British Journal of Nutrition (2022), 128, 324–333 doi:10.1017/S0007114521002944

Eating architecture in adults at increased risk of type 2 diabetes: associations with body fat and glycaemic control

Lijun Zhao[1,2,3], Xiao Tong Teong[1,2,3], Kai Liu[1,2,3], Bo Liu[1,2,3], Yohannes Adama Melaku[4], Andrew Vincent[1], Emily Manoogian[5], Satchidananda Panda[5], Gary A. Wittert[1,2,3], Amy Hutchison[1,2,3] and Leonie K. Heilbronn[1,2,3]*

[1]*Adelaide Medical School, University of Adelaide, Adelaide, SA 5000, Australia*
[2]*NHMRC Centre of Research Excellence in Translating Nutritional Science to Good Health, University of Adelaide, Adelaide, SA, Australia*
[3]*Lifelong Health Theme, South Australian Health and Medical Research Institute, Adelaide, SA 5000, Australia*
[4]*Adelaide Institute for Sleep Health, College of Medicine and Public Health, Flinders University, Adelaide, SA 5000, Australia*
[5]*Salk Institute for Biological Studies, La Jolla, CA, USA*

(Submitted 23 February 2021 – Final revision received 5 July 2021 – Accepted 2 August 2021 – First published online 5 August 2021)

Abstract

Eating architecture is a term that describes meal frequency, meal timing and meal size and the daily variation in each of these. The aim of this study was to determine the relationship between components of eating architecture on body fat and markers of glycaemic control in healthy adults at increased risk of type 2 diabetes (T2DM). Participants (*n* 73, 39 males, age 58·8 (8·1) years, BMI 33·4 (4·4) kg/m^2) recorded food intake and wore accelerometers and continuous glucose monitors (CGM) for 7–14 d under free-living conditions. Body fat and glycated Hb (HbA1c) were also measured. The mean and day-to-day variation (calculated as the standard deviation during the monitoring period) of each component of eating architecture were calculated. Multivariable linear regression models were constructed for three separate outcome variables (body fat mass, mean CGM glucose and HbA1c) for each component of eating architecture before and after adjustment for confounders. Higher variability in the time of first meal consumption was associated with increased body fat mass after adjusting for confounders ($\beta = 0{\cdot}227$, 95 % CI: 0·019, 0·434, $P = 0{\cdot}033$). Increased variability in the time lag from waking to first meal consumption was also positively associated with increased HbA1c after adjustment ($\beta = 0{\cdot}285$, 95 % CI: 0·040, 0·530, $P = 0{\cdot}023$). Low day-to-day variability in first meal consumption was associated with lower body fat and improved glucose control in adults at increased risk of T2DM. Routine consumption of meals may optimise temporal regulation to anticipate and respond appropriately to a glucose challenge.

Key words: **Meal timing: Meal regularity: Obesity: Glycaemia control: Breakfast**

Eating architecture refers to when and how much, rather than what, we eat[1,2], and encompasses the concepts of meal frequency, meal size (or energetic density), meal regularity and meal timing (Fig. 1). There is renewed interest in the concept of eating architecture as meal timing has emerged as a strong external cue that regulate circadian clock genes in peripheral tissues, such as liver, gut and adipose tissue in rodent models[3,4]. In humans, delaying breakfast by 5 hours delayed the expression of *period 2* by 1 hour in adipose tissue from healthy individuals[3]. Whereas eating dinner late at night inverted the daily rhythm of salivary microbiota[5] and increases the cortisol nadir, impairing glycaemic control the following morning[6]. The most studied form of eating architecture in the literature is 'breakfast skipping'. Breakfast skipping is associated with an increased risk of developing type 2 diabetes (T2DM) in epidemiological studies[7–10]. Other studies suggest that skipping breakfast plus concomitant late evening meals was associated with poorer glycaemic control in patients with T2DM[11,12]. Randomised controlled trials investigating whether breakfast skipping alters health have produced mixed results[13–15]. In the largest study conducted to date, breakfast skipping did not produce a greater body weight loss in 147 free-living adults attempting to lose weight over 16 weeks *v.* breakfast eaters[15]. However, a recent systematic review of seven randomised clinical trials showed that breakfast skipping reduced body weight by 0·5 kg, but increased low-density cholesterol by 9 mg/dl[16]. Late night eating and irregular energy intake and snacking between meals are also associated with increased risk of

Abbreviations: CGM, continuous glucose monitors; IF, intermittent fasting; T2DM, type 2 diabetes.

* **Corresponding author:** Leonie K. Heilbronn, email leonie.heilbronn@adelaide.edu.au

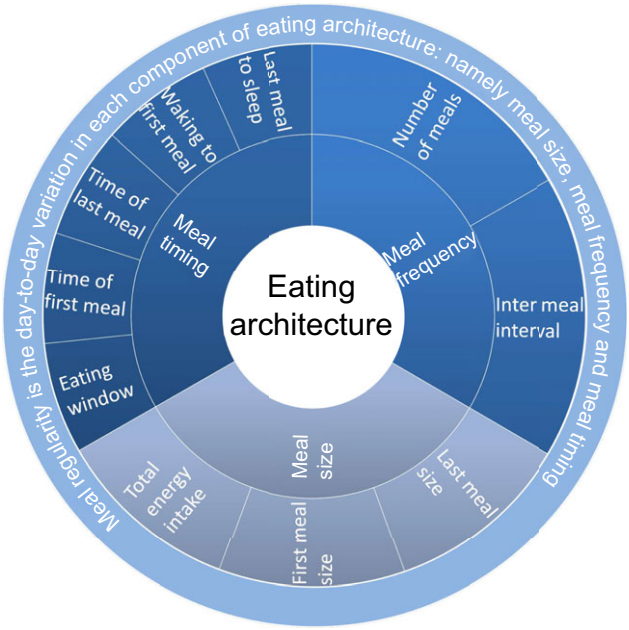

Fig. 1. Eating architecture components.

adiposity and cardiovascular diseases (CVD) and poorer glucose control[6,17–21]. Irregular energy intake and snacking between meals has also been positively associated with BMI, waist circumference[22] and increased CVD risk at > 10 years follow-up[23].

Typically, all of the epidemiological studies referenced above have relied on 24-h recalls or have asked a single question regarding usual eating habits. However, meals are highly personalised and highly variable from day to day[22,24,25]. To our knowledge, there is no study that has investigated the variation in components of eating architecture and measures of obesity or glucose control in real time over 1–2 weeks either in the general population or in those at increased risk of obesity or T2DM, who would likely benefit most from this knowledge given they are more likely to have irregular eating patterns[26,27] and dampened peripheral clocks in adipose tissue and skeletal muscle[28,29]. Therefore, we hypothesised that high variability in components of eating architecture, and particularly the first meal of the day, would positively associate with outcomes, body fat mass as a marker of obesity, HbA1c and mean 24-h glucose by CGM as markers of overall glycaemic control in men and women at increased risk of T2DM.

