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ORIGINAL ARTICLE

Epidemiology/Genetics

A hypothetical intervention of the timing of dietary intake on weight and body composition after initial weight loss

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Abstract

Objective: This study estimated the effect of hypothetical interventions of higher and lower frequency of breakfast and post-dinner snack consumption (breakfast consumption 0-4 vs. 5-7 times/week and post-dinner snack consumption 0-2 vs. 3-7 times/week) on changes in body weight and composition over 18 months after a successful 6-month standard behavioral weight-loss program.

Methods: The study analyzed data from the Innovative Approaches to Diet, Exercise and Activity (IDEA) study.

Results: If all participants consumed a breakfast meal 5 to 7 times/week over 18 months, they would have regained 2.95 kg of body weight on average (95% CI: 2.01 to 3.96), which is 0.59 kg (95% CI: −0.86 to −0.32) lower than if all participants consumed breakfast 0 to 4 times/week. If all participants consumed a post-dinner snack 0 to 2 times/week, they would have regained 2.86 kg of body weight on average (95% CI: 0.99 to 5.25), which is 0.83 kg (95% CI: −1.06 to −0.59) lower than if all consumed a post-dinner snack 3 to 7 times/week.

Conclusions: Regular breakfast consumption and minimizing post-dinner snacking may modestly mitigate weight and body fat regain over 18 months after initial weight loss.

INTRODUCTION

The primary challenge in obesity care and prevention is long-term body weight maintenance, particularly after weight loss [1, 2]. Body weight maintenance has multiple determinants, including a growing body of evidence that informs the hypothesis that, in addition to diet quality and energy intake, the timing of eating occasions may influence metabolic and weight-related health outcomes owing to the influence on circadian rhythms [3, 4]. Eating occasions that bookend the daily meal pattern have drawn particular interest, given the potential interactions with metabolism and circadian patterns [5, 6]. Although these observations have led to weight-loss interventions aiming to leverage the hypothesized basic biological phenomena, the optimal meal timing strategy for weight management remains poorly defined [7, 8].

In particular, the role of the timing of eating occasions on weight maintenance after initial weight loss remains largely unaddressed. To begin informing this question, we estimated the causal effects of hypothetical randomized dietary interventions using existing cohort data. Specifically, we estimated the effects of habitual sustained breakfast meal intake versus avoidance/irregular breakfast meal intake and avoidance/rare consumption of post-dinner snacks versus habitual post-dinner snacks on 18-month weight-loss maintenance in a population that had lost significant weight after 6 months of a standard weight-loss program. We estimated absolute and relative change in weight and body composition variables and applied modeling assumptions that appropriately account for time-varying confounding [9]. Based on basic biological, clinical, and observational epidemiologic research, we hypothesized that habitual sustained breakfast consumption and avoidance or rare consumption of after-dinner snacks would be more favorable dietary approaches for mitigating weight regain after initial weight loss.

METHODS

First, we outline a hypothetical randomized trial design to test the question of interest. Then we describe the methods we used to emulate this randomized trial using the available observational data.

Target trial specification

Table 1 summarizes the key components of the target trial. Briefly, the trial would enroll young adults with overweight and obesity into a standard 6-month behavioral weight-loss intervention. After 6 months, usually the nadir of weight loss, they would be randomly assigned to a dietary strategy intended to inform whether the timing of eating occasions impacts weight-loss maintenance. Each eligible participant would be followed from assignment until withdrawal/loss to follow-up or administrative end of follow-up (18 months after assignment), whichever happens first. The primary outcomes would be weight, body fat, and lean body mass change.

Dietary strategies

Participants would be randomly assigned after 6 months of the weight-loss intervention to one of the following dietary strategies for 18 months to test the hypotheses related to mitigating weight gain: (1) regular breakfast meals (breakfast 5-7 times/week); (2) irregular to rare breakfast (breakfast 0-4 times/week); (3) avoidance to rare post-dinner eating (post-dinner snacks 0-2 times/week); (4) frequent to habitual post-dinner eating (post-dinner snacks 3-7 times/week).

Causal contrasts and statistical analysis

The target trial's primary (intent-to-treat) effect would be estimated by comparing the body weight and composition change since the randomization to each breakfast and post-dinner snack strategy (with adjustment for loss to follow-up, if necessary). However, the information provided by the intent-to-treat effect would be limited if, as expected, many individuals deviated from their dietary assignments during the 18-month follow-up. In this setting, a contrast of the body weight and fat change that would have been observed if all individuals had adhered to their assigned dietary strategy (i.e., per-protocol effect) may be more relevant for informing the potential effects of the dietary approaches [10]. These estimates can be generated in the target trial using a marginal structural model (MSM) with inverse-probability weights (IPW) [11, 12]. Briefly, IPW of MSM is an alternative to the parametric g-formula. The standardized outcome estimates are calculated as a weighted average of the outcome estimates conditional on the time-varying confounders, with the distribution of the time-varying confounders used as weights. Unlike standard statistical methods, weighting can appropriately adjust for confounding and selection bias caused by time-varying covariates affected by prior exposure. If our emulation procedures had been successful, the estimates would have a straightforward interpretation because the target trial is well defined. The robustness of the estimates and causal inference is achieved by minimizing unmeasured confounding (selection of confounders through a thorough review of existing studies), selection bias (incomplete follow-up expanded to include questionnaire nonresponses and incomplete responses to dietary questions), measurement error (quality control of the assessments and data in the Innovative Approaches to Diet, Exercise and Activity [IDEA] study), and model misspecification (using directed acyclic graphs to select potential confounders) and maximizing consistency (indicated range of dietary exposure like frequency of breakfast and post-dinner snack consumption and the starting points and durations of the dietary interventions and follow-up periods) [9, 10, 13].

To identify potential subgroups of participants for whom the dietary strategies may be more beneficial, analyses can be conducted separately in subsets of the study population defined at baseline according to pre-baseline breakfast consumption (regular vs. irregular

Study Importance

What is already known?

- Maximum weight loss with behavioral approaches tends to plateau after 6 months, whereby the fundamental challenge becomes minimizing weight regain following the initial weight loss.
- The timing of eating occasions, specifically breakfast and post-dinner snack consumption, is hypothesized to influence weight regain after weight loss.

What does this study add?

- Regular breakfast consumption and minimizing post-dinner snacking might have a modest impact on lessening weight and body fat regain over 18 months after initial weight loss.

