereating/overeating occasions, both of which indicate the inability to adhere to a prescribed meal plan.

Thesis Question

How does participant compliance vary between a low eating frequency protocol and a high eating frequency protocol?

Methods

Participants

Participants were recruited for theFRESHstudy with flyers, promotional material and online advertisements managed by the University of Washington and the Fred Hutchinson Cancer Research Center (FHCRC.) Flyers and promotional materials were distributed at the University of Washington, the FHCRC, farmers markets, neighborhood block parties, local events, and other various locations in Seattle, Washington (WA.) Online advertisements were posted on email newsletters and social networking sites. The office for minority recruitment at the FHCRC were utilized to assist with recruitment.

Eligible participants were normal, overweight, and obese males and females [body mass index (BMI) = 18.5 – 24.9 kg/m^2 and 28.0 – 40.0 kg/m^2,] ages 18-50 years and living in Seattle, WA. Participants with a BMI greater or equal to 40 kg/m^2 were excluded because of the greater likelihood of obesity-related disease states and abnormal levels of biomarkers. Other exclusion criteria include the presence of diseases requiring dietary modification, including physician diagnosed cardiovascular disease or diabetes mellitus, use of medications that may impact study results including non-steroidal anti-inflammatory drugs (NSAIDS), abnormal fasting glucose (>100 mg/dL), history of disordered or restrained eating and severe food restrictions. Participants received $300.00 compensation for partaking in the study.

theFRESHstudy Procedures

All experimental protocols were approved by the Institute Review Office at the FHCRC. Potential participants were required to pass an online eligibility screening that consisted of a questionnaire and an in-person fasting blood glucose test. The questionnaire asked about health history, current medications, height and weight. The initial screening also included an eating

disorders/restrained eating screener. Eligible participants were then invited to attend a Screening Visit at the FHCRC to provide written informed consent, and take a finger prick test to assess fasting blood glucose. Participants whose fasting blood glucose was >100 mg/dL were not eligible for the study but thanked for their interest. Participants with a fasting blood glucose <100 mg/dL were asked to sign a second informed consent to participate in the dietary intervention.

Each participant completed two 21-day, isocaloric intervention phases, with a 14-day washout period between treatment arms. The order of conditions was randomized using a computer system developed by a biostatitian at the FHCRC. The two intervention phases were low EF (three eating occasions per day) and high EF (six eating occasions per day.) Highly structured eating plans were provided, but participants were considered free-living and were expected to purchase and prepare their own foods. Eating plans were based on pre-calculated food choices for a variety of energy needs (1200-3000 kcal) to provide 100% ($\pm$ 10%) of daily energy needs for weight maintenance and around 90% of dietary reference index (DRI) for required and essential nutrients. Similar to the Academy of Nutrition and Dietetics Food Exchange System, food choices were defined as servings of study food groups, e.g. starch, fruit, milk, vegetables, protein and fat, allotted for each meal and day from which participants planned their meals (Russolillo-Femenias et al., 2017.) For instance, a participant prescribed with a 2000 kcal meal plan would aim to meet nine starch, five fruit, two milk, four vegetable, eight protein and six fat food choices in a given day. These food choices would be distributed throughout the day according to high or low EF treatment arm.

Participants were required to attend four Clinic Visits at the FHCRC Prevention Center at day one (baseline) and day 21 (endpoint) of each phase. The baseline appointment included an extensive meeting with study staff to go over the study protocol. The endpoint appointment

included an appetite testing session during which participants report hunger, desire to eat, fullness, thirst, nausea and food cravings every 30 minutes. At both the baseline and endpoint appointments, anthropometric measurements and fasting blood draws were obtained from each participant.

For each intervention phase, participants completed a daily online diet checklist where they reported food selection, amount and type of physical activity, sleep, and appetite. Internet-based mobile messaging was used to coordinate text messaging, appointment reminders, and various participant surveys. Participants received a daily text message reminder to complete their checklist, and were able to complete the checklist with their smart phones, tablets or computers. In addition to these digital reminders, the study team reached out to participants who had difficulty adhering to the study protocol and worked with them to manage obstacles that stood in the way of intervention completion. For this report, only data on extra eating occasions (EEO) and under- and overeating occasions will be used.

