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Association of Eating and Sleeping Intervals With Weight Change Over Time: The Daily24 Cohort

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Background

We aim to evaluate the association between meal intervals and weight trajectory among adults from a clinical cohort.

Methods and Results

This is a multisite prospective cohort study of adults recruited from 3 health systems. Over the 6-month study period, 547 participants downloaded and used a mobile application to record the timing of meals and sleep for at least 1 day. We obtained information on weight and comorbidities at each outpatient visit from electronic health records for up to 10 years before until 10 months after baseline. We used mixed linear regression to model weight trajectories. Mean age was 51.1 (SD 15.0) years, and body mass index was 30.8 (SD 7.8) kg/m2; 77.9% were women, and 77.5% reported White race. Mean interval from first to last meal was 11.5 (2.3) hours and was not associated with weight change. The number of meals per day was positively associated with weight change. The average difference in annual weight change (95% CI) associated with an increase of 1 daily meal was 0.28 kg (0.02–0.53).

Conclusions

Number of daily meals was positively associated with weight change over 6 years. Our findings did not support the use of time-restricted eating as a strategy for long-term weight loss in a general medical population.

Clinical Perspective

What Is New?

- In this electronic health record-based cohort study of 547 participants from 3 health systems, the number of daily meals was positively associated with weight change over 6.3 years, but the time interval between first and last meal was not associated with weight change.

What Are the Clinical Implications?

- The frequency, rather than the timing, of meals is a stronger determinant of weight change over time.
- When counselling patients about weight gain prevention, limiting the frequency of large meals is more beneficial than restricting eating windows.

Overweight and obesity are well-established modifiable chronic disease risk factors that affect >70% of US adults.**1** The limited success of behavioral approaches targeting calorie restriction, modified diet composition, and increased physical activity to control overweight and obesity have prompted the development of alternative strategies that can increase success rates.**2**, **3**, **4**, **5** Experimental and mechanistic studies suggest that the timing of food intake (eg, through intermittent fasting or time-restricted feeding) could regulate metabolic function and reduce body weight.**2**, **6**, **7**, **8** Specifically, time-restricted feeding, restricting food intake to 4 to 12 hours per day without reduced calorie intake, has been associated with improved body weight homeostasis and is a proposed weight reduction strategy.**9**, **10**, **11** However, in randomized clinical trials, time-restricted meal regimens resulted in similar weight loss compared with eating throughout the day**12**, **13**, **14**, **15** but had beneficial effects on cardiometabolic risk factors, including abdominal fat loss, glucose regulation, insulin resistance, blood pressure, and lipid profile.**7**, **14**, **16** Nevertheless, these studies were limited by small sample sizes, relatively short durations, and populations with specific conditions such as prediabetes**13** or overweight/obesity.**12**, **14**

Questions remain about the potential benefits of time-restricted eating patterns, especially the challenges with maintaining this eating behavior.**17** Observational studies are better suited to evaluate long-term changes, but no population-based studies have been specifically designed to evaluate the association between meal intervals and changes in weight over time. In a secondary data analysis from a weight loss trial of 420 Spanish participants followed for 20 weeks showed that later lunch eaters (after 3 pm) had less weight loss compared with early lunch eaters (before 3 pm) with equivalent caloric intake and physical activity.**18** However, previous studies were not able to evaluate meal intervals as they lacked real-time assessments of eating time.

In addition to windows between meals, the role of the frequency and size of meals on weight has been also controversial.**19** Cross-sectional studies have shown that a greater meal frequency was either not associated,**20** or associated with a reduced prevalence of abdominal**21**, **22** and general obesity,**22**, **23** while 2 large-scale prospective cohort studies showed that greater meal frequency was associated with increased weight gain and body mass index (BMI).**24**, **25**

The primary objective of this cohort study was to evaluate the longitudinal association between time from first to last meal with weight trajectories over time among adults in a population-based clinical cohort with detailed real-time information collected using a dedicated smartphone application. The secondary objectives were to evaluate the associations of time from wake-up to first meal, last meal to sleep, sleep duration, and the number of meals with weight trajectories.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. We recruited a cohort of adults from 3 health care systems included in the PaTH Clinical Research Network (Johns Hopkins Health System, Geisinger Health System, and University of Pittsburgh Medical Center).**26** PaTH is a Partner Network of PCORnet (National Patient-Centered Clinical Research Network). Institutional review board approval was obtained at The Johns Hopkins School of Medicine, which has a reliance agreement with the other institutional review boards. All research participants gave informed consent.