How might these results change the direction of research or the focus of clinical practice?

- The analytic approach and results in this research helped define and compare dietary strategies that could be used to inform randomized interventions and potential recommendations for weight-maintenance programs in the face of the lack of long-term randomized trials investigating the timing of eating occasions on weight maintenance.

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TABLE 1 Specification and emulation of a target trial of meal timing interventions among young adults with BMI of 25.0 to <40.0 kg/m^2 using observational data from the IDEA study

Component	Target trial specifications	Target trial emulation
Aim	To estimate the effect of the timing of eating occasions that likely influence circadian metabolic and energy intake considerations, specifically breakfast and post-dinner snack intake, on body weight, body fat, and lean mass maintenance for 18 months after initial weight loss among young US adults with overweight and obesity.	Same. Because of the lack of timing of eating occasions measures in the observational data, we assumed that regular breakfast consumption stands for regular early morning eating and rare evening (post-dinner) snack consumption stands for rare post-dinner eating.
Eligibility criteria	Age 18-35 years and pre-baseline BMI of 25.0-40.0 kg/m^2. Exclusion criteria: had past or planned weight-loss surgery, current participation in another weight-loss intervention study.	Same. We also required complete questions on breakfast and evening snack frequency, body composition and weight data, and plausible energy intake (<600 or >6000 kcal/d for women and <800 or >8000 kcal/d for men) at pre-baseline and baseline. Baseline is defined as the 6-month follow-up to allow for adjustment for pre-baseline confounding (0-month follow-up).
Treatment strategies	Each individual would be assigned to one of the following strategies: • Regular early morning eating (breakfast 5-7 times/week), • Irregular to rare early morning eating (breakfast 0-4 times/week), • Avoidance to rare post-dinner evening eating (evening snacks 0-2 times/week), • Frequent to habitual post-dinner evening eating (evening snacks 3-7 times/week). Participants assigned to a dietary strategy are expected to maintain their dietary intake within the range prespecified by the corresponding intervention.	Same. We assumed that breakfast consumption frequency accurately reflects early morning eating frequency and that post-dinner snack frequency reflects post-dinner evening eating frequency.
Treatment assignment	Participants are randomly assigned to a strategy at baseline and aware of their assigned strategy.	We attempted to emulate randomized assignment by adjusting for pre-baseline and baseline covariates: age, sex, ethnicity, income, breakfast frequency, post-dinner snack frequency, education, physical activity, smoking, alcohol consumption, sleep duration, BMI, diet quality, total energy intake, depression, and initial weight loss between 0 and 6 months.
Follow-up	From assignment until withdrawal/loss to follow-up or administrative end of follow-up (18 months after assignment), whichever happens first.	Same. Incomplete follow-up is defined as nonparticipation in the outcome measure or nonresponses to the dietary frequency questionnaire. The complete follow-up period is 18 months.
Outcome	Change in body weight, body fat, and lean mass composition 3 years after baseline.	Same for 18 months of follow-up.
Causal contrast of interest	Intention-to-treat effect, that is, the effect of being assigned to a regular early morning eating frequency versus rare early morning eating frequency at baseline. Per-protocol effect, that is, the effect that would have been observed if all participants adhered to their assigned strategy over the 18-month follow-up.	Observational analogue of the per-protocol and intent-to-treat analysis adjusted for adherence.
Statistical analysis	Apply MSM to compare 18-month estimates between groups receiving each treatment strategy and no treatment group with adjustment for pre- and post-baseline covariate factors associated with adherence to strategies and loss to follow-up.	Same.

Abbreviation: MSM, marginal structural model.

to rare) or post-dinner snack consumption (frequent to habitual vs. avoidance to rare). Particularly, we selected the subgroups with no exposure at pre-baseline for the treatment to estimate the effect of the initiation of regular breakfast consumption and initiation of avoidance of post-dinner snack in unexposed groups.

Target trial emulation

We emulated the described target trial using data from the IDEA study [14], a randomized clinical trial that was one of the studies within the Early Adult Reduction of Weight through Lifestyle intervention (EARLY) Trials consortium.

Observational data

The participants with BMI of 25.0 to <40.0 kg/m^2 were enrolled at the University of Pittsburgh between October 2010 and October 2012 using direct mail, mass media advertisements, or referral from clinical research registries. Males and females aged 18 to 35 years reported detailed clinical and lifestyle information at enrollment and every 6 months, including diet, cigarette smoking, alcohol consumption, sleep practices, physical activity, and sociodemographic factors. The protocol of the study is mentioned elsewhere [15].

Eligibility criteria

To emulate the target trial using these observational data (Table 1), we identified individuals in the cohort who met all eligibility criteria. We applied all eligibility criteria to participants in the IDEA study and excluded participants who did not have information on breakfast and post-dinner snack frequency, body composition, and weight measures or who had implausible energy intake (<600 or >6000 kcal/d for women and <800 or >8000 kcal/d for men) at 0 and 6 months.

Modifications to the target trial protocol

Eligible individuals were followed from baseline assessments until censoring (lack of outcome measures or incomplete responses to dietary questions) or 18 months after baseline, whichever happened first. To allow for adjustments of pre-baseline covariates, we used data from the 0-month time point or original study baseline.

Dietary strategies

The dietary strategies described earlier cannot be directly emulated because dietary observational data lacked the time stamp of eating occasion measures. Based on the assessment of daily meal patterns in the study, breakfast was implied to be the first eating occasion/meal of the day, and an evening snack occurred separately and after a dinner meal [15]. Therefore, we assumed that breakfast consumption accurately reflects morning eating frequency and post-dinner snack frequency reflects late evening eating frequency. For the analyses, we defined dietary strategies as 0 to 4 (irregular to rare) and 5 to 7 (regular) times/week for breakfast and 0 to 2 (avoidance to rare) and 3 to 7 (frequent to habitual) times/week for a post-dinner snack (online Supporting Information S1). Eligible individuals were analyzed according to the following dietary strategies: (1) regular breakfast meals (breakfast 5-7 times/week); (2) irregular to rare breakfast (breakfast 0-4 times/week); (3) avoidance to rare post-dinner eating (post-dinner snacks 0-2 times/week); (4) frequent to habitual post-dinner eating (post-dinner snacks 3-7 times/week).