Extra Eating Occasions

The primary variable used to measure participant compliance was self-reported extra eating occasions (EEOs.) At the end of the daily checklist, participants were asked, “Did you have any additional eating or drinking occasions today?” If the participant selected, “yes,” they were prompted, “Please briefly describe the time(s), type and amount of food and beverages you had at your additional eating occasions today.” The type and amount of these extra food and beverages were re-coded to match the study-specified food choice groups. A single EEO was defined as one or more reported food choice(s.) Participant responses to this question were collected for each day of each treatment arm and stored in the study database using RedCap®.

Data Management: Extra Eating Occasions

The data were organized in Excel®, with each food choice category as a column heading. The food composition of each reported EEO was recorded as a numerical value underneath the corresponding food choice column. For instance, if a participant reported consuming an EEO that consisted of two "fat" food choices, a "2" would be indicated under the "Fat" column. A "0" in all six food choice columns implied that an EEO was not consumed for that day. A column entitled, "Total EEO," was added next to the food choice columns to quantify the total EEO in each day. In addition, a row entitled, "Total EEO Food Choices," was added beneath the completion of each intervention phase. This row summed the number of food choices the participant consumed in all of the EEOs during that particular treatment arm. The intersection between the, "Total EEO," column and the, "Total EEO Food Choices," row represented the total number of the EEOs a participant consumed throughout the specified treatment arm, irrespective of food choice (Figure 1). This process was repeated twice for each participant, one for the high EF arm and one for the low EF arm.

Subject ID	Event Name	Starch	Fruit	Milk	Vegetable	Protein	Fat	**Total EEO**
1	LowEFDay1	0	0	0	0	0	0	0
1	LowEFDay2	0	0	0	0	0	0	0
1	LowEFDay3	0	0	0	0	0	0	0
1	LowEFDay4	0	0	0	0	0	0	0
1	LowEFDay5	0	0	0	0	0	0	0
1	LowEFDay6	0	0	0	0	0	0	0
1	LowEFDay7	0	1	0	0	0	0	1
1	LowEFDay8	0	0	0	0	0	0	0
1	LowEFDay9	0	0	0	0	0	0	0
1	LowEFDay10	1	0	0	0	0	2	3
1	LowEFDay11	0	0	0	0	0	0	0
1	LowEFDay12	3	0	0	0	0	1	4
1	LowEFDay13	0	0	0	0	0	0	0
1	LowEFDay14	0	0	0	0	0	0	0
1	LowEFDay15	0	0	0	0	0	0	0
1	LowEFDay16	2	0	0	0	0	2	4
1	LowEFDay17	0	0	0	0	0	0	0
1	LowEFDay18	0	0	0	0	0	0	0
1	LowEFDay19	0	0	0	0	0	0	0
1	LowEFDay20	0	0	0	0	0	0	0
1	LowEFDay21	0	0	0	0	0	0	0
Total EEO Food Choices		6	1	0	0	0	5	12

Figure 1: Sample Participant-reported Extra Eating Occasions (EEO) during Low Eating Frequency (EF) Arm

Once all the totals were calculated, a table was generated to consolidate the data. The table reported each participant's total EEOs for both treatment arms. EEO means were also calculated. Finally, the difference between the high EF EEOs and the low EF EEOs were calculated for data analysis (Table 3; Appendix A).

As a secondary analysis of EEO, the distribution of food choices in each EEO was recorded in a table, split by EF intervention phase. One side of the table displayed the total number of food choices each participant consumed during the low EF arm. The same was repeated for the high EF arm (Table 4; Appendix B). These data were graphically displayed to

visually examine the general food composition of EEOs and to explore if the amount of food choices varied between treatment arms (Figure 4).

Undereating and Overeating Occasions

The secondary variable to measure participant compliance was undereating and overeating occasions. Under- and overeating occasions were defined as any deviation in food choices from those prescribed in each participant's eating plan. When participants recorded their meals in the online daily checklist, they were asked to, "Select the number of choices of each food you had," during that meal. The food choices reported were compared to those in their prescribed kcal plan to determine undereating and overeating occasions.