Materials and methods

Participants

Data analysed in this study were baseline information from two registered clinical trials (ClinicalTrials.gov Identifier: NCT03590158 and NCT03689608, respectively), which were collected between July 2018 and June 2020. Ethics approval for both studies was obtained from Central Adelaide Local Health Network (CALHN) Human Research Ethics Committee and participants provided written informed consent. Use of the MyCircadianClock application was approved by Salk Institute Institutional Review Board[30,31]. Inclusion criteria were aged between 35 and 75 years old, score 12 or greater on the Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK) calculator[32], without diabetes, non-shift workers, weight-stable (< 5 % fluctuation in their body weight for past 6-months at study entry). All participants were assessed for their risk of developing diabetes by the Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK) score determined by gender, ethnicity, BMI, waist circumference, exercise level, family or personal hypoglycaemia history and vegetable and fruit consumption[32]. A score of 9 to 11 indicates intermediate risk (1 in 30 will develop diabetes within 5 years), 12 to 15 indicates high risk (1 in 14), 16 to 19 indicates very high risk (1 in 7) and ≥ 20 indicates 1 in 3 will develop diabetes within 5 years. Participants who took medications that might affect glucose metabolism and HbA1c, and smokers were excluded. Women who were pregnant or lactating at the time of study enrolment were not eligible.

Eligible participants underwent a 1- to 2-week baseline monitoring period prior to the baseline metabolic test. During this monitoring period, participants were fitted with an Actigraph (wGT3X-BT, ActiGraph LLC) to measure sleep patterns and physical activity (steps per day) (ActiLife software, version 6.13.3). A continuous glucose monitor (CGM; FreeStyle Libre Pro, Abbott) was also fitted on the back of the upper arm of the non-dominant hand. This measured blood glucose levels every 15 min for the duration of the baseline monitoring period. One of two smartphone applications (app), myCircadianClock (mCC; https://mycircadianclock.org/)[30,31] and Easy Diet Diary (https://xyris.com.au/products/easy-diet-diary/)[33], were used to photograph and annotate meal timing and eating/drinking events.

Of the 122 participants from both studies who wore CGM, forty-nine participants excluded from the analysis for the following reasons: incomplete food records (thirty-four participants; meal timing not documented or poorly documented), missing ActiGraph data (four participants) and missing CGM data (seven participants with < 72 h CGM data, four participants with technical issues where the CGM failed to collect data). As such, a total of seventy-three (46·6 % females) participants were included in the final analysis (Fig. 2).

At the end of the baseline monitoring period, whole body composition was assessed by dual-energy X-ray absorptiometry (Lunar Prodigy; GE Health care, Madison, Wisconsin) and analysed by EnCore software (GE Healthcare; version 16.2). Body weight was measured on calibrated scales with participants in the fasted state, in a gown and after voiding. Waist circumference was measured at the mid-point between the participant's lowest rib and the top of the iliac crest. Blood samples were taken to evaluate HbA1c using commercially available enzymatic kits on an AU480 clinical analyzer (Beckman Coulter, Inc.). Sleep on and sleep off time were obtained from ActiGraph and markers reflecting sleep–meal relationship were calculated as defined in the following section.

Continuous glucose monitoring

Days for which any of CGM data were not recorded was excluded from the analysis, including the day when the CGM

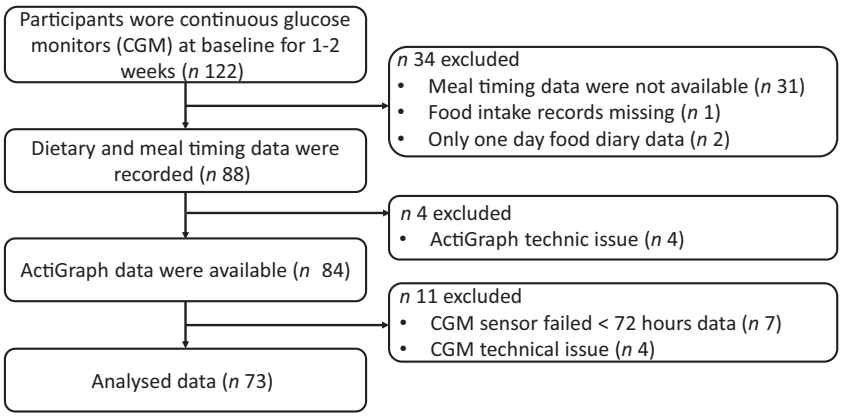

Fig. 2. Participant flow chart.

was put on, and the day when it was taken off. If the CGM accidentally fell off at any point prior to the scheduled end of testing, that day was also excluded. 24-h mean blood glucose was calculated as the mean of the daily 96 readings and 24-h SD as the standard deviation of these 96 readings. The 24-h mean glucose in the following analysis was calculated as the average glucose on all recording days. Each CGM glucose reading was counted as one data point, and the data were summarised from midnight to midnight for each participant. For diurnal variations of glucose metrics, daytime was defined as 06.00 to 00.59 and night time as 01.00 to 05.59 (only <0·5 % of eating events occurred during these hours, Fig. 3(b)).

Smart phone applications for food intake

Participants who used the mCC app were asked to photograph all eating events prior to any food and/or drink consumption (*n* 28). Annotation was used to describe what they ate, while the app provides a timestamp to note when they ate. Participants who used the Easy Diet Diary app also photographed all eating events and annotated the food they ate (*n* 45). They were required to record the time the meal was consumed manually as an annotation. Only participants with ≥ 2 recording days and meal frequency ≥ 2 times per day were included in the analysis. Total energy, fat, protein, carbohydrate and fibre intakes were estimated from the food images and annotations by nutritionally trained researchers using FoodWorks (Version 10, Xyris Software) with meal timing aligned from the apps. The reliability of digital photographs to estimate energy intake by trained investigators has previously been validated against weighed food records. In this study, they were utilised to obtain a timestamp of food consumption as we were primarily interested in meal timing[34].

Definition of eating event, meal and snacks and eating architecture components

The metabolic recording day was defined as from 03.00 on day 1 to 03.00 on day 2 in our dataset as very few eating events occurred between 03.00 and 04.00 (Fig. 3(b)). The following definitions were applied to food intake data that generated through FoodWorks based on the information from smartphone apps.