Treatment assignment

We attempted to emulate the randomization to the specified treatment groups at the 6-month point (baseline for this analysis) by adjusting for pre-baseline (time 0), time-invariant, and other "pre-intervention" confounders (age, sex, ethnicity, income, breakfast frequency, post-dinner snack frequency, education, physical activity, smoking, alcohol consumption, sleep duration, BMI, diet quality, total energy intake, depression, initial weight loss between 0 and 6 months) via IPW.

Primary outcome

The primary outcomes are changes in body weight and body composition (fat mass and lean mass) 18 months after baseline. The IDEA study measured body composition using a GE Lunar iDXA dual-energy x-ray absorptiometer (GE Healthcare, Madison, Wisconsin) every 6 months of the follow-up. A calibrated digital scale that measures weight to 0.1 kg was used to assess body weight. Absolute changes in body weight and body composition were calculated as the following: measured value at 24 months – values of the same measure at 6 months, where a negative change means a reduction in body weight or body composition. Relative changes in body weight and body composition were calculated as (100 × [(value at 24 months – value of the same measure at 6 months) / value of the same measure at 6 months]), where a negative change means a reduction in body weight or body composition [16].

Statistical analysis

We implemented parametric MSM to estimate the causal effect of each dietary strategy on body fat and weight maintenance between 6 and 24 months [12, 17]. To emulate the random strategy assignment at baseline and adherence to the treatment for 18 months, we adjusted for all baseline confounding factors required to maximize the exchangeability (comparability) of the groups defined by initiation of the treatment strategies [18]. The probability of treatment strategy was estimated at 6 (baseline), 12, and 18 months of the follow-up.

Participants with a missing measure of the outcome or nonresponse to the breakfast or post-dinner snack frequency questionnaire were censored at the time of nonresponse or at 18 months of follow-up.

We selected a list of potential confounders using directed acyclic graphs to avoid unnecessary conditioning on covariates. The final model for the weights included the following baseline covariates measured at pre-baseline (month 0): age, sex, race, smoking, education, BMI, vigorous and moderate physical activity, breakfast frequency, post-dinner snack frequency, energy intake, diet quality, alcohol intake, sleep duration, and depression, as well as the following time-varying covariates measured at all previous time points and at the times of treatment: vigorous and moderate physical activity, body mass/body fat change since pre-baseline, breakfast frequency, post-dinner snack frequency, energy intake, diet quality, alcohol intake, sleep duration, and depression. The estimates of IPW, which are used to estimate the marginal causal effect, are not subject to multicollinearity, unlike the estimates from standard regression analysis. Additionally, IPW is also protected from the collinearity between the same covariates measured at several time points [19].

The last observation carried forward was used to impute income and smoking status if not measured in a particular interval [20]. Other covariates were imputed using the Monte Carlo multiple imputation method, assuming that data were missing at random, and the models used to perform the imputation were correctly specified (Supporting Information Table S8) [21]. Owing to the extensive range of IPW, weights were truncated at the 5th and 95th percentiles. This decision was made to improve the trade-off between variance and residual confounding by measured covariates, understanding the bias-variance trade-off associated with weight truncation [11]. Because the estimated weight distribution may serve as an indicator of the "positivity assumption," we examined the distribution of weights. We carefully assessed the distribution of the resulting IPW, which consistently averaged 1, to ensure appropriate adjustment for potential confounders.

Nonparametric bootstrapping with 100 samples was used to construct percentile-based 95% confidence intervals (CIs) of the estimated mean differences between the estimated outcomes of treatments (breakfast 0-4 vs. 5-7 times/week, post-dinner snack 0-2 vs. 3-7 times/week).

Sensitivity analysis. We used various cutoff points to define the thresholds of the treatment strategies (0, 1-2, 3-4, 5-6, and 7 times/week). However, for the final analysis, we collapsed the 0 and 1 to 2 times groups as well as the 5 to 6 and 7 times groups to ensure positivity (owing to the small sample size of groups 0, 1-2, 5-6, and 7 times on their own, the positivity assumption did not hold). We assessed whether the initiation of treatment strategies in some participants had a different effect on body weight and composition maintenance compared with no treatment in the same participants. We also performed an intent-to-treat analysis adjusting for adherence for all participants, including those who did not adhere to the treatment assigned at baseline. We also assessed the robustness of our estimates to various analytical decisions. Specifically, we (1) evaluated whether observed associations could have been driven by a small number of persons with extreme weights by applying various truncation rules to the treatment and censoring weights, (2) defined different cutoff points for exposure categories, (3) additionally adjusted for smoking as a time-varying confounder, (4) assessed dinner consumption and before bed eating as a primary exposure, and (5) used only age, sex, race, education, and BMI at baseline as baseline confounders. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Baseline characteristics of participants

Out of 647 screened participants of the IDEA study, 372 were eligible for this analysis (Figure 1). Of 372 eligible individuals, 71% were female (Tables 2 and 3). The mean age was 30 years, the mean BMI was 31, mean body fat was 41%, mean body weight was 91 kg, 24% had ≥150 min/week of moderate-intensity physical activity, and 64% had ≥75 min/week of vigorous-intensity physical activity. In addition, 69% of participants consumed breakfast 5 to 7 times/week ($n = 245$), and 41% of participants consumed post-dinner snacks 0 to 2 times/week ($n = 151$), most of whom were White, had baccalaureate degrees, and were nonsmokers. The crude mean weight-loss percentage during the first 6 months of the weight-loss intervention was 10.2% in the eligible population.

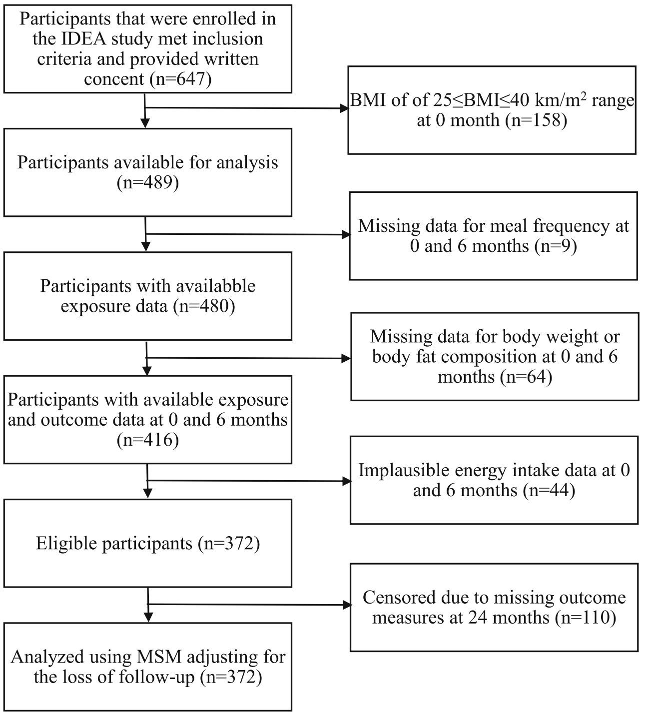

FIGURE 1 Selection of participants to study meal frequency and body weight and composition among young adults with BMI of 25.0 to <40.0 kg/m^2 using data from the Innovative Approaches to Diet, Exercise and Activity (IDEA) study. MSM, marginal structural model