Study Participants

Potentially eligible participants were adults aged ≥18 years with electronic health records (EHR) in 1 of the 3 health systems, who had at least 1 weight and 1 height measurement registered in the EHR within the 2 years before the enrollment window (February 1, 2019–July 31, 2019). Patients received a recruitment email or a patient portal message with an invitation to participate and a personalized enrollment link. Interested subjects completed a web-based consent form and a baseline online questionnaire. We excluded subjects who were not proficient in English, as the consent, survey, and mobile app were only available in English.

Data Collection

Daily24 Mobile App

With feedback from end users and patient stakeholders, our team designed the Daily24 mobile application for participants to record their timing of waking up, sleeping, and each eating occasion for each 24-hour window in real-time.**27** The details of the design, functionality, and screen shots of the mobile app are described in a manuscript by Woolf and colleagues.**27** Briefly, the only eating behaviors assessed were meal timing (ie, when meals were consumed) and approximate meal size. For each eating occasion, participants first indicated the time using a 24-hour wheel and then selected the type and estimated size of meal from a drop-down menu (ie, small meal [<500 calories], medium [500–1000 calories], or large [>1000 calories]) (Figure S1).**28** Emails, short message service text messages, and in-app notifications encouraged participants to use the app as much as possible during the first 4 weeks after downloading the app and then again in subsequent “power weeks” (1 per month for 6 months). For sleep duration, participants indicated on the 24-hour wheel the time of falling asleep the previous night and the time of waking up in the current day. Nighttime awakening and daytime naps were not captured. The entries for a given day were considered complete when the participant selected the “done for the day.” To ensure data quality, participants were not allowed to enter information more than 48 hours, retrospectively. If the participants had questions, they reached out to the study staff through emails, phone calls, or text messages. We used multiple engagement strategies to encourage frequent app use during the study period, including text reminders, badges, and raffles.

Based on the timing of sleep and eating occasions, for each day we calculated the duration of the interval from the first to the last meal, from waking to the first meal, and from the last meal to sleep. Sleep duration was calculated as the time from falling asleep to waking up. Meal and sleep intervals were calculated only for complete daily entries, and data from all complete days were averaged across all complete days for each participant.

Study Surveys

Participants completed an online survey at enrollment and were asked to report their weight at baseline and in a 4-month follow-up survey. Race, sex, education, income, smoking status, weight intentions, and behavioral variables were self-reported from the survey at enrollment. Physical activity was collected using the International Physical Activity Questionnaire**29** and categorized into low, moderate, and high activity levels based on duration and intensity. Food intake was collected using the Dietary Screener Questionnaire.**30**

Electronic Health Records

For each participant, we obtained all weight and height information available from up to 10 years before enrollment until 10 months after enrollment from EHR data collected in outpatient visits. Enrollment weight was identified as the EHR weight measurement at the closest visit before the enrollment date. BMI was calculated as weight in kilograms divided by height in meters squared. Baseline and pre-enrollment BMI measurements were calculated from weight and height measurements available in the EHR. For pre-enrollment weights, we used as many outpatient EHR weight measurements as available. For post-enrollment weights, because of the fewer weight measurements available because of the short follow-up period, we used all available outpatient EHR weight measurements, as well as the self-reported weight from the 4-month follow-up survey. The Bland–Altman plot showed good agreement between EHR-derived and the self-reported enrollment weight (Figure S2; Intraclass Correlation Coefficient=0.97). Comorbidities including chronic kidney disease, acute myocardial infarction, chronic obstructive pulmonary disease, heart failure, hypertension, ischemia heart disease, and stroke were obtained from EHR diagnoses and procedure codes obtained from each health system's PCORNet Common Data Model.**31**

Deidentified Token and Data Linkages

A deidentified alphanumeric token (9 characters) was embedded in all enrollment links. Upon consent, participants were asked to provide identifying information (full name, date of birth, and email) enabling staff to confirm eligibility and link each participants' survey data to the EHR. Month of birth was inserted into the token as a check digit. Following enrollment, participants received a text message on their mobile phones with a unique link that included the token to the Daily24 registration form allowing linkage of all participant data (survey, EHR, mobile app).