1. *Eating event*: any food/drink (except water) consumed at a unique time was considered an eating event[31,35]; this included drinks such as black coffee or artificial sweeteners[36,37].
2. *Hourly percentage of eating events*: percentage of all eating events in 1 h bin. It was calculated as eating events at each hour divided by the total eating events.
3. *Meal*: classified as all eating event only if they occurred within 15 min of a preceding eating event, including main meals and snacks.
4. *Meal frequency*: the number of meals on each recording day including meals after midnight.
5. *Inter-meal* interval: the average time difference between two subsequent meals during each recording day (e.g., if there were two eating events 14 min apart within a meal, and then another meal 2 h later, inter-meal interval was counted from the second eating event); then mean values of recording days were calculated.
6. *Time of the first meal*: depicted as the time of first meal (HH:MM) which occurred after 03.00.
7. *Time of the last meal:* depicted as the time of last meal (HH:MM). If the time of a meal occurred after midnight but before 03.00, this was recorded as the time of the last meal of the previous day.
8. *Eating window:* the duration between the first and the last meal within a day (hours) and was obtained by subtracting the first from the last recorded time of eating from the 95 % (2·5 %tile to 97·5 %tile) of all energy-containing eating events occur during the monitoring period.
9. *Percentage of energy in first/last meal:* the energy content of the first/last meal divided by total energy intake on each recording day.
10. *Total energy intake:* the mean daily energy intake.
11. *Meal timing relative to sleep onset/wake*: time lag from wake to the first meal (wake to first meal) and time lag from the last meal to sleep onset (last meal to sleep onset).
12. *Meal regularity*: day-to-day variation of each component of the eating architecture. Calculated as the standard deviation of each eating architecture component during the monitoring period for each participant.

Outcome measures

Outcome measures included body fat mass, 24-h mean glucose and HbA1c. The body fat mass covariate-unadjusted model (model 1) was first adjusted for age, sex, fat free mass, app type (shown as model 2) and further adjusted for physical activity,

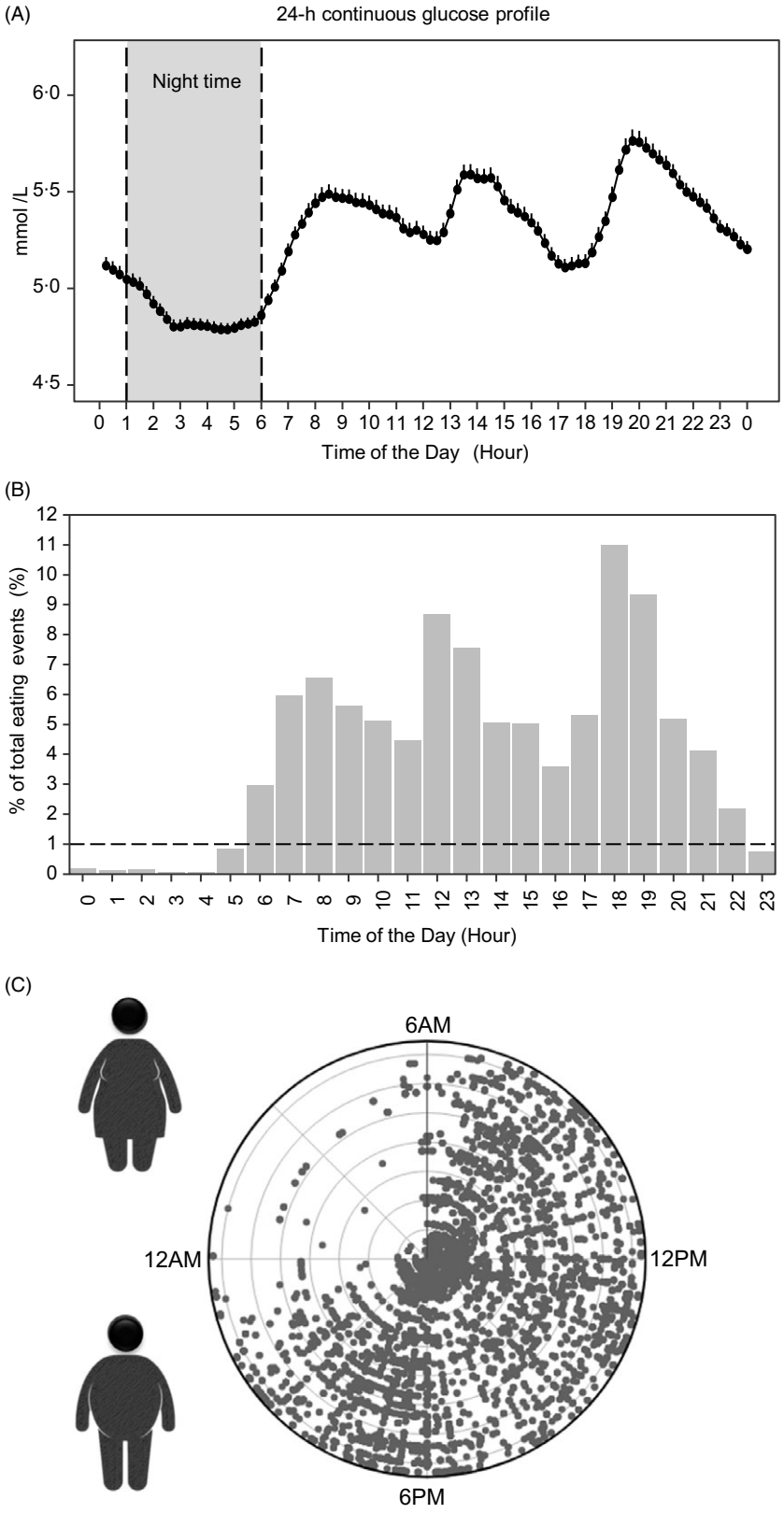

Fig. 3. Distribution of eating events around the day and 24-hour continuous glucose profile.

British Journal of Nutrition

total energy intake and total sleep time (shown as model 3). The HbA1c and glucose unadjusted models (model 1) were first adjusted for age, sex, app type, waist circumference, BMI (shown as model 2) and further adjusted for the percentage of energy intake from carbohydrates (shown as model 3).

Statistical methods

Calculations of eating architecture components were performed after synchronising data from food records, activity and sleep patterns and continuous glucose levels in real time. Data are presented as mean ± SD. Mann–Whitney *U* test was applied to assess the difference between mean percentage of energy in first meal and mean percentage of energy in last meal. Linear regression models were constructed with each eating architecture component as predictors. To ensure that the assumption of normality did not affect the performance of the models, we assessed quanitle–quanitle plots of the residuals of each model. Where necessary, dependent variables were log transformed before the regression (body fat mass). Each eating architecture variable was investigated independently of the others, i.e. each model had only one eating architecture component included as the predictor. All regression coefficients (β) were reported as standardised estimates with a 95 % confidence interval. Plots and statistical analysis were performed using R software (version 3.6.1; The R Foundation for Statistical Computing, Vienna, Austria) and its interaction software jamovi (Version 1.1) with the significance level set at 0·05.