TABLE 2 Pre-baseline[a] characteristics of 372 eligible participants by breakfast consumption frequency, the IDEA study

	Breakfast frequency (times/wk)			
	Overall (*n* = 372)	**0 to 2 (*n* = 67)**	**3 to 4 (*n* = 60)**	**5 to 7 (*n* = 245)**
Female sex, *n* (%)	264 (70.97)	45 (67.16)	45 (75)	174 (71.02)
Race, *n* (%)				
White	305 (81.99)	49 (73.13)	39 (65)	217 (88.57)
Black	57 (15.32)	17 (25.37)	18 (30)	22 (8.98)
Asian	10 (2.69)	1 (1.49)	3 (5)	6 (2.45)
Education, *n* (%)				
HS, GED, or some college	84 (22.58)	21 (31.34)	23 (38.33)	40 (16.33)
College or baccalaureate	156 (41.94)	26 (38.81)	21 (35)	109 (44.49)
Graduate degree	132 (35.48)	20 (29.85)	16 (26.67)	96 (39.18)
Annual household income, *n* (%)				
<$5000	146 (39.25)	26 (38.81)	31 (51.67)	89 (36.33)
$5000 through $11,999	161 (43.28)	31 (46.27)	19 (31.67)	111 (45.31)
$12,000 through $15,999	65 (17.47)	10 (14.93)	10 (16.67)	45 (18.37)
Current smoker, *n* (%)	30 (8.06)	9 (13.43)	9 (15)	12 (4.9)
Moderate PA[b], *n* (%)				
<150 min/wk	284 (76.34)	51 (76.12)	39 (65)	194 (79.18)
≥150 min/wk	88 (23.66)	16 (23.88)	21 (35)	51 (20.82)
Vigorous PA[b], *n* (%)				
<75 min/wk	131 (35.22)	31 (46.27)	19 (31.67)	81 (33.06)
≥75 min/wk	241 (64.78)	36 (53.73)	41 (68.33)	164 (66.94)
Regular dieting[c], *n* (%)	163 (43.82)	21 (31.34)	27 (45)	115 (46.94)
Depression[d], *n* (%) (d/wk)				
<1	288 (77.42)	51 (76.12)	50 (83.33)	187 (76.33)
1-2	64 (17.2)	10 (14.93)	8 (13.33)	46 (18.78)
3-4	17 (4.57)	5 (7.46)	2 (3.33)	10 (4.08)
5-7	3 (0.81)	1 (1.49)	.	2 (0.82)
Dinner[e], *n* (%) (times/wk)				
0-2	5 (1.34)	1 (1.49)	2 (3.33)	2 (0.82)
3-4	7 (1.88)	3 (4.48)	2 (3.33)	2 (0.82)
5-7	360 (96.77)	63 (94.03)	56 (93.33)	241 (98.37)
Post-dinner snack[f], *n* (%) (times/wk)				
0-2	151 (40.59)	25 (37.31)	26 (43.33)	100 (40.82)
3-4	94 (25.27)	20 (29.85)	13 (21.67)	61 (24.9)
5-7	127 (34.14)	22 (32.84)	21 (35)	84 (34.29)
Eating within an hour of bedtime[e], *n* (%) (times/wk)				
0-2	227 (61.02)	34 (50.75)	34 (56.67)	159 (64.9)
3-4	78 (20.97)	21 (31.34)	8 (13.33)	49 (20)
5-7	67 (18.01)	12 (17.91)	18 (30)	37 (15.1)
Age, mean (SD) (y)	30.1 (3.8)	30 (3.9)	30.1 (3.9)	30.2 (3.8)
BMI, mean (SD) (kg/m^2)	31.7 (4)	31.7 (3.8)	32.8 (4.5)	31.4 (3.9)
Body weight, mean (SD) (kg)	91.4 (15.6)	90.6 (14.4)	95.4 (18.1)	90.7 (15.2)
Body fat, mean (SD) (%)	40.8 (6.3)	41.7 (5.8)	41.6 (5.9)	40.4 (6.4)
Body weight change[f], mean (SD) (%)	−9.2 (6.6)	−7.8 (6.6)	−7.4 (6.4)	−10 (6.6)
Alcohol[g], mean (SD) (d/mo)	6.5 (5)	6.6 (5)	6.4 (5.1)	6.5 (5)

(Continues)

TABLE 2 (Continued)

	Breakfast frequency (times/wk)			
	Overall (n = 372)	0 to 2 (n = 67)	3 to 4 (n = 60)	5 to 7 (n = 245)
Sleep on weekdays[h], mean (SD) (h/d)	7.7 (2.1)	8.2 (2.4)	7.6 (1.9)	7.6 (2)
Total energy intake, mean (SD) (calories/d)	1900.5 (866.7)	1950.6 (935.5)	1928.4 (1130.6)	1879.9 (771.4)
Diet quality, mean (SD) (HEI out of 100)	64.6 (11.1)	60.1 (9.2)	61.4 (12)	66.5 (10.8)

Abbreviations: HEI, Healthy Eating Index; HS, high school; GED, general equivalency diploma; PA, physical activity.
[a]Pre-baseline refers to the assessment of the characteristics at 0 months of the IDEA study.
[b]"Vigorous-intensity activities" are activities that require hard physical effort and cause large increases in breathing or heart rate; "moderate-intensity activities" are activities that require moderate physical effort and cause small increases in breathing or heart rate.
[c]The participants who responded positively to the following statement: "Since my weight goes up and down, I have gone on reducing diets more than once," referring to the experience prior to the weight-loss intervention.
[d]The participants who responded positively to the following statement: "I felt depressed," referring to the experience 1 week prior to the pre-baseline (month 0) assessment.
[e]Referring to the meal consumption frequency in a typical week prior to the pre-baseline (month 0) assessment.
[f]Weight change during the first 6 months of the conventional weight-loss intervention. Relative body weight (percentage) change is calculated as (100 × [(absolute body weight [kilograms] at 6 months − absolute body weight [kilograms] at 0 months)/(absolute body weight [kilograms] at 0 months)]). A negative estimate means a decrease in body weight during the follow-up period.
[g]The participants responded to the following question: "During the past 30 days, how many days did you have at least one drink of any alcoholic beverage?" referring to the experience prior to the pre-baseline (month 0) assessment.
[h]Referring to the period between which the participants usually went to bed in the evening (turn out the lights in order to go to sleep) and the time they usually got out of bed in the morning in the past month prior to the pre-baseline (month 0) assessment.