Data Management: Undereating and Overeating Occasions

The raw data listed the number of food choices in each eating occasion for every day of the treatment arm. For instance, six "fat" food choice columns were present for all participants in the high EF treatment arm when the protocol required consumption of six eating occasions per day. Participants' daily caloric (kcal) goal were also indicated in the raw data (Table 2). While most participants maintained one kcal goal throughout the study, some participants had to switch their prescribed eating plan midway through the study to appropriately meet their energy requirements for weight maintenance.

The raw data were divided into two separate Excel® documents, one for each EF intervention phase. Individual spreadsheet tabs were formed within each document and divided by kcal goal, ranging from 1600-2600 kcal. The data were transferred to the corresponding spreadsheet according to EF arm and prescribed kcal goal. The data for participants who switched their prescribed eating plan within an intervention phase were grouped into the kcal

goal that was initially prescribed to the participant for clarity, although the change in kcal goal was noted in gray-colored text.

A column was added next to each food choice category to calculate the daily total food choice, e.g. a "Total Daily Fat" column was added after the three columns of starch food choices for participants in the low EF arm. In addition, a row was added beneath the completion of each intervention phase labeled, "Participant Total," to determine the total number of food choices consumed by the participant for the entire treatment arm. This process was repeated for each food choice and EF treatment arm (Figure 2).

Once the total daily food choices were summed for each participant, undereating and overeating occasions were coded by text color. Undereating occasions were noted in red-colored font and overeating occasions were distinguished in blue-colored font. Both under- and overeating occasions were determined by comparing participant consumption to the researchers' pre-calculated food choice for each kcal goal (Table 2). To further distinguish between undereating and overeating occasions, "Undereating Occasions" and "Overeating Occasions" columns were added next to each "Total Daily [food choice]" column. In these columns, any type of noncompliance from the prescribed food choice was denoted with a "1" (Figure 2.)

Subject ID	Event Name	1st fat	2nd fat	3rd fat	4th fat	5th fat	6th fat	Total Daily Fat	Undereating Occasions	Overeating Occasions	Kcal goal
1	HighEFDay1	1	1	1	1	1	1	**6**			2400
1	HighEFDay2	1	1	1	1	1	1	**6**			2400
1	HighEFDay3	1	1	1.5	1.5	0	2	**7**		**1**	2400
1	HighEFDay4	0	1	1.5	1	1	1	**5.5**	**1**		2400
1	HighEFDay5	1	1	1	1	1	1	**6**			2400
1	HighEFDay6	1	1	1	1	1	1	**6**			2400
1	HighEFDay7	1	1	1	1	1	1	**6**			2400
1	HighEFDay8	1	1	1	1	0	3	**7**		**1**	2400
1	HighEFDay9	1	1	1	1	1	1	**6**			2400
1	HighEFDay10	1	1	1	1	1	1	**6**			2400
1	HighEFDay11	1	1	0	0	1	2	**5**	**1**		2400
1	HighEFDay12	1	1	1	1	1	1	**6**			2400
1	HighEFDay13	1	1	1	1	1.5	1.5	**7**		**1**	2400
1	HighEFDay14	1	1	1	1	1	1	**6**			2400
1	HighEFDay15	1	1	1	1	1	1	**6**			2400
1	HighEFDay16	1	1	1	1	1	1	**6**			2400
1	HighEFDay17	1	1	1	1	1	1	**6**			2400
1	HighEFDay18	1	1	1	1	1.5	1	**6.5**		**1**	2400
1	HighEFDay19	1	1	1	1	1	1	**6**			2400
1	HighEFDay20	1	1	1	1	1	1	**6**			2400
1	HighEFDay21	1	1	1	1	1	1	**6**			2400
Participant Total		**20**	**21**	**21**	**20.5**	**20**	**25.5**	**128/126**	**2/21**	**4/21**	

Figure 2: Sample Participant Recorded Food Choices for Fat during High Eating Frequency (EF) Arm.
[Red indicates undereating occasions for 2400 kcal goal Blue indicates overeating consumption for 2400 kcal goal.]