Results

Baseline characteristics

Caucasians (*n* 73, 34 females, 39 males, mean ± SD, age 58·8 ± 8·1 years, BMI 33·4 ± 4·4 kg/m^2) with elevated waist circumference (113 ± 13 cm) were included in the final analysis (Table 1). The average body fat mass and lean mass were 38·6 ± 10·4 kg and 59·2 ± 11·9 kg, respectively. Sleep patterns showed that the total sleep time was 7·7 ± 1·1 h with sleep onset time at 22:48 ± 1:07 and sleep offset time at 6:56 ± 0:59. The group mean of average 24-h glucose was 5·3 ± 0·6 mmol/l (Fig. 3(a)), and HbA1c was 5·5 ± 0·4 %. The glucose distribution over 24-h is shown in Fig. 3(a); mean glucose during the daytime was 5·4 ± 0·6 mmol/l and 4·9 ± 0·6 mmol/l during the night.

Eating architecture

Eating events peaks occurred at 08.00, 12.00 and 18.00 (Fig. 3(b)). The 95% (2·5–97·5 percentile) eating window was 11·5 ± 2·0 h, with a variation in the day-to-day eating window of 2·0 ± 1·5 h (Table 2, note: the SD in this table represents the daily variation between participants). A polar plot shows the eating events spread against the clock time (Fig. 3(c)) and more clearly depicts the day-to-day within-individual variation in meal timing. The mean inter-meal duration was 187 ± 59 min with a mean day-to-day variation of 46 ± 24 min. The mean time of the first meal and last meal was 08:30 ± 01:24 and 19:48 ± 13:24, respectively, with a similar day-to-day variation of 84 min. Meal frequency was on average 5·0 ± 1·5 times/day with 1·2 ± 0·6 times/d variation between days. Average reported daily total energy intake was 8405 ± 2056 kJ with 2250 ± 1326 kJ day-to-day variation in daily energy intake, and more food was consumed during the last meal of the day than the first meal of the day (26·1 ± 13·7 % *v.* 19·6 ± 9·44 %, $P < 0·001$). Substantial day-to-day variations in percentage of energy intake in the first (10·5 ± 6·7 %) and last (14·6 ± 7·1%) meals were observed. The average time lag from waking to first meal was 114 ± 57 min, and time lag from last meal to sleep was 197 ± 90 min, with 78 ± 48 min and 88 ± 81 min daily variation, respectively.

Table 1. Participants' characteristics (Mean values and standard deviations)

	All (*n* 73)	
	Mean	SD
Sex (*n*, female/male)	34/39	
Age at recruitment (year)	58·8	8·1
Height (m)	1·7	0·1
Weight (kg)	98·2	16·3
BMI (kg/m^2)	33·4	4·4
Waist circumference (cm)	113	13
Glycated haemoglobin (%)	5·5	0·4
Body fat mass (kg)†	38·6	10·4
Fat-free mass (kg)†	59·2	11·9
Sleep onset time (HH:MM)‡	22:48	01:07
Sleep offset time (HH:MM)‡	06:56	00:59
Total sleep time (h)‡	7·7	1·1
Steps per day (steps)‡	10 351	5447

† *n* 67.
‡ *n* 69.

Table 2. Characteristics of eating pattern components (Mean values and standard deviations)

	All (*n* 73)	
	Mean	SD
Meal timing		
Eating window (h)	11·5	2·0
Inter-meal interval (min)	187	59
Time of first meal (HH:MM)	08:30	01:24
Time of last meal (HH:MM)	19:48	01:24
Time lag from last meal to sleep (min)†	197	90
Time lag from wake to first meal (min)†	114	57
Meal frequency		
Number of meals/day (times/d)	5·0	1·5
Meal size		
Total daily energy intake (kJ)	8405	2056
Percentage of energy in first meal (%)	19·6	9·4
Percentage of energy in last meal (%)	26·1	13·7
Meal regularity		
Eating window (h)	2·0	1·5
Time of first meal (min)	84	78
Time of last meal (min)	84	60
Inter-meal interval (min)	46	24
Time lag from last meal to sleep onset (min)†	88	81
Time lag from wake to first meal (min)†	78	48
Meal frequency (times/d)	1·2	0·6
Total daily energy intake (kJ)	2252	1326
Percentage of energy in first meal (%)	10·5	6·7
Percentage of energy in last meal (%)	14·6	7·1

† *n* 69.

British Journal of Nutrition

Table 3. Associations between body fat mass and each component of eating pattern after adjustment of confounders* (coefficient values and 95 % confidence intervals)

	Model 1			Model 2			Model 3		
	P trend	*β*	95 % CI	*P* trend	*β*	95 % CI	*P* trend	*β*	95 % CI
Meal timing									
Eating window	0·02	−0·30	−0·54, −0·05	0·14	−0·16	−0·36, 0·05	0·25	−0·12	−0·32, 0·09
Inter-meal intervals	0·69	0·05	−0·21, 0·31	0·77	0·03	−0·19, 0·25	0·59	0·07	−0·18, 0·31
Time of first meal	0·05	0·26	0·01, 0·51	0·03	0·22	0·02, 0·41	0·09	0·17	−0·03, 0·37
Time of last meal	0·22	−0·16	−0·41, 0·10	0·84	−0·02	−0·24, 0·19	0·99	0·11	−0·21, 0·21
Last meal – sleep	0·04	0·27	0·02, 0·52	0·55	0·07	−0·15, 0·28	0·69	0·05	−0·18, 0·27
Waking – first meal	0·29	0·14	−0·12, 0·40	0·60	0·05	−0·15, 0·25	0·82	0·02	−0·18, 0·23
Meal frequency									
Number of meals	0·27	−0·14	−0·40, 0·11	0·40	−0·09	−0·30, 0·12	0·36	−0·11	−0·34, 0·12
Meal size									
First meal size	0·97	0·01	−0·25, 0·26	0·53	0·07	−0·14, 0·27	0·63	0·05	−0·16, 0·26
Last meal size	0·04	0·26	0·01, 0·51	0·30	0·12	−0·11, 0·34	0·33	0·11	−0·12, 0·33
Meal regularity									
Meal timing									
Eating window	0·82	−0·03	−0·29, 0·23	0·13	0·16	−0·05, 0·37	0·17	0·16	−0·07, 0·38
Inter-meal intervals	0·81	−0·03	−0·29, 0·23	0·76	0·03	−0·17, 0·23	0·61	0·05	−0·14, 0·24
Time of first meal	0·52	0·08	−0·17, 0·34	0·03	0·22	0·02, 0·42	0·03	0·23	0·02, 0·43
Time of last meal	0·46	−0·10	−0·35, 0·16	0·92	−0·01	−0·22, 0·19	0·67	−0·04	−0·25, 0·16
Last meal – sleep	0·78	−0·04	−0·31, 0·23	0·81	0·03	−0·19, 0·25	0·87	0·02	−0·21, 0·25
Waking – first meal	0·85	−0·03	−0·29, 0·24	0·86	−0·02	−0·23, 0·19	0·51	−0·07	−0·26, 0·13
Meal frequency									
Number of meals	0·18	−0·17	−0·43, 0·08	0·99	0·00	−0·23, 0·23	0·71	−0·04	−0·28, 0·19
Meal size									
First meal size	0·50	−0·09	−0·35, 0·17	0·94	0·01	−0·21, 0·23	0·66	−0·05	−0·28, 0·18
Last meal size	0·96	−0·01	−0·27, 0·25	0·87	−0·02	−0·22, 0·18	0·33	−0·10	−0·29, 0·10