Body fat and body weight maintenance: emulated trial results

Table 4 and Supporting Information Figure S3 show the estimated change in body weight and fat and lean mass from month 6 to month 24 under strategies of consuming breakfast 0 to 4 versus 5 to 7 times/week. Compared with the 3.56 kg (95% CI: 0.67 to 5.63) increase in body weight under 0 to 4 times/week breakfast frequency, the body weight increase would be 2.97 kg or 0.59 kg (95% CI: −0.86 to −0.32) lower if all participants had followed the strategy of 5 to 7 breakfasts per week. These estimates should be interpreted as if all participants adhered to the assigned treatment strategies at 6, 12, and 18 months of the follow-up. Similar trends were observed in body fat maintenance. The proportion of participants who followed the hypothetical intervention strategies in the source data set is shown in Supporting Information Table S1.

Table 4 also shows the estimated change in body weight and composition under strategies of consuming post-dinner snacks 0 to 2 and 3 to 7 times/week. Compared with the 3.7 kg (95% CI: 2.3 to 4.9) increase in body weight under 3 to 7 times/week post-dinner snack frequency, the body weight increase would be 2.87 kg or 0.83 kg (95% CI: −1.06 to −0.59) lower in the strategy of 0 to 2 post-dinner snacks per week. Similarly, these estimates should be interpreted as per-protocol as if participants adhered to the assigned treatment strategies at 6, 12, and 18 months of the follow-up. Similar trends were observed in body fat maintenance. Lean body mass increased by 0.22 kg (95% CI: −0.29 to −0.16) during the follow-up among those who avoided consuming post-dinner snacks regularly.

The estimates from the analysis emulating an intent-to-treat analysis adjusted for adherence should be interpreted as if all participants were assigned to treatment at baseline (month 6), but some were non-adherent at 12 or 18 months of the follow-up, which was adjusted for in the analysis. The results were in a similar direction with the estimates obtained from emulating a per-protocol analysis.

Supporting Information Table S2 presents this analysis using relative measures of body weight (percentage) and body fat (percentage) change as the outcome of interest.

Table 5 and Supporting Information Figure S4 show the sensitivity analysis results of restricted populations. The estimates suggest that if the participants who consumed breakfast 0 to 4 times/week at pre-baseline (time 0) were to follow the strategy of breakfast 5 to 7 times/week during the 18-month intervention they would regain 2.21 kg, or 1.23 kg (95% CI: −1.78 to −0.67) less body weight than if they continued consuming 0 to 4 breakfasts per week, where we estimated they would gain 3.44 kg (95% CI: 1.57 to 5.64) of body weight. Owing to the small sample size informing the models and a limited number of participants to intervene on, the estimates for post-dinner snack interventions among those who habitually consumed post-dinner snacks at pre-baseline are not presented in this analysis.

Supporting Information Table S3 presents this analysis using relative measures of body weight (percentage) and body fat (percentage) change as the outcome of interest. Supporting Information Tables S4-S7 present sensitivity analyses using extreme threshold cutoff points for breakfast consumption strategies (0–6 and 7 times/week). The estimates did not materially change under any of the sensitivity analyses. Owing to the relatively small sample size and a limited number of participants to intervene on (post-dinner snack 0 times/week strategies), some estimates have inflated precision and thus they are not presented in this analysis (Supporting Information Table S4).

TABLE 3 Pre-baseline[a] characteristics of 372 eligible participants by post-dinner snack consumption frequency, the IDEA study

	Post-dinner snack frequency, times/wk			
	Overall (*n* = 372)	0 to 2 (*n* = 67)	3 to 4 (*n* = 60)	5 to 7 (*n* = 245)
Female sex, *n* (%)	264 (70.97)	111 (73.51)	55 (58.51)	98 (77.17)
Race, *n* (%)				
Asian	10 (2.69)	6 (3.97)	3 (3.19)	1 (0.79)
Black	57 (15.32)	21 (13.91)	9 (9.57)	27 (21.26)
White	305 (81.99)	124 (82.12)	82 (87.23)	99 (77.95)
Education, *n* (%)				
College or baccalaureate	156 (41.94)	72 (47.68)	41 (43.62)	43 (33.86)
HS, GED, or some college	84 (22.58)	31 (20.53)	17 (18.09)	36 (28.35)
Graduate degree	132 (35.48)	48 (31.79)	36 (38.3)	48 (37.8)
Annual household income, *n* (%)				
$12,000 through $15,999	65 (17.47)	20 (13.25)	22 (23.4)	23 (18.11)
$5000 through $11,999	161 (43.28)	61 (40.4)	44 (46.81)	56 (44.09)
Less than $5000	146 (39.25)	70 (46.36)	28 (29.79)	48 (37.8)
Current smoker, *n* (%)	30 (8.06)	8 (5.3)	8 (8.51)	14 (11.02)
Moderate PA[b], *n* (%)				
<150 min/wk	284 (76.34)	110 (72.85)	76 (80.85)	98 (77.17)
≥150 min/wk	88 (23.66)	41 (27.15)	18 (19.15)	29 (22.83)
Vigorous PA[b], *n* (%)				
<75 min/wk	131 (35.22)	32 (21.19)	40 (42.55)	59 (46.46)
≥75 min/wk	241 (64.78)	119 (78.81)	54 (57.45)	68 (53.54)
Regular dieting[c], *n* (%)	163 (43.82)	56 (37.09)	43 (45.74)	64 (50.39)
Depression[d], *n* (%)				
<1 time/wk	3 (0.81)	2 (1.32)	0	1 (0.79)
1-2 times/wk	17 (4.57)	6 (3.97)	5 (5.32)	6 (4.72)
3-4 times/wk	288 (77.42)	120 (79.47)	72 (76.6)	96 (75.59)
5-7 times/wk	64 (17.2)	23 (15.23)	17 (18.09)	24 (18.9)
Dinner[e], *n* (%)				
0-2 times/wk	5 (1.34)	3 (1.99)	0	2 (1.57)
3-4 times/wk	7 (1.88)	3 (1.99)	1 (1.06)	3 (2.36)
5-7 times/wk	360 (96.77)	145 (96.03)	93 (98.94)	122 (96.06)
Breakfast[e], *n* (%)				
0-2 times/wk	67 (18.01)	25 (16.56)	20 (21.28)	22 (17.32)
3-4 times/wk	60 (16.13)	26 (17.22)	13 (13.83)	21 (16.54)
5-7 times/wk	245 (65.86)	100 (66.23)	61 (64.89)	84 (66.14)
Eating within an hour of bedtime[e], *n* (%)				
0-2 times/wk	227 (61.02)	126 (83.44)	64 (68.09)	37 (29.13)
3-4 times/wk	78 (20.97)	19 (12.58)	24 (25.53)	35 (27.56)
5-7 times/wk	67 (18.01)	6 (3.97)	6 (6.38)	55 (43.31)
Age, mean (SD) (y)	30.1 (3.8)	30 (3.7)	30 (4)	30.3 (3.9)
BMI, mean (SD) (kg/m^2)	31.7 (4)	31.4 (3.9)	31.9 (4.2)	31.7 (4.1)
Body weight, mean (SD) (kg)	91.4 (15.6)	90.3 (14.8)	92.9 (15.5)	91.6 (16.6)
Body fat, mean (SD) (%)	40.8 (6.3)	41 (6.1)	39.8 (6.3)	41.4 (6.4)
Body weight change[f], mean (SD) (%)	−9.2 (6.6)	−10.1 (6.8)	−10.2 (6.1)	−7.4 (6.4)
Alcohol[g], mean (SD) (d/mo)	6.5 (5)	6.6 (4.9)	6.8 (4.6)	6.1 (5.4)