The total number of undereating and overeating occasions was summed and consolidated in a separate Excel® spreadsheet (Figure 3). In this spreadsheet, the total number of prescribed food choices was calculated for each participant. For instance, Participant 1 was assigned to a 2400 kcal goal which allots to 10 starch food choices per day (Table 2.) As Participant 1 completed the treatment arm in 21 days, the value "210" was added to the "Total Daily Starch" column (Figure 3). This process was repeated for each participant. The values in the "Total Daily Starch," "Undereating Occasions," and "Overeating Occasions" were summed for all 30 participants. The summed value of "Undereating Occasions" was subtracted from the summed value of "Total Daily Starch" to determine the observed number of undereating occasions. Similarly, the summed value of "Overeating Occasions" was added to the summed value of "Total Daily Starch" to determine the observed number of overeating occasions (Figure 3). The same process was completed for the high EF treatment arm. The final values of observed undereating and overeating occasions were utilized for data analysis within the Excel® Spreadsheet (Figure 3).

subject_id	Total Daily Starch (prescribed by kcal goal)	Undereating Occasions	Overeating Occasions
1	210	5	1
2	180	14	3
3	210	19	2
4	168	2	17
5	210	0	0
6	210	0	12
7	210	12	0
8	168	0	0
9	168	1	5
10	157	14	1
11	210	0	2
12	168	1	1
13	147	0	3
14	210	3	0
15	252	21	0
16	147	1	0
17	147	9	0
18	168	6	0
19	168	4	1
20	147	6	2
21	184	1	0
22	147	9	6
23	147	1	3
24	147	0	0
25	252	1	0
26	220	1	2
27	168	1	9
28	168	1	3
29	176	4	6
30	252	1	1
Totals	5516	138	80
Observed Eating Occasions		**5378**	**5596**

Figure 3: Observed Starch Food Group Choices for all Participants in the Low Eating Frequency (EF) Arm

Compliance Data Analysis

Prior to analysis, the data were inspected to determine missing values and to examine the distribution. The primary goal of data analysis was to test if and how participant compliance differed between the low EF treatment arm and the high EF treatment arm

Data analyses were performed using formula functions in Microsoft Excel 2016®. A two-tailed T-test was conducted to analyze EEO as a primary indicator of participant compliance. A chi-squared test was performed to test for proportions of undereating and overeating occasions. Both statistical formulas were used to determine p-values for significance, which was set at $p<0.05$.

Results

The results are based on data from participants who completed both intervention phases of theFRESHstudy protocol by March 31, 2018. A total of 30 participants (10 males, 20 females) completed both intervention phases by the assigned date. On average, participants were 32.8 years of age, with a mean height of 168.9 cm, weight of 69.6 kg, and 24.4 kg/m^2. The following races and ethnicities were represented by the study population: Caucasian (66.7%,) Asian (26.7%,) Hispanic/Latino (13.3%,) and Black/African American (3%.) Two participants (6.7%) identified themselves as more than one race (Table 1).

A two-tailed t-test was conducted to assess the mean differences in reported EEO between the low EF arm and the high EF arm. There was minimal noncompliance (< 1 EEO per person per day) and no significant differences by treatment arm (p = 0.44) (Table 3). The results indicated that in both EF treatment arms, starch and fat food groups were the primary sources of EEOs reported by participants who completed the study protocol (Table 4; Figure 4).