* Linear regression analyses were performed to estimate strength of associations between log 10 transformed body fat mass and each component of eating architecture without covariate adjustment model 1 and multivariable models adjusting for age, gender, fat-free mass, application-type model 2, and model 2 plus the physical activity, total energy intake and total sleep time model 3. *β* are the standardised coefficients; 95 % CI.

Associations between components of eating architecture and metabolic health markers

As shown in Table 3, later consumption of the first meal was associated with increased body fat mass before (model 1, $P = 0{\cdot}05$, $\beta = 0{\cdot}26$, 95 % CI: 0·01, 0·51) and after adjustment of age, sex, fat-free mass and app type (model 2, $P = 0{\cdot}03$, $\beta = 0{\cdot}22$, 95 % (CI): 0·02, 0·41). A trend was evident after further adjustment of physical activity, total energy intake and total sleep time (model 3, $P = 0{\cdot}09$, $\beta = 0{\cdot}17$, 95 % CI: −0·03, 0·37) (Table 3). Higher day-to-day variability in the time of first meal consumption was associated with higher body fat mass after adjusted for age, sex, fat-free mass and app type (model 2: $P = 0{\cdot}03$, $\beta = 0{\cdot}22$, 95 % CI: 0·02, 0·42) and further adjusted by physical activity, total energy intake and total sleep time (model 3: $P = 0{\cdot}03$, $\beta = 0{\cdot}23$, 95 % CI: 0·02, 0·43) (Table 3). There were no significant associations between other eating architecture components and body fat mass after adjustment for confounders as shown in Table 3. There were no significant associations between any eating architecture components and mean glucose by CGM as shown in Supplementary Table S1. There was a positive association between HbA1c and day-to-day variation in the time lag from waking to the first meal before (model 1, $P = 0{\cdot}02$, $\beta = 0{\cdot}30$, 95 % CI: 0·06, 0·54) and after adjustment for age, sex, app type, BMI and waist circumference (model 2, $P = 0{\cdot}02$, $\beta = 0{\cdot}28$, 95 % CI: 0·04, 0·52) and further adjustment for percentage of energy intake from carbohydrates (model 3, $P = 0{\cdot}02$, $\beta = 0{\cdot}29$, 95 % CI: 0·04, 0·53) (Table 4).

Discussion

In this cross-sectional study in adults at risk of T2DM, eating breakfast earlier and smaller variation in the daily timing of breakfast were both associated with decreased body fat mass. Less day-to-day variation in the size of the first meal and the time lag from waking to the first meal were also associated with improved glycaemic control in this population.

Observational studies have shown associations between meal irregularity and cardio-metabolic health[9,18,22,25,38–45]. Most of the previous population-based studies have investigated the relationship between frequency of breakfast consumption and weight status by categorising participants into either daily breakfast consumers or have combined never eating breakfast with irregular breakfast consumption[25,39,41–45]. Additionally, the data are typically collected by a single 24-h recall or a single question about breakfast habits[38,43,46], which may not represent habitual eating patterns[47]. Guinter *et al.* were first to investigate the day-to-day regularity in breakfast consumption in the Sister study cohort of 46 037 women in relation to weight status after stratifying the frequencies of breakfast consumption per week (0 d/week, 1–2 d/week, 3–4 d/week, 5–6 d/week and 7 d/week)[25]. Compared with irregular breakfast eaters (3–4 d/week), regular daily breakfast eaters (7 d/week) and those who never ate breakfast (0 d/week) were less likely to be obese and showed a decreased risk of 5-year incidence of overweight and obesity[25]. However, this study did not examine the relationship between day-to-day variation in breakfast size or timing and obesity and

British Journal of Nutrition

Table 4. Associations between glycated haemoglobin HbA1c and each component of eating pattern after adjustment of confounders* (coefficient values and 95 % confidence intervals)

	Model 1			Model 2			Model 3		
	P trend	*β*	95 % CI	*P* trend	*β*	95 % CI	*P* trend	*β*	95 % CI
Meal timing									
Eating window	0·97	0·01	−0·23, 0·24	0·30	−0·13	−0·38, 0·12	0·30	−0·13	−0·39, 0·12
Inter-meal intervals	0·38	−0·11	−0·34, 0·13	0·53	−0·08	−0·33, 0·17	0·53	−0·01	−0·33, 0·17
Time of first meal	0·91	−0·01	−0·25, 0·22	0·74	0·04	−0·21, 0·29	0·74	0·04	−0·22, 0·30
Time of last meal	0·99	0·00	−0·24, 0·24	0·50	−0·09	−0·34, 0·17	0·49	−0·09	−0·36, 0·17
Last meal – sleep	0·94	0·01	−0·24, 0·26	0·34	0·13	−0·14, 0·39	0·34	0·13	−0·14, 0·39
Waking – first meal	0·22	0·15	−0·09, 0·39	0·08	0·21	−0·02, 0·44	0·08	0·21	−0·03, 0·45
Meal frequency									
Number of meals	0·86	0·02	−0·21, 0·26	0·79	−0·03	−0·27, 0·21	0·79	−0·33	−0·28, 0·21
Meal size									
Total daily energy intake	0·40	0·10	−0·14, 0·34	0·96	0·00	−0·25, 0·25	0·99	0·00	−0·26, 0·25
First meal size	0·56	−0·07	−0·31, 0·17	0·83	−0·03	−0·26, 0·21	0·08	−0·03	−0·03, 0·22
Last meal size	0·95	−0·01	−0·24, 0·23	0·54	0·08	−0·18, 0·33	0·54	0·80	−0·18, 0·34
Meal regularity									
Meal timing									
Eating window	0·99	0·00	−0·24, 0·24	0·78	−0·04	−0·28, 0·21	0·780	−0·04	−0·29, 0·22
Inter-meal intervals	0·58	0·06	−0·17, 0·30	0·72	0·04	−0·19, 0·28	0·714	0·05	−0·20, 0·29
Time of first meal	0·98	0·00	−0·23, 0·24	0·69	−0·05	−0·31, 0·20	0·694	−0·05	−0·31, 0·21
Time of last meal	0·93	0·01	−0·24, 0·25	0·99	−0·00	−0·24, 0·24	0·990	−0·00	−0·24, 0·24
Last meal – sleep	0·39	−0·11	−0·36, 0·14	0·39	−0·11	−0·38, 0·15	0·387	−0·12	−0·39, 0·15
Waking – first meal	0·02	0·30	0·06, 0·54	0·02	0·28	0·04, 0·52	0·023	0·29	0·04, 0·53
Meal frequency									
Number of meals	0·97	−0·01	−0·24, 0·23	0·60	−0·07	−0·34, 0·19	0·600	−0·07	−0·34, 0·20
Meal size									
Total daily energy intake	0·80	0·03	−0·21, 0·27	0·64	−0·59	−0·31, 0·19	0·644	−0·59	−0·31, 0·19
First meal size	0·82	−0·03	−0·26, 0·21	0·83	−0·03	−0·29, 0·23	0·827	−0·03	−0·29, 0·24
Last meal size	0·33	0·12	−0·12, 0·35	0·17	0·16	−0·07, 0·40	0·166	0·17	−0·07, 0·41