(Continues)

TABLE 3 (Continued)

	Post-dinner snack frequency, times/wk			
	Overall ($n = 372$)	**0 to 2 ($n = 67$)**	**3 to 4 ($n = 60$)**	**5 to 7 ($n = 245$)**
Sleep on weekdays[h], mean (SD) (h/d)	7.7 (2.1)	7.8 (2)	7.7 (2.3)	7.8 (1.9)
Total energy intake, mean (SD) (calories/d)	1900.5 (866.7)	1731.1 (708.6)	1839.2 (790.5)	2147.2 (1026.8)
Diet quality, mean (SD) (HEI out of 100)	64.6 (11.1)	65.2 (10.8)	63.4 (10.4)	64.7 (11.9)

Abbreviations: GED, general equivalency diploma; HEI, Healthy Eating Index; HS, high school; PA, physical activity.

[a]Pre-baseline refers to the assessment of the characteristics at 0 months of the IDEA study.

[b]"Vigorous-intensity activities" are activities that require hard physical effort and cause large increases in breathing or heart rate; "moderate-intensity activities" are activities that require moderate physical effort and cause small increases in breathing or heart rate.

[c]The participants who responded positively to the following statement: "Since my weight goes up and down, I have gone on reducing diets more than once," referring to the experience prior to the weight-loss intervention.

[d]The participants who responded positively to the following statement: "I felt depressed," referring to the experience 1 week prior to the pre-baseline (month 0) assessment.

[e]Referring to the meal consumption frequency in a typical week prior to the pre-baseline (month 0) assessment.

[f]Weight change during the first 6 months of the conventional weight-loss intervention. Relative body weight (%) change is calculated as (100 × [(absolute body weight [kilograms] at 6 months − absolute body weight [kilograms] at 0 months)/absolute body weight (kilograms) at 0 months]). A negative estimate means a decrease in body weight during the follow-up period.

[g]The participants responded to the following question: "During the past 30 days, how many days did you have at least one drink of any alcoholic beverage?" referring to the experience prior to the pre-baseline (month 0) assessment.

[h]Referring to the period between which the participants usually went to bed in the evening (turn out the lights in order to go to sleep) and the time they usually got out of bed in the morning in the past month prior to the pre-baseline (month 0) assessment.

DISCUSSION

This manuscript analyzes observational data that estimated the causal effects of hypothetical meal timing-related dietary interventions on weight maintenance after a weight-loss intervention in young adults. The results suggest that limiting or avoiding post-dinner meals (post-dinner snack) and habitual consumption of a morning meal (breakfast) may have modest benefits for mitigating weight and body fat regain over 18 months in young adults after clinically significant weight loss. The estimated effect was of greater magnitude (i.e., less weight regain) if all participants who ate breakfast 0 to 4 times before weight loss increased their breakfast meal intake to 5 to 7 times as part of a hypothetical intervention.

The validity of our effect estimates cannot be directly benchmarked because no randomized trials have assessed the effect of implementing early or avoiding late daytime eating on weight-loss maintenance. However, the potential impact of the timing of food intake on weight and body fat is informed by an understanding of metabolism and circadian rhythms. Indeed, the timing of food intake relative to melatonin onset is associated with the percentage of body fat and BMI, which suggests that consumption of food during the circadian evening and/or night, independent of more traditional risk factors such as amount or content of food intake and activity level, plays an important role in body composition [22, 23]. Further evidence supports that diet-circadian rhythm influences body weight, appetite, glucose, and lipid metabolism [23–26]. A fundamental question we aimed to inform is what the potential impact of leveraging this knowledge has on weight and body composition dynamics in individuals who had lost weight over 6 months.

Other salient research also informs this topic. A recent randomized controlled trial aimed to evaluate the effect of late versus early evening meal consumption on weight loss in women and found that eating an earlier evening meal resulted in favorable changes in weight loss during a 12-week weight-loss program [26].