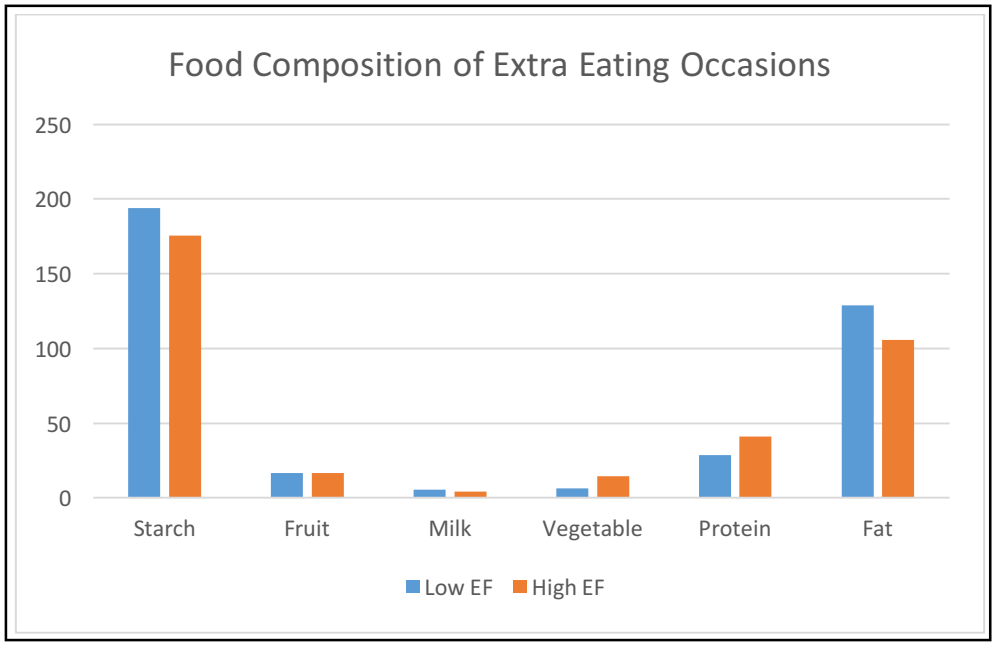

Figure 4: Food Composition of Extra Eating Occasions (EEO) for Both Eating Frequency (EF) Treatment Arms

The chi-squared analysis revealed that the observed number of undereating occasion and overeating occasions were significant compared to the expected number of eating occasions in both EF treatment arms (low EF treatment arm: $p=0.02$; high EF treatment arm: $p < 0.001$) (Table 5; Table 6; Appendix C; Appendix D).

Discussion

Key Findings

The purpose of this study was to observe the differences, if any, between participant compliance to a low EF versus high EF protocol. The analysis of EEOs revealed that there are no significant differences between reported EEOs in the low EF treatment arm versus those in the high EF treatment arm. This finding suggests that both EF treatment arms had similar degrees of participant compliance, when utilizing EEOs as the primary variable of compliance. Additionally, the average number of EEOs was minimal (<1 EEO/person/meal) and participants who consumed EEOs were more inclined to choose foods in starch and fat food groups for both EF protocols.

The secondary analysis aimed to understand how compliance to the prescribed number of food choices differed between low versus high EF patterns. The finding revealed that observed undereating and overeating occasions were significant (low EF: $p = 0.02$; high EF: $p<0.001$) in both treatment arms. Echoing the primary analysis of EEO, this finding suggests that participant compliance did not differ between EF protocols. Overall, the results indicate that participant compliance did not vary between EF patterns.

These findings cannot be compared and validated by other studies, as there is an overall lack of literature on EF compliance. Consequently, this study provides foundational material to inform the development of future EF protocols. The findings may also guide future registered dietitians in making clinical recommendations related to EF frequency, as adherence to dietary recommendations is an important component to improved health outcomes.

Strengths

The study has several notable strengths. This is the first study of its kind to measure participant compliance to a prescribed EF protocol. Second, the study investigated two variables of compliance. This allowed for multiple angles to be taken to measure self-reported data to the protocol. Third, participants were randomized into treatment groups. This design reduced the possibility of confounding by independent variables not accounted for. Additionally, participants reported that the accessibility and accountability of the daily online checklist were effective reminders of study engagement. Finally, participants reported that the use of food group exchanges made it simple to navigate their eating plans as free-living participants. This suggests that the collected self-reported data reflected an accurate depiction of participants' daily intake.

Limitations

The analysis reflected a small sample (n=30) of healthy adults living in Seattle, WA and cannot be generalizable to the greater population of adults living outside the study territory. In addition to a small study population, each EF protocol had a short duration of 21 days, on average. Thus, participant compliance to theFRESHstudy protocol does not reflect prolonged use of each EF pattern.

The study was prone to certain biases and confounding factors. The study may have contained reporting and recall biases, as both the primary and secondary variables of compliance were based on self-report. Finally, participants who did not complete both EF treatment arms were excluded from data collection, which may have subjected the study to confounding factors.

Implications/ Future Direction

In the context of theFRESHstudy, the findings imply that compliance to a prescribed number of food choices has a significant impact on participant compliance, compared with

compliance to the prescribed number of eating occasions. Future research is urged to validate these outcomes with future data points as theFRESHstudy continues. Additionally, it would be useful to compare the self-reported data in this report to objective measures and biological markers of compliance.