* Linear regression analyses were performed to estimate strength of associations between glycated haemoglobin HbA1c and each component of eating architecture without covariate adjustment model 1 and multivariable models adjusting for age, gender, body mass index, waist circumference, application type model 2 and model 2 plus the percentage of carbohydrates model 3. *β* are the standardised coefficients; 95 % CI.

did not assess cardiometabolic risk. Pot's research team developed a method to score meal regularity based on the variability in energy intake per meal relative to the 5-consecutive-day mean energy intake of that meal (i.e., calculated breakfast, lunch, evening meal, between meals and total daily energy intake separately), with a higher score reflecting a more irregular eating pattern[22,40]. In that study, more irregular energy intake at breakfast was associated with an increased risk of metabolic syndrome in 1768 adults[22]. Further prospective analysis confirmed the positive association between irregular energy intake, particularly at breakfast, lunch and between meals, and cardiometabolic risk after 10 and 17 years follow-up[40]. In the present study, we only observed associations with the first meal of the day and did not observe any significant relationships between the last meal of the day and glucose control or obesity.

In the present study, we found that higher day-to-day variability in the time lag from waking to the first meal was associated with higher HbA1c. Adults with type 1 and T2DM who eat regular meals have better glycaemic control than those who eat irregularly timed meals[11,48]. Xiao *et al.* examined the associations between timing of energy intake relative to sleep and BMI in 872 middle-to-old-aged adults utilising six non-consecutive 24-h dietary recalls over 12 months. In that study, a higher percent of total daily energy intake consumed within 2 h after waking and a lower percent of total energy intake consumed within 2 h before bedtime was associated with lower BMI[18]. However, glucose status was not evaluated.

Randomised clinical trials have reported the importance of breakfast consumption and breakfast size in glucose control[49–52]. Jakubowicz *et al.* established that high-energy breakfast with low-energy dinner improved glucose tolerance in women with obesity[49] and improved glycaemic control in patients with T2DM[50] as compared with the reverse feeding pattern. A high-energy breakfast rich in carbohydrates also upregulated clock gene expression in white blood cells as compared with breakfast skipping[53]. Consuming a large breakfast (47 % energy requirements) and small dinner (13 % of energy requirements) also upregulated expression of clock genes and reduced HbA1c after 12 weeks *v.* eating six isoenergetic meals over the day in fourteen adults with T2DM[54]. In the latter study, meal frequency, inter-meal interval, time of the last meal, the length of eating window, the size of the first meal and the last meal, time lag from last meal to sleep were all different between the two arms making it impossible to untangle which factor was the main contributing factor to the glycaemic benefit. Overall, these studies suggest that skewing food intake towards earlier in the day allows for appropriate temporal regulation of glucose metabolism, a finding that is supported by the results of the present study.

Meal timing considerations could also be important during intermittent fasting (IF) diets. IF is a diet pattern in which zero or minimal energies are consumed 1 to 4 d per week, followed by *ad libitum* eating on the remaining days[55]. Some controversial results exist as to whether IF is superior for metabolic health

when compared with continuous energy restriction[56–58]. Some of the discrepancies could be the result of meal timing on fasting and non-fasting days. In anticipation of a fasting day, it is possible that some individuals may choose to eat late-night snacks. Furthermore, fasting protocols have been initiated after breakfast[56], lunch[59] and dinner[59–61]. Ending the fasting period at the onset of the rest phase (akin to dinner in humans) inverted peripheral clock gene expression in mice[62]. Whilst the impacts of meal timing during IF have not been adequately studied in humans, IF initiated after breakfast did not alter clock genes in human adipose tissue and skeletal muscle[55]. However, future studies should assess eating architecture in both CR and IF interventions. In addition, time-restricted eating (a subtype of IF, in which daily energy intake is restricted to between 6 and 11 h) is a dietary tool that has emerged as a practical intervention for improving cardiometabolic health[63–70]. However, many questions as to the optimal time to initiate time-restricted eating also remain to be tested.

The present analysis was a cross-sectional study with a relatively small sample size, which limited the number of multi-variables that could be adjusted for. This also limited the exploration of the impact of combining components of eating architecture which are likely to interact with each other[11,44,45,71]. Additional limitations include that food intake was not assessed by weighed food records, subjective appetite was not measured, and that data were lost from a number of participants due to incomplete food records (28 %), technical issues with accelerometry (3 %) or CGM loss (9 %) resulting in the final sample size was 73. Finally, the outcomes from the present study cannot be extrapolated to the general population. Thus, more prospective studies with larger sample sizes and in wider population groups are needed to evaluate the long-term risk of obesity or chronic diseases with respect to irregular eating patterns. The strengths of this work are that this is the first study synchronising data from objective food records, activity and sleep patterns and continuous glucose levels in real time for 1–2 weeks to capture meal size, frequency, timing and meal regularity. The use of smartphone apps may offer a practical tool for collecting personalised food diaries in real time in the future, as opposed to paper-based questionnaires or 24-h diet recall. This is also the first study to evaluate the components of eating architecture in relation to body fat mass and glucose control among adults at increased risk of T2DM.

In conclusion, the results from the present analysis show that eating breakfast earlier, and at a consistent time each day was associated with decreased body fat mass, and improved glycaemic control as indicated by lower HbA1c, in adults with increased risk of T2DM. Routine consumption of meals may therefore optimise temporal regulation to anticipate and respond appropriately to a glucose challenge.

Acknowledgements

We thank the participants who participated in this study and acknowledge that the software and dashboard to calculate the time lag of the meal relative to sleep was created by Aran Wittert.

The research was funded by diabetes Australia and National Health and Medical Research Council (NHMRC) project grant. LZ is supported by a beacon of enlightenment scholarship from the University of Adelaide.