Statistical Analysis

We compared the baseline characteristics for all participants by BMI categories using ANOVA for means, Kruskal–Wallis for medians, and the $\chi 2$ tests for percentages. We evaluated the association between average meal and sleep-related time intervals and weight trajectories. The primary analysis included all weight measurements available for each participant. In secondary analyses, we separated the weight trajectories in 2 periods, pre-enrollment and post-enrollment.

We created linear mixed effect models to evaluate the associations between each exposure and the longitudinal weight trajectories. The models included time since enrollment, the exposure of interest as a continuous variable (each exposure in a separate model), and interaction terms for the time variable and the exposure. These interaction terms provided estimates for the differences in the slope in the weight trajectory per unit change in exposure. The linear mixed models included random intercepts and random slopes for time. In secondary analyses, time since enrollment was modeled as a linear spline with a knot at enrollment time (time 0).

To control for potential confounders, we evaluated 3 models with progressive degrees of adjustment. Model 1 adjusted for age at enrollment, sex, health center, race, education, physical activity, and height. Model 2 additionally adjusted for smoking, time-varying comorbidities including diabetes, chronic kidney disease, acute myocardial infarction, chronic obstructive pulmonary disease, heart failure, hypertension status, ischemic heart disease, stroke, and number of complete days of using the app for each participant. Additionally, we assessed the associations of all primary and secondary exposure variables of interest in a single, mutually adjusted model.

In sensitivity analyses, we restricted the analyses to participants who completed data entry for ≥21 days, to participants who did not plan to make changes to timing of meals, to participants with same meal patterns for at least the past 2 years, and to weight measurements up to 2 years before enrollment. Two-sided $P<0.05$ was considered statistically significant. All statistical analyses were performed using Stata version 16.0 (StataCorp LP, College Station, TX). With 547 participants and 12 805 records, the covariance matrix among weight measurements of 0.9 and the SD of slope of 0.5, we were able to detect a limit of annual weight change of 0.42 kg, with a CI of 0.95, which was computed from a t distribution using a 2-sided, multivariate statistic.

RESULTS

Enrollment was determined by electronic consent and completion of baseline surveys (n=1017). Enrolled participants then received instructions on how to download the Daily24 mobile application. We excluded participants who did not download the Daily24 app or did not use it for at least 1 day (n=470). The final sample included 547 (54%) participants (Figure S3). Differences between and determinants of participants who downloaded and did not download the application are reported separately.**32** Briefly, participants who downloaded and used the application were younger and more educated (Table S1).

Among the 547 in our sample, the mean (SD) number of weight measurements in the EHR were 23.7 (22.9) overall, 21.3 (21.5) before enrollment, and 3.4 (3.1) in the 6 months after enrollment. The mean (SD) follow-up time of weights in the EHR was 6.3 (SD 2.9) years (Table 1). The mean (SD) times from first to last meal, wake up to first meal, last meal to sleep, and sleep duration of study participants were 11.5 (2.3), 1.6 (1.9), 4.0 (2.1), and 7.5 (1.2) hours, respectively (Table 2). Participants with higher BMI levels at enrollment were more likely to be Black and older, have diabetes or hypertension, have a longer duration from last mealtime to sleep, and were more likely to have lower education, physical activity, less fruit/vegetable consumption, and shorter duration from first to last meal.

Table 1. Characteristics of Study Participants by BMI Categories at Time of Enrollment