Time-restricted eating is a dietary strategy that focuses on consolidating all calorie intake in a restricted period of the day (usually 6-11 hours) and avoiding eating outside of this period. The short-term TREAT trial demonstrated that time-restricted eating was associated with a modest decrease (1.17%) in weight. However, the estimates suggest that longer trials are needed to detect the long-term effect of meal timing on weight regain [27]. If we stopped our emulated trial at 12 weeks post intervention initiation, the estimated weight difference would also be close to null (Supporting Information Figures S1 and S2). In addition, because our study population was younger with a slightly lower range of baseline BMI than the TREAT trial, the dynamic of weight change is expected to be different from that in participants from that trial. The ongoing Rhythm trial aims to evaluate whether restricting the timing of energy intake to a short-defined period during wakefulness can improve fuel use patterns and enhance circadian rhythms in metabolic tissues to optimize health, but results have yet to be reported [28]. Breakfast is commonly defined as any caloric intake after an overnight fast or fasting period of ≥8 hours [29]. A randomized trial that analyzed the effectiveness of the recommendation for eating breakfast on weight loss in adults trying to lose weight in a free-living setting concluded there was no discernable effect of the recommendation for breakfast consumption on weight loss [30]. Other recent trials suggest that late evening meals result in less favorable changes in weight during weight-loss programs [26, 31, 32]. These prior studies are related but are fundamentally different from our question and analysis, as we were focused on weight maintenance/mitigation of weight regain.

In observational research, a large European cohort study that followed up participants for 10 years suggests that daily breakfast consumption has no association with weight maintenance during the

TABLE 4 Estimates[a] of the effect of dietary strategies on the maintenance of total body weight (kilograms), body fat mass (kilograms), body lean mass (kilograms), and relative body fat (percentage) among all eligible participants of the IDEA study during the 18-month follow-up after initial weight loss, per-protocol and intent-to-treat analysis

	Total body weight (kg)[d]		Body fat mass (kg)[e]		Body lean mass (kg)[f]	
Treatment strategy[b,c]	Mean change (95% CI)	Mean difference (95% CI)	Mean change (95% CI)	Mean difference (95% CI)	Mean change (95% CI)	Mean difference (95% CI)
Per-protocol analysis						
Breakfast[g]						
0-4 times/wk	3.56 (0.67 to 5.63)	Reference	2.94 (0.44 to 4.84)	Reference	0.62 (0.15 to 1.06)	Reference
5-7 times/wk	2.95 (2.01 to 3.96)	−0.59 (−0.86 to −0.32)	2.34 (1.51 to 3.13)	−0.57 (−0.82 to −0.33)	0.61 (0.4 to 0.91)	−0.01 (−0.06 to 0.05)
Post-dinner snack[g]						
0-2 times/wk	2.86 (0.99 to 5.25)	−0.83 (−1.06 to −0.59)	2.29 (0.95 to 4.12)	−0.59 (−0.78 to −0.39)	0.58 (0.12 to 1.22)	−0.22 (−0.29 to −0.16)
3-7 times/wk	3.7 (2.29 to 4.9)	Reference	2.89 (1.44 to 3.87)	Reference	0.8 (0.47 to 1.09)	Reference
Intent-to-treat analysis adjusted for adherence						
Breakfast[g]						
0-4 times/wk	4.1 (1.67 to 6.48)	Reference	3.38 (1.43 to 5.38)	Reference	0.72 (−0.18 to 1.71)	0.37 (0.34 to 0.39)
5-7 times/wk	3.01 (0.98 to 4.13)	−1.39 (−1.45 to −1.33)	2.45 (0.95 to 3.96)	−1 (−1.06 to −0.95)	0.56 (−0.44 to 0.96)	Reference
Post-dinner snack[g]						
0-2 times/wk	2.43 (0.18 to 4.32)	−1.18 (−1.22 to −1.14)	1.8 (−0.42 to 3.5)	−1.23 (−1.27 to −1.19)	0.65 (0.18 to 1.12)	0.05 (0.04 to 0.06)
3-7 times/wk	3.72 (1.56 to 5.29)	Reference	3.14 (1.07 to 4.57)	Reference	0.58 (0.16 to 1.04)	Reference

[a]Estimates are based on marginal structural model with inverse-probability weights (IPW) accounting for selection bias due to censoring and treatment selection. IPW adjust for pre-baseline covariates (age, sex, ethnicity, income, breakfast frequency, post-dinner snack frequency, education, physical activity, smoking, alcohol consumption, sleep duration, BMI, diet quality, total energy intake, depression, initial body fat change) and time-varying covariates (income, breakfast frequency, evening snack frequency, physical activity, alcohol consumption, sleep duration, diet quality, total energy intake, depression).

[b]Breakfast frequency is categorized as regular breakfast frequency (consumption of breakfast 5-7 times a week) and irregular to rare breakfast frequency (consumption of breakfast 0-4 times a week).

[c]Post-dinner snack frequency is categorized as frequent to habitual post-dinner snack frequency (consumption of post-dinner snack 3-7 times a week) and avoidance to rare post-dinner snack frequency (consumption of post-dinner snack 0-2 times a week).

[d]Total body weight (kilograms) change is calculated as (absolute body weight [kilograms] at 24 months − absolute body weight [kilograms] at 6 months). A negative estimate means a decrease in absolute body weight during the 18-month follow-up period.

[e]Body fat mass (kilograms) change is calculated as (body fat mass [kilograms] at 24 months − body fat mass [kilograms] at 6 months). A negative estimate means a decrease in body fat mass during the 18-month follow-up period.

[f]Body lean mass (kilograms) change is calculated as (body lean mass [kilograms] at 24 months − body lean mass [kilograms] at 6 months). A negative estimate means a decrease in body lean mass during the 18-month follow-up period.

[g]All eligible participants.

TABLE 5 Estimates[a] of the effect of dietary strategies on the maintenance of total body weight (kilograms), body fat mass (kilograms), body lean mass (kilograms), and relative body fat (%) among selected subsets of participants of the IDEA study during the 18-month follow-up after initial weight loss, per-protocol and intent-to-treat analysis