Beyond the scope of theFRESHstudy, this report provides novel insight on participant compliance to a prescribed eating frequency protocol, where there is little literature available. As exploration of EF pattern gains momentum, future participant compliance studies are warranted to improve research outcomes.

Tables

Table 1: Characteristics of the Study Population

		All Participants (n=30)	Males (n=10)	Females (n=20)
Age in yrs (μ,σ)		32.8 (7.3)	36.5 (8.5)	31.4 (6.3)
Height in cm (μ,σ)		168.9 (8.8)	178.2 (8.1)	164.2 (4.1)
Weight in kg (μ,σ)		69.6 (15.7)	79.2 (17.3)	64.8 (15.7)
BMI in kg/m^2 (μ,σ)		24.4 (5.0)	24.9 (5.2)	24.1 (5.0)
Race/Ethnicity	**Hispanic/Latino (n,%)**	4 (13.3)	1 (10)	3 (15)
	Asian (n,%)	8 (26.7)	3 (15)	5 (25)
	Black/African American (n,%)	1 (3)	1 (10)	0 (0)
	Caucasian (n,%)	20 (66.7)	6 (60)	14 (70)
	More than One Race (n,%)	2 (6.7)	1 (10)	1 (5)

Table 2: Prescribed Caloric Intake Levels and Corresponding Daily Food Choices

Prescribed kcal	Starch	Fruit	Milk	Vegetables	Protein	Fat
1200	6	3	1	2	5	3
1400	7	3	2	2	5	4
1600	7	4	2	3	6	4
1800	8	4	2	4	8	5
2000	9	5	2	4	8	6
2200	10	5	2	4	9	7
2400	10	4	4	4	12	6
2600	12	4	4	4	12	7
2800	12	6	4	4	12	7
3000	16	4	4	5	13	7

Table 3: Difference in Extra Eating Occasions (EEO) between Treatment Arms

	EEO for High EF (EEO/person/day)	EEO for Low EF (EEO/person/day)
Totals μ (σ)	0.56 (0.83)	0.68 (1.2)
	t-statistic	**p-value**
	-0.79	0.44

Table 4: Food Composition of Extra Eating Occasions (EEO) per Treatment Arm

	Low EF EEO/person/day						High EF EEO/person/day					
	Starch	**Fruit**	**Milk**	**Vegetable**	**Protein**	**Fat**	**Starch**	**Fruit**	**Milk**	**Vegetable**	**Protein**	**Fat**
Totals (μ, σ)	0.3 (0.5)	0 (0.1)	0 (0)	0 (0)	0 (0.1)	0.2 (0.4)	0.3 (0.4)	0 (0)	0 (0)	0 (0.1)	0.1 (0.2)	0.2 (0.3)

Table 5: Observed vs. Expected Eating Occasions for Low Eating Frequency (EF) Arm

Observed Eating Occasions*

	Starch	Fruit	Milk	Vegetable	Protein	Fat	Total
Undereating Occasions	5378	2405	1416	2225	5291	3212	19927
Overeating Occasions	5596	2673	1667	2490	5609	3502	21537
Total	10974	5078	3083	4715	10900	6714	41464

Expected Eating Occasions

	Starch	Fruit	Milk	Vegetable	Protein	Fat	Total
Undereating Occasions	5273.9	2440.4	1481.6	2266	5238.3	3226.7	19927
Overeating Occasion	5700.1	2637.6	1601.4	2449	5661.6	3487.3	21537
Total	10974	5078	3083	4715	10900	6714	41464

Chi-square Statistic	**p-value**
13.1	0.0223

**Observed undereating occasions were calculated by subtracting undereating occasions from the prescribed number of food choices. Observed overeating occasions were calculated by adding overeating occasions to the prescribed number of food choices. The chi-squared statistic was computed using these numbers as proportions.*

Table 6: Observed vs. Expected Eating Occasions for High Eating Frequency (EF) Arm

Observed Eating Occasions*

	Starch	Fruit	Milk	Vegetable	Protein	Fat	Total
Undereating Occasions	5422	2428	1497	2238	5480	3253	20318
Overeating Occasions	5751	2777	1824	2580	5773	3610	22315
Total	11173	5205	3321	4818	11253	6863	42633