	Overall	**BMI categories, kg/m2**			***P* value**[†]
		<25	**25–<30**	**≥30**	
No.	547	138	169	240	
Follow-up time, y	6.3 (2.9)	6.2 (3.1)	6.2 (3.1)	6.4 (2.8)	
Before enrollment	5.9 (2.8)	5.9 (2.9)	5.8 (3.0)	6.0 (2.7)	
After enrollment	0.6 (0.4)	0.6 (0.3)	0.6 (0.4)	0.7 (0.4)	
Annual weight change, kg/y					
Before enrollment	−0.1 (2.8)	0.3 (1.9)	−0.1 (2.2)	−0.3 (3.4)	0.12
After enrollment	0.1 (34.2)	0.4 (27.8)	2.6 (31.1)	−2.9 (41.8)	0.55
Age, y	49.3 (15.0)	46.4 (17.3)	49.7 (15.5)	50.7 (13.0)	0.02
Men, %	110 (20.1)	26 (18.8)	47 (27.8)	37 (15.4)	0.008
Race, %					<0.001
White	437 (79.9)	213 (85.5)	236 (79.5)	339 (72.0)	
Black	67 (12.2)	13 (5.2)	37 (12.5)	99 (21.0)	
Asian	16 (2.9)	17 (6.8)	7 (2.4)	5 (1.1)	
Other (≥2 races)	27 (4.0)	6 (2.4)	17 (5.7)	28 (5.9)	
Education ≥College, %	428 (78.2)	120 (87.0)	139 (82.2)	169 (70.4)	0.001
Current smoking, %	10 (1.8)	2 (1.4)	2 (1.2)	6 (2.5)	0.58
Fruit and vegetables, cup equivalent/day	3.0 (1.4)	3.2 (1.4)	2.8 (1.4)	2.9 (1.4)	0.03
Sugar sweetened beverages, tsp equivalent/day	0.7 (1.2)	0.6 (1.0)	0.8 (1.2)	0.8 (1.3)	0.38
Dairy, cup equivalent/day	1.1 (0.9)	1.1 (0.9)	1.0 (0.8)	1.2 (1.0)	0.05

Physical activity, %					<0.001
Low	184 (33.6)	22 (15.9)	49 (29.0)	113 (47.1)	
Moderate	208 (38.0)	58 (42.0)	65 (38.5)	85 (35.4)	
High	155 (28.3)	58 (42.0)	55 (32.5)	42 (17.5)	
Night eating syndrome, %	6 (14)	0 (0)	1 (7)	5 (21)	0.29
Health-related app use in past 6 mo, %					0.03
0	85 (15.5)	33 (23.9)	24 (14.2)	28 (11.7)	
≤5	406 (74.2)	93 (67.4)	129 (76.3)	184 (76.7)	
>5	56 (10.2)	12 (8.7)	16 (9.5)	28 (11.7)	
Diabetes, %	59 (10.8)	3 (2.2)	13 (7.7)	43 (17.9)	<0.001
Chronic kidney disease, %	54 (9.9)	9 (6.5)	11 (6.5)	34 (14.2)	0.01
Acute myocardial infarction, %	1 (0.2)	0 (0.0)	1 (0.6)	0 (0.0)	0.33
Chronic obstructive pulmonary disease, %	80 (14.6)	14 (10.1)	20 (11.8)	46 (19.2)	0.03
Heart failure, %	13 (2.4)	5 (3.6)	3 (1.8)	5 (2.1)	0.53
Hypertension, %	200 (36.6)	26 (18.8)	50 (29.6)	124 (51.7)	<0.001
Ischemic heart disease, %	38 (6.9)	7 (5.1)	11 (6.5)	20 (8.3)	0.47
Stroke, %	22 (4.0)	4 (2.9)	9 (5.3)	9 (3.8)	0.54

*BMI at the time of enrollment was the electronic health records weight measurement at the closest visit before the enrollment date. Data are mean (SD) or number (percentage). BMI indicates body mass index.
†*P* values were derived from ANOVA or χ2 tests.

Table 2. Interval Duration of Study Participants by BMI Categories at the Outpatient Visit Closest to Enrollment

	Overall	**BMI categories, kg/m2**			***P* value‡**
		<25	**25–<30**	**≥30**	
No.	547	138	169	240	
Time from first to last meal, h*	11.5 (2.3)	11.9 (2.2)	11.5 (2.1)	11.2 (2.4)	0.008
Time from wake up to first meal, h*	1.6 (1.9)	1.5 (1.9)	1.6 (2.0)	1.8 (1.8)	0.49
Time from last meal to sleep, h*	4.0 (2.1)	3.4 (1.2)	4.1 (2.6)	4.2 (2.0)	0.001
Sleep duration, h*	7.5 (1.2)	7.6 (1.0)	7.4 (1.0)	7.5 (1.4)	0.21
No. of meals per day†	3.0 (2.6–3.4)	3.0 (2.5–3.3)	3.0 (2.5–3.4)	3.0 (2.6–3.4)	0.48