Treatment strategy[b,c]	Total body weight (kg)[d]		Body fat mass (kg)[e]		Body lean mass (kg)[f]	
	Mean change (95% CI)	Mean difference (95% CI)	Mean change (95% CI)	Mean difference (95% CI)	Mean change (95% CI)	Mean difference (95% CI)
Breakfast[g]						
Only participants who consumed breakfast 0-4 times/wk at pre-baseline						
0-4 times/wk	3.44 (1.57 to 5.64)	Reference	3.05 (1.12 to 5.23)	Reference	0.4 (−0.19 to 0.94)	Reference
5-7 times/wk	2.26 (−2.39 to 6.67)	−1.23 (−1.78 to −0.67)	1.63 (−2.12 to 5.47)	−1.45 (−1.93 to −0.98)	0.63 (−0.24 to 1.5)	0.24 (0.13 to 0.35)
Only participants who consumed breakfast 5-7 times/wk at pre-baseline						
0-4 times/wk	2.86 (0.64 to 6.65)	Reference	2.53 (0.54 to 5.14)	Reference	0.27 (−0.55 to 1.42)	Reference
5-7 times/wk	3.01 (2.07 to 3.97)	0.04 (−0.34 to 0.43)	2.46 (1.55 to 3.29)	−0.17 (−0.45 to 0.11)	0.56 (0.33 to 0.85)	0.27 (0.15 to 0.39)
Post-dinner snack[g]						
Only participants who consumed post-dinner snacks 0-2 times/wk at pre-baseline						
0-2 times/wk	2.77 (0.02 to 5.22)	−1.15 (−1.53 to −0.78)	1.95 (−1.03 to 4.23)	−1.57 (−1.89 to −1.24)	0.83 (0.26 to 1.38)	0.44 (0.34 to 0.54)
3-7 times/wk	3.9 (1.41 to 6.33)	Reference	3.5 (1.43 to 5.24)	Reference	0.38 (−0.36 to 1.05)	Reference

[a]Estimates are based on marginal structural model with inverse-probability weights (IPW) accounting for selection bias due to censoring and treatment selection. IPW adjust for pre-baseline covariates (age, sex, ethnicity, income, breakfast frequency, post-dinner snack frequency, education, physical activity, smoking, alcohol consumption, sleep duration, BMI, diet quality, total energy intake, depression, initial body fat change) and time-varying covariates (income, breakfast frequency, evening snack frequency, physical activity, alcohol consumption, sleep duration, diet quality, total energy intake, depression).
[b]Breakfast frequency is categorized as regular breakfast frequency (consumption of breakfast 5-7 times a week) and irregular to rare breakfast frequency (consumption of breakfast 0-4 times a week).
[c]Post-dinner snack frequency is categorized as frequent to habitual post-dinner snack frequency (consumption of evening snack 3-7 times a week) and avoidance to rare post-dinner snack frequency (consumption of post-dinner snack 0-2 times a week).
[d]Total body weight (kilograms) change is calculated as (absolute body weight [kilograms] at 24 months − absolute body weight [kilograms] at 6 months). A negative estimate means a decrease in absolute body weight during the 18-month follow-up period.
[e]Body fat mass (kilograms) change is calculated as (body fat mass [kilograms] at 24 months − body fat mass [kilograms] at 6 months). A negative estimate means a decrease in body fat mass during the 18-month follow-up period.
[f]Body lean mass (kilograms) change is calculated as (body lean mass [kilograms] at 24 months − body lean mass [kilograms] at 6 months). A negative estimate means a decrease in body lean mass during the 18-month follow-up period.
[g]Per-protocol analysis.

follow-up period [33, 34]. Similar findings were made in the US National Weight Control Registry cohort study [34]. A prospective investigation of the association between breakfast consumption and long-term weight gain in a US adult male population observed that men who frequently consumed breakfast had less weight gain compared with those who skipped breakfast [34]. Related, night eating habits were associated with dyslipidemia and hypertriglyceridemia among 17,534 workers and their spouses in Japan [36].

Other studies have demonstrated that breakfast skipping impaired fasting lipids and postprandial insulin sensitivity and might lead to weight gain in the presence of higher energy intake [37]. This could be mediated by circadian interruptions and increased fat accumulation due to decreased fat oxidation at night [38–40]. A cross-sectional study of 872 middle-to-older aged adults suggested that higher dietary consumption after waking up and lower consumption close to bedtime were associated with lower BMI. However, the relationship differed by chronotype, suggesting the importance of considering the timing of food intake relative to sleep timing when studying the associations of meal timing with obesity and metabolic health [41].

Given the evidence on this topic, this study's research and analytic design provide a better framework for explicit discussion of methodologic considerations and alternative explanations for findings [18]. First, specifying the target trial clarifies the question of interest as a trial would do, including the indicated range of dietary exposure, like frequency of breakfast and post-dinner snack consumption, and the starting points and durations of the dietary interventions and follow-up periods. This framework aims to reduce the risk of bias and improve data interpretation [18]. Second, unlike traditional outcome regression, MSM with IPW appropriately adjusts for time-varying confounders affected by previous exposure [42]. In weight-loss research, time-varying confounders are present when weight-loss progress affects the future dietary habits of participants, and weight loss itself can be affected by past dietary habits, for example, the timing of eating. Last, we performed several analyses to address the potential effectiveness of newly assigned treatment to unexposed individuals and negative exposure control as a tool for detecting bias in observational studies [43].

Nevertheless, our approach does not eliminate the potential for uncontrolled confounding, measurement error, and model misspecification. Like in any observational study, we cannot rule out the possibility of uncontrolled confounding, despite adjustments for many potential confounders. An estimated null effect of lunch frequency on weight maintenance (which was not expected to be influenced by lunch frequency) is reassuring but not proof of a lack of confounding. In addition, we relied on self-report of breakfast and post-dinner snacks, and therefore, some degree of measurement error in the diet was expected. Because of logistics difficulties, a questionnaire is common to assess the adherence to timing for food intake strategies. Therefore, per-protocol effect estimation is also susceptible to measurement error in randomized trials [44]. Additionally, the lack of a time stamp in regard to the typical meal frequencies assessed precludes being more specific in the hypothetical interventions modeled and any conclusions beyond the occurrence of the eating occasion. Finally, the results may not be generalizable to populations with different dietary habits (because the effects are estimated in comparison with regular dietary practices), age distributions (because the ability to maintain lost weight differs in different age cohorts), or other distributions of other confounders [45].

In summary, we estimated that avoiding post-dinner meals (post-dinner snack) and habitual consumption of a morning meal (breakfast) modestly reduce body weight and fat regain over 18 months after initial weight loss among young adults with overweight and obesity defined by BMI. Furthermore, initiating habitual sustained breakfast consumption might be more beneficial for weight-loss maintenance over 18 months in people who did not habitually consume a breakfast meal before weight loss. The analytic approach and results in this research helped define and compare dietary strategies that could be used to inform randomized interventions and potential recommendations for weight-maintenance programs in the face of the lack of long-term randomized trials investigating the timing of eating occasions on weight maintenance.O

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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