Trials in this study were conducted in South Australia Health and Medical Research Institute, Adelaide. L. K. H, A. H., G. A. W. designed the research. L. K. H., A. H., B. L., X. T. T., K. L. and L. Z. collected data. L. Z., X. T. T. and K. L. estimated energy intake via FoodWorks. G. A. W. provided clinical support and supervision. E. M. and S. P. supplied the myCircadianClock application. Y. A. M. and A. V. provided statistical support. L. Z. performed the statistical analysis and draft the manuscript. All authors contributed to data interpretation and preparation of the manuscript. L. K. H. had full access to the data and had primary responsibility for the final publication.

S. P. is the author of the book 'The Circadian Code' for which he receives author royalty from PenguinRandomHouse Company. The other authors declared no conflict of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114521002944

References

1. Leech RM, Worsley A, Timperio A, *et al.* (2015) Understanding meal patterns: definitions, methodology and impact on nutrient intake and diet quality. *Nutr Res Rev* **28**, 1–21.
2. Magklis E, Howe LD & Johnson L (2019) Eating style and the frequency, size and timing of eating occasions: a cross-sectional analysis using 7-day weighed dietary records. *Sci Rep* **9**, 15133.
3. Wehrens SMT, Christou S, Isherwood C, *et al.* (2017) Meal timing regulates the human circadian system. *Curr Biol* **27**, 1768–1775e3.
4. Hatori M, Vollmers C, Zarrinpar A, *et al.* (2012) Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. *Cell Metab* **15**, 848–860.
5. Collado MC, Engen PA, Bandín C, *et al.* (2018) Timing of food intake impacts daily rhythms of human salivary microbiota: a randomized, crossover study. *FASEB J* **32**, 2060–2072.
6. Gu C, Brereton N, Schweitzer A, *et al.* (2020) Metabolic effects of late dinner in healthy volunteers-a randomized crossover clinical trial. *J Clin Endocrinol Metab* **105**, 2789–2802.
7. Bi H, Gan Y, Yang C, *et al.* (2015) Breakfast skipping and the risk of type 2 diabetes: a meta-analysis of observational studies. *Public Health Nutr* **18**, 3013–3019.
8. Ballon A, Neuenschwander M & Schlesinger S (2019) Breakfast skipping is associated with increased risk of type 2 diabetes among adults: a systematic review and meta-analysis of prospective cohort studies. *J Nutr* **149**, 106–113.
9. Ma X, Chen Q, Pu Y, *et al.* (2020) Skipping breakfast is associated with overweight and obesity: a systematic review and meta-analysis. *Obes Res Clin Pract* **14**, 1–8.
10. Wicherski J, Schlesinger S & Fischer F (2021) Association between breakfast skipping and body weight-a systematic review and meta-analysis of observational longitudinal studies. *Nutrients* **13**, 272.
11. Azami Y, Funakoshi M, Matsumoto H, *et al.* (2019) Long working hours and skipping breakfast concomitant with late evening meals are associated with suboptimal glycemic control among young male Japanese patients with type 2 diabetes. *J Diabetes Investig* **10**, 73–83.