No. of large meals per day†	0.2 (0.0–0.6)	0.2 (0.0–0.6)	0.2 (0.0–0.5)	0.3 (0.0–0.6)	0.67
No. of medium meals per day†	1.3 (0.9–1.7)	1.2 (0.9–1.6)	1.2 (0.9–1.6)	1.4 (1.0–1.8)	0.08
No. of small meals per day†	1.2 (0.7–1.8)	1.1 (0.6–1.7)	1.3 (0.7–1.9)	1.2 (0.7–1.7)	0.60

BMI indicates body mass index.
*Data are mean (SD).
†Data are median (interquartile).
‡*P* values were derived from ANOVA or Kruskal–Wallis tests.

Time from first to last meal, wake up to first meal, last meal to sleep, and total sleep duration at enrollment were not associated with weight change over follow-up time (Figure, Table 3). In models adjusted for potential confounders (Model 1), each 1-hour increase in time from first to last meal at baseline was associated with a 0.005 kg (95% CI, −0.08 to 0.09) average annual weight change. The annual weight changes over follow-up associated with time from wake up to sleep, time from last meal to sleep, and sleep duration were 0.02 kg (95% CI, −0.08 to 0.12), 0.07 kg (95% CI, −0.03 to 0.17), and 0.11 kg (95% CI, −0.06 to 0.28), respectively. Results of the fully adjusted model (Model 2) were similar to Model 1. These associations were consistent during the period before and after enrollment, except for time from last meal to sleep, which showed an inverse trend with weight change after enrollment (Table 3).

Table 3. Average Difference of Annual Weight Change (kg) and 95% CIs Per Unit Increase in Interval Durations

	Overall		**Before enrollment**		**After enrollment**	
	Model 1	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Time from first to last meal, h	0.005 (−0.08 to 0.09)	−0.04 (−0.13 to 0.06)	0.01 (−0.08 to 0.09)	−0.04 (−0.14 to 0.06)	−0.03 (−0.73 to 0.67)	0.15 (−0.64 to 0.94)
Time from wake up to first meal, h	0.02 (−0.08 to 0.12)	0.06 (−0.06 to 0.17)	0.00 (−0.10 to 0.11)	0.04 (−0.07 to 0.15)	0.65 (−0.15 to 1.45)	0.62 (−0.27 to 1.50)
Time from last meal to sleep, h	0.07 (−0.03 to 0.17)	0.06 (−0.04 to 0.16)	0.09 (−0.02 to 0.19)	0.07 (−0.03 to 0.18)	−0.54 (−1.36 to 0.27)	−0.64 (−1.47 to 0.19)
Sleep duration, h	0.11 (−0.06 to 0.28)	0.18 (−0.01 to 0.37)	0.10 (−0.07 to 0.27)	0.17 (−0.02 to 0.37)	0.49 (−0.87 to 1.85)	0.36 (−1.23 to 1.94)
No. of meals per day	0.33 (0.09 to 0.56)†	0.28 (0.02 to 0.53)†	0.33 (0.08 to 0.57)†	0.27 (0.01 to 0.53)†	0.34 (−1.63 to 2.32)	0.60 (−1.56 to 2.76)
No. of large meals per day	0.69 (0.19 to 1.18)†	0.56 (0.05 to 1.07)†	0.64 (0.13 to 1.15)†	0.51 (−0.01 to 1.03)	2.52 (−1.44 to 6.49)	2.64 (−1.52 to 6.80)
No. of medium meals per day	0.97 (0.64 to 1.29)†	0.99 (0.65 to 1.33)†	0.95 (0.61 to 1.28)†	0.96 (0.61 to 1.31)†	1.62 (−1.00 to 4.24)	2.25 (−0.50 to 4.99)
No. of small meals per day	−0.30 (−0.53 to −0.07)†	−0.37 (−0.61 to −0.12)†	−0.27 (−0.51 to −0.04)†	−0.34 (−0.59 to −0.09)†	−1.12 (−2.97 to 0.74)	−1.32 (−3.31to 0.67)

*Model 1 adjusted for age at consent (continuous, year), sex (men; women), center (Geisinger; Johns Hopkins University; Pittsburgh), race (White; Black; Asian; Pacific Islander, American Indian, others; ≥2 races), education (≤high school; some college; ≥college), physical activity (low; moderate; high), height (continuous, meter).