Expected Eating Occasions

	Starch	Fruit	Milk	Vegetable	Protein	Fat	Total
Undereating Occasions	5324.8	2480.6	1582.7	2296.2	5362.9	3270.8	20318
Overeating Occasions	5848.2	2724.4	1738.3	2521.8	5890.1	3592.2	22315
Total	11173	5205	3321	4818	11253	6863	42633

Chi-squared Statistic	**p-value**
22.3	$p<0.001$

**Observed undereating occasions were calculated by subtracting undereating occasions from the prescribed number of food choices. Observed overeating occasions were calculated by adding overeating occasions to the prescribed number of food choices. The chi-squared statistic was computed using these numbers as proportions.*

References

1. Cameron, J.D., Cyr, M., Doucet, E. (2009) Increased meal frequency does not promote greater weight loss in subjects who were prescribed an 8-week equi-energetic energy-restricted diet. *British Journal of Nutrition*. 103(8): 1098-1101.
2. Dashti, H.S. and Mogensen, K.M. (2016) Recommending Small, Frequent Meals in the Clinical Care of Adults. *Nutrition in Clinical Practice*. doi: 10.1177/0884533616662995
3. Desroches, S., Lapointe, A., Ratte, S., Gravel, K., Legare, F., Thirsk, J. (2013) Interventions to enhance adherence to dietary advice for preventing and managing chronic diseases in adults. *Cochrane Database of Systematic Reviews*. 2(CD008711). doi: 10.1002/14651858.CD008722.pub2.
4. Greenberg, I., Stampfer, M.J., Schwarzfuchs, D., Shai, I. (2009) Adherence and Success in Long-Term Weight Loss Diets: The Dietary Intervention Randomized Controlled Trial (DIRECT). *The Journal of the American College of Nutrition*. 28(2):159-168.
5. Hutchison, A.T. and Heilbronn, L.K. (2016) Metabolic impacts of altering meal frequency and timing – Does when we eat matter? *Biochimie* 124:187-197.
6. Jones, B.L. (2018) Making time for family meals: Parental influences, home eating environments, barriers and protective factors. *Physiology & Behavior*. doi:10.1016/j.physbeh.2018.03.035.
7. Kristensen, M., Pelletier, X., Ross, A.B., Thielecke, F. (2017) A High Rate of Non-Compliance Confounds the Study of Whole Grains and Weight Maintenance in a Randomised Intervention Trial – The Case for Greater Use of Dietary Biomarkers in Nutrition Intervention Studies.
8. Leech, R.M., Worsley, A., Timperio, A., McNaughton, S.A. (2015) Understanding meal patterns: definitions, methodology and impact on nutrient intake and diet quality. *Nutrition Research Reviews* 28: 1-21.
9. Murakami, K. and Livingstone, B.E. (2016) Associations between Meal and Snack Frequency and diet Quality in US Adults: National Health and Nutrition Examination Survey 2003-2012. *Journal of the Academy of Nutrition and Dietetics*. 116 (7):1101-1113.
10. Ohkawara, K., Cornier, M.A., Kohrt W.M. Melanson, E.L. (2013) Effects of increased meal frequency on fat oxidation and perceived hunger. *Obesity (Silver Spring)*. 21(2):336-342. doi: 10.1002/oby.20032
11. Perrigue, M.M., Drewnowski, A., Wang, C-Y., Neuhouser, M.L. (2015) Higher Eating Frequency Does Not Decrease Appetite in Healthy Adults. *The Journal of Nutrition*. 146(1): 59-64. doi: 10.3945/jn.115.216978
12. Raynor, H.A., Goff, M.R., Pool S.A., Chen, G. (2015) Eating Frequency, Food Intake, and Weight: A Systematic Review of Human and Animal Experimental Studies. *Frontiers in Nutrition*. Doi: 10.3389/fnut.2015.0038.
13. Russolillo-Femenias, G., Menal-Puey, S., Alfredo Martinez, J., and Iva Marques-Lopes. (2017) A Practical Approach to the Management of Micronutrients and Other Nutrients of Concern in Food Exchange List for Meal Planning. *Journal of the Academy of Nutrition and Dietetics*. Published online: October 5, 2017.