Model 2 additionally adjusted for current smoking (yes, no), time-varying diabetes (yes, no), chronic kidney disease (yes, no), acute myocardial infarction (yes, no), chronic obstructive pulmonary disease (yes, no), heart failure (yes, no), hypertension status (yes, no), ischemia heart disease (yes, no), stroke (yes, no), and number of complete days for using app (continuous, days).

†indicates $P<0.05$.

Total daily number of large and medium meals was associated with increased weight over follow-up time, while total number of small meals was associated with decreasing weight. The average annual weight changes (95% CI) associated with a daily increase of one large, medium, or small meal were 0.69 kg (95% CI, 0.19–1.18), 0.97 kg (95% CI, 0.64–1.29), and −0.30 kg (95% CI, −0.53 to −0.07), respectively. These associations of number of meals with weight trajectory were consistent before enrollment and after enrollment, although the associations after enrollment did not reach the level of statistical significance.

In sensitivity analyses excluding participants who used the app for a shorter duration (ie, <21 days of usage, Table S2), the association between time from wake up to first meal with weight gain was stronger. We also performed sensitivity analyses among participants who self-reported not planning to change their meal timing (ie, used to assess stability of their eating patterns over time) (Table S3), among participants with <5% weight change in 3 months after enrollment (Table S4), among participants with weight measures up to 2 years before enrollment (Table S5), among participants with same meal patterns for at least the past 2 years (Table S6), and in analyses in which interval variables were mutually adjusted for one another (Tables S7 and S8). Results from these additional analyses were consistent with the main analysis.

DISCUSSION

In this EHR-based retrospective and prospective cohort composed of men and women with linked mobile application recorded data, online surveys, and repeated EHR outpatient weight measurements, the window of time between first to last meal was not associated with weight change over an average of about 6 years of follow-up. However, the average daily number of large and medium meals was associated with increased weight over time, suggesting that the meal frequency and meal sizes, rather than the timing of meals, was a stronger determinant of weight gain over time. Our analysis also suggested that some dietary behaviors, such as the total number of meals per day, may be representative of long-term dietary patterns and were associated with weight trajectories up to 10 years before the time of dietary measurements.

Although experimental studies have suggested that time-restricted eating could improve circadian rhythms and play a role in metabolic regulation,**7**, **33** our study did not detect an association in a population with a wide range of body weights. In a small pilot study (n=8) of participants whose dietary assessment was collected with a mobile application, reducing the daily eating duration contributed to weight loss over 16 weeks.**10** In another pilot study (n=10) of elderly overweight adults, time-restricted feeding resulted in 2.6 kg weight loss after 4 weeks' time-restricted feeding intervention.**34** Nevertheless, in randomized clinical trials of up to 116 overweight or obese participants, up to 1 year after intervention, time-restricted eating did not increase weight loss compared with no intervention or consistent meal timing schedule.**12**, **13**, **14** Our finding of a lack of association between the time from first to last meal and weight changes was consistent with the results of these clinical trials.

Importantly, we found an association between the eating of more frequent and larger meals per day and weight increase, indicating that total overall caloric intake is the major driver of weight gain. In randomized clinical trials of women who are lean (n=9),**35** overweight (n=10),**36** or obese (n=30),**37** greater meal frequency without additional caloric restriction did not change body weight after follow-up between 2 to 8 weeks. Conversely, a crossover trial of 15 adults with normal-weight showed that reduced meal frequency led to weight loss at 8 weeks.**38** Two large longitudinal studies, the Adventist Health Study 2 with 50 660 participants and 7 years of follow-up, and the Health Professionals Follow-up Study with 20 064 participants and 10 years of follow-up, found an association between greater eating frequency and increased weight gain.**24**, **25** On the contrary, the NHANES (National Health and Nutrition Examination Survey) I

Epidemiologic Follow-up Study, with 7147 participants and 10 years of follow-up, did not find an association between eating frequency and weight changes.**39** Finally, cross-sectional studies have shown different associations between eating frequency and BMI, ranging from positive,**40** to null,**20** to inverse associations.**21**, **22**, **23** The discrepant findings may be attributable to lack of standard approaches to define or measure eating behaviors, as eating frequency was measured using single-day 24-hour dietary recall,**21**, **23**, **40** daily food booklet,**20** or questionnaire that included both snacks and meals.**22** Discrepancy may also be attributable to differences in study design, or to differences in adjustment for confounders.

The mechanisms for the association between meal frequency and weight gain is unknown. While some studies suggested that increased meal frequency could lead to higher energy intake,**19**, **20** other randomized trials did not show an effect of eating frequency on total energy intake or expenditure.**41**, **42**, **43**, **44** Conversely, higher eating frequency could be associated with meals with fewer meal sizes in both men and women.**45** Our understanding of the effects of varying meal frequency is still incomplete, and additional research in this area is warranted.

In the prospective component of our analysis, participants with shorter time from wake up to first meal and with longer time from last meal to sleep appeared to have less weight increase. This trend suggested that consuming energy early in the day might facilitate weight control. This finding is consistent with 2 cohort studies conducted in Spain**18** and the United Kingdom.**46** Also, other cross-sectional and prospective cohort studies have found that skipping breakfast and night eating were associated with increased adiposity.**47**, **48** In fact, the American Dietetic Association guideline on weight management suggests that energy consumption during the day is preferable to eating in the evening.**49** On the other hand, meta-analyses of randomized clinical trials showed that skipping breakfast reduced weight in the short term.**50** These inconsistent results could indicate differences in the short-term versus the long-term effects of meal timing on weight change. The distribution of total energy consumed in the day may not have immediate short-term effects on weight, as reflected in clinical trials, but could implicate a long-term effect on energy metabolism and weight changes. More large-scale prospective studies with precise measurements of meal timing are needed to understand the long-term associations.

Some limitations need to be considered in the interpretation of our findings. First, about half of all enrolled participants did not use the Daily24 app and had to be excluded from this analysis. Excluded participants were younger and less educated, so the study population may not be representative of the entire cohort population. Second, the follow-up after enrollment was short (mean of 0.6 years) compared with before-enrollment period (mean of 5.9 years), and the associations between eating exposures and weight for the prospective associations were less precise likely because of fewer weight measurements. Third, we were not able to determine the intentionality of the weight loss before enrollment and cannot rule out the possibility of reverse causation because of pre-existing illness. Nevertheless, in sensitivity analysis restricting to participants who did not plan to make changes to dietary patterns, and to participants with <5% weight loss after enrollment, the results were similar. Fourth, we used averages of the eating periods across the days of Daily24 app use. Even though we adjusted for the number of meals, we could not evaluate complex time-restricted eating or fasting behaviors such as fasting 1 day per week or skipping the middle meal each day. Fifth, meal sizes were estimated by the participants and not standardized between participants. Dietary quality in this study was not evaluated. Finally, participants were recruited from patients engaged in care at 3 health systems, so the findings may not be generalizable to the general population who may seek care less frequently.

The strengths of our study included repeated measures of weight and other clinical covariates from the EHR, the evaluation of long-term association between eating window and weight change, detailed information and adjustment on obesity risk factors and covariates, and the real-time assessment of eating behaviors. Participants were able to record their meal and sleep episodes any time for multiple days, and the measurements could be less subject to recall bias compared with 24-hour recall or food frequency questionnaire, the methods mostly used in previous studies. However, we have not evaluated the validity of the dietary measurements by the mobile application against more traditional food frequency registries.

In conclusion, in this clinically based prospective cohort, the number of large and medium meals was positively associated with weight change, while number of small meals was inversely associated with weight change. The distribution of energy intake earlier during the day appeared to be associated with less weight increase after enrollment. Duration from first to last meal, as well as other meal patterns, did not show a clear association with weight trajectory. Our findings did not support the use of time-restricted eating as a strategy for long-term weight loss. Further large-scale studies with long follow-up time are needed to better characterize the association for time of eating with weight change.

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Disclosures

Outside of this work, Dr Clark served as a scientific advisor for NovoNordisk and Boehringer Ingelheim. Dr Woolf helped found DaiWare, which developed the software under a service contract with Johns Hopkins University and with funding from the American Heart Association. There are no current plans to commercialize the Daily24 app used in this project, and this project was not initiated with any funds from DaiWare. None of the other authors report any disclosures.

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Footnotes

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