Appendices

Appendix A: Difference in Extra Eating Occasions (EEO) between Treatment Arms - All

Subject ID	EEO Mean for High EF (EEO/day)	EEO Mean for Low EF (EEO/day)	Difference [EEO (High EF) - EEO (Low EF)
1	0.26	0.57	-6.5
2	0.65	0.64	3.5
3	3.4	3.8	-10
4	2.07	1.4	14
5	0	0	0
6	0.12	0.43	-6.5
7	0	0.1	-2
8	0	0	0
9	1.1	0.6	10.5
10	0.76	0.43	7
11	0.29	0.31	0.5
12	0.12	0.05	1.5
13	0.07	0.14	-1.5
14	0.17	0.38	-4.5
15	0	0	0
16	0	0	0
17	0.57	0	12
18	0	0	0
19	0.24	1.5	-27.2
20	2.23	3.9	-32.5
21	0	0	0
22	0.48	1.4	-18.5
23	0.83	0.14	14.5
24	0.21	0.21	0
25	0.36	0.43	1
26	1.86	0	41

27	1	3.91	-78.7
28	0	0	0
29	0	0	0
30	0	0.04	-1
Mean Totals (σ)	0.56 (0.83)	0.68 (1.2)	

t-statistic = -0.79

p-value = 0.44

Appendix B: Food Composition of Extra Eating Occasions (EEOs) per Treatment Arm – All

	Low EF (EEO μ/day)						High EF (EEO μ/day)					
Subject ID	**Starch**	**Fruit**	**Milk**	**Vegetable**	**Protein**	**Fat**	**Starch**	**Fruit**	**Milk**	**Vegetable**	**Protein**	**Fat**
1	0.3	0	0	0	0	0.2	0.2	0	0	0	0	0
2	0.4	0.1	0	0	0	0.2	0.2	0.1	0	0.1	0.1	0.2
3	1.9	0.1	0	0.1	0.5	1.3	1.3	0.1	0	0.1	0.9	0.9
4	0.7	0.2	0	0.1	0.1	0.2	1	0.1	0	0.2	0.3	0.5
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0.3	0	0	0	0	0	0.1	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0.2	0	0	0	0	0.3	0.5	0	0	0	0	0.5
10	0.3	0	0	0	0.2	0	0.5	0	0	0	0	0.3
11	0.1	0	0	0	0.2	0	0.2	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0.1	0	0	0	0.1	0	0.1	0	0	0	0	0
14	0.1	0	0	0	0	0.2	0	0.1	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0.4	0	0	0	0	0.1
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0.7	0.1	0	0	0	0.7	0.1	0	0	0	0	0.1
20	1.8	0.1	0	0	0	2	1.1	0	0	0	0	1.1
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0.5	0.1	0	0	0	0.45	0.2	0	0	0	0	0.2
23	0	0	0	0	0	0.1	0.3	0.1	0	0	0	0.3
24	0.1	0	0	0	0	0	0.1	0	0	0	0	0
25	0.3	0	0.1	0	0	0	0.1	0.1	0	0	0	0
26	0	0	0	0	0	0	0.9	0.1	0	0.2	0.4	0.2
27	1.4	0	0	0	0.1	0.4	0.7	0	0	0	0	0.3

28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0
Total μ (σ)	0.3 (0.5)	0 (0)	0 (0)	0 (0)	0 (0.1)	0.2 (0.4)	0.3 (0.4)	0 (0)	0 (0)	0 (0.1)	0.1 (0.2)	0.2 (0.3)

Appendix C: Chi-Squared Analysis for Low Eating Frequency (EF) Treatment Arm

	Starch	Fruit	Milk	Vegetables	Protein	Fat
Undereating Occasions (X^2)	2.1	0.5	2.9	0.7	0.5	0.1
Overeating Occasions (X^2)	1.9	0.5	2.7	0.7	0.5	0.1

Chi-square statistic	**p-value**
13.1	$p < 0.02$

Appendix D: Chi-Squared Analysis for High Eating Frequency (EF) Treatment Arm

	Starch	Fruit	Milk	Vegetables	Protein	Fat
Undereating Occasions (X^2)	1.8	1.1	4.6	1.5	2.5	0.1
Overeating Occasions (X^2)	1.6	1.0	4.2	1.3	2.3	0.1

Chi-square statistic	**p-value**
22.3	$p < 0.001$