12. St-Onge MP, Ard J, Baskin ML, *et al.* (2017) Meal timing and frequency: implications for cardiovascular disease prevention: a scientific statement from the American heart association. *Circulation* **135**, e96–e121.
13. Schlundt DG, Hill JO, Sbrocco T, *et al.* (1992) The role of breakfast in the treatment of obesity: a randomized clinical trial. *Am J Clin Nutr* **55**, 645–651.
14. Geliebter A, Astbury NM, Aviram-Friedman R, *et al.* (2014) Skipping breakfast leads to weight loss but also elevated cholesterol compared with consuming daily breakfasts of oat porridge or frosted cornflakes in overweight individuals: a randomised controlled trial. *J Nutr Sci* **3**, e56.
15. Dhurandhar EJ, Dawson J, Alcorn A, *et al.* (2014) The effectiveness of breakfast recommendations on weight loss: a randomized controlled trial. *Am J Clin Nutr* **100**, 507–513.
16. Bonnet JP, Cardel MI, Cellini J, *et al.* (2020) Breakfast skipping, body composition, and cardiometabolic risk: a systematic review and meta-analysis of randomized trials. *Obesity* **28**, 1098–1109.
17. Nas A, Mirza N, Hägele F, *et al.* (2017) Impact of breakfast skipping compared with dinner skipping on regulation of energy balance and metabolic risk. *Am J Clin Nutr* **105**, 1351–1361.
18. Xiao Q, Garaulet M & Scheer F (2019) Meal timing and obesity: interactions with macronutrient intake and chronotype. *Int J Obes* **43**, 1701–1711.
19. Lopez-Minguez J, Saxena R, Bandín C, *et al.* (2018) Late dinner impairs glucose tolerance in MTNR1B risk allele carriers: a randomized, cross-over study. *Clin Nutr* **37**, 1133–1140.
20. McHill AW, Phillips AJ, Czeisler CA, *et al.* (2017) Later circadian timing of food intake is associated with increased body fat. *Am J Clin Nutr* **106**, 1213–1219.
21. Allison KC, Hopkins CM, Ruggieri M, *et al.* (2020) Prolonged, controlled daytime versus delayed eating impacts weight and metabolism. *Curr Biol* **31**, 650–657.
22. Pot GK, Hardy R & Stephen AM (2014) Irregular consumption of energy intake in meals is associated with a higher cardiometabolic risk in adults of a British birth cohort. *Int J Obes* **38**, 1518–1524.
23. Pot GK, Almoosawi S & Stephen AM (2016) Meal irregularity and cardiometabolic consequences: results from observational and intervention studies. *Proc Nutr Soc* **75**, 475–486.
24. Zeevi D, Korem T, Zmora N, *et al.* (2015) Personalized nutrition by prediction of glycemic responses. *Cell* **163**, 1079–1094.
25. Guinter MA, Park YM, Steck SE, *et al.* (2020) Day-to-day regularity in breakfast consumption is associated with weight status in a prospective cohort of women. *Int J Obes* **44**, 186–194.
26. Leech RM, Worsley A, Timperio A, *et al.* (2017) Temporal eating patterns: a latent class analysis approach. *Int J Behav Nutr Phys Act* **14**, 3.
27. Leech RM, Timperio A, Livingstone KM, *et al.* (2017) Temporal eating patterns: associations with nutrient intakes, diet quality, and measures of adiposity. *Am J Clin Nutr* **106**, 1121–1130.
28. Stenvers DJ, Jongejan A, Atiqi S, *et al.* (2019) Diurnal rhythms in the white adipose tissue transcriptome are disturbed in obese individuals with type 2 diabetes compared with lean control individuals. *Diabetologia* **62**, 704–716.
29. Wefers J, Connell NJ, Fealy CE, *et al.* (2020) Day-night rhythm of skeletal muscle metabolism is disturbed in older, metabolically compromised individuals. *Mol Metab* **41**, 101050.
30. Prasad MA, Manoogian E, Zuraikat FM, *et al.* (2020) 2005-P: a smartphone intervention to promote time-restricted eating reduces body weight and blood pressure in adults with overweight and obesity diabetes. *Nutrients* **69**.
31. Gill S & Panda S (2015) A smartphone app reveals erratic diurnal eating patterns in humans that can be modulated for health benefits. *Cell Metab* **22**, 789–798.
32. Chen L, Magliano DJ, Balkau B, *et al.* (2010) AUSDRISK: an Australian Type 2 Diabetes Risk Assessment Tool based on demographic, lifestyle and simple anthropometric measures. *Med J Aust* **192**, 197–202.
33. Ambrosini GL, Hurworth M, Giglia R, *et al.* (2018) Feasibility of a commercial smartphone application for dietary assessment in epidemiological research and comparison with 24-h dietary recalls. *Nutr J* **17**, 5.
34. Naaman R, Parrett A, Bashwari D, *et al.* (2021) Assessment of dietary intake using food photography and video recording in free-living young adults: a comparative study. *J Acad Nutr Diet* **121**, 749–761.
35. Gupta NJ, Kumar V & Panda S (2017) A camera-phone based study reveals erratic eating pattern and disrupted daily eating-fasting cycle among adults in India. *PLoS One* **12**, e0172852.
36. Reis CEG, Dórea JG & da Costa THM (2019) Effects of coffee consumption on glucose metabolism: a systematic review of clinical trials. *J Tradit Complement Med* **9**, 184–191.
37. Sylvetsky AC (2018) Metabolic effects of low-calorie sweeteners: a brief review. *Obesity* **3**, S25–S31.
38. Shin A, Lim SY, Sung J, *et al.* (2009) Dietary intake, eating habits, and metabolic syndrome in Korean men. *J Am Diet Assoc* **109**, 633–640.
39. Wennberg M, Gustafsson PE, Wennberg P, *et al.* (2016) Irregular eating of meals in adolescence and the metabolic syndrome in adulthood: results from a 27-year prospective cohort. *Public Health Nutr* **19**, 667–673.
40. Pot GK, Hardy R & Stephen AM (2016) Irregularity of energy intake at meals: prospective associations with the metabolic syndrome in adults of the 1946 British birth cohort. *Br J Nutr* **115**, 315–323.
41. Uemura M, Yatsuya H, Hilawe EH, *et al.* (2015) Breakfast skipping is positively associated with incidence of type 2 diabetes mellitus: evidence from the aichi workers' cohort study. *J Epidemiol* **25**, 351–358.
42. Ha K & Song Y (2019) Associations of meal timing and frequency with obesity and metabolic syndrome among Korean adults. *Nutrients* **11**, 2437.
43. Wang W, Grech A, Gemming L, *et al.* (2020) Breakfast size is associated with daily energy intake and diet quality. *Nutr* **75**, 110764.
44. Mekary RA, Giovannucci E, Cahill L, *et al.* (2013) Eating patterns and type 2 diabetes risk in older women: breakfast consumption and eating frequency. *Am J Clin Nutr* **98**, 436–443.
45. Mekary RA, Giovannucci E, Willett WC, *et al.* (2012) Eating patterns and type 2 diabetes risk in men: breakfast omission, eating frequency, and snacking. *Am J Clin Nutr* **95**, 1182–1189.
46. Sierra-Johnson J, Undén AL, Linestrand M, *et al.* (2008) Eating meals irregularly: a novel environmental risk factor for the metabolic syndrome. *Obesity* **16**, 1302–1307.
47. McHill AW, Hilditch CJ, Fischer D, *et al.* (2020) Stability of the timing of food intake at daily and monthly timescales in young adults. *Sci Rep* **10**, 20849.
48. Ahola AJ, Mutter S, Forsblom C, *et al.* (2019) Meal timing, meal frequency, and breakfast skipping in adult individuals with type 1 diabetes – associations with glycaemic control. *Sci Rep* **9**, 20063.
49. Jakubowicz D, Barnea M, Wainstein J, *et al.* (2013) High caloric intake at breakfast *v.* dinner differentially influences weight loss of overweight and obese women. *Obesity* **21**, 2504–2512.
50. Jakubowicz D, Wainstein J, Ahrén B, *et al.* (2015) High-energy breakfast with low-energy dinner decreases overall daily hyperglycaemia in type 2 diabetic patients: a randomised clinical trial. *Diabetologia* **58**, 912–919.
51. Jakubowicz D, Wainstein J, Landau Z, *et al.* (2017) High-energy breakfast based on whey protein reduces body weight,

postprandial glycemia and HbA1C in Type 2 diabetes. *J Nutr Biochem* **49**, 1–7.
52. Jakubowicz D, Wainstein J, Ahren B, *et al.* (2015) Fasting until noon triggers increased postprandial hyperglycemia and impaired insulin response after lunch and dinner in individuals with type 2 diabetes: a randomized clinical trial. *Diabetes Care* **38**, 1820–1826.
53. Jakubowicz D, Wainstein J, Landau Z, *et al.* (2017) Influences of breakfast on clock gene expression and postprandial glycemia in healthy individuals and individuals with diabetes: a randomized clinical trial. *Diabetes Care* **40**, 1573–1579.
54. Jakubowicz D, Landau Z, Tsameret S, *et al.* (2019) Reduction in glycated hemoglobin and daily insulin dose alongside circadian clock upregulation in patients with type 2 diabetes consuming a three-meal diet: a randomized clinical trial. *Diabetes Care* **42**, 2171–2180.
55. Zhao L, Hutchison AT, Wittert GA, *et al.* (2020) Intermittent fasting does not uniformly impact genes involved in circadian regulation in women with obesity. *Obesity* **1**, S63–S67.
56. Hutchison AT, Liu B, Wood RE, *et al.* (2019) Effects of intermittent versus continuous energy intakes on insulin sensitivity and metabolic risk in women with overweight. *Obesity* **27**, 50–58.
57. Trepanowski JF, Kroeger CM, Barnosky A, *et al.* (2017) Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults: a randomized clinical trial. *JAMA Intern Med* **177**, 930–938.
58. Harvie MN, Pegington M, Mattson MP, *et al.* (2011) The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: a randomized trial in young overweight women. *Int J Obes* **35**, 714–727.
59. Hoddy KK, Kroeger CM, Trepanowski JF, *et al.* (2014) Meal timing during alternate day fasting: impact on body weight and cardiovascular disease risk in obese adults. *Obesity* **22**, 2524–2531.
60. Varady KA, Bhutani S, Klempel MC, *et al.* (2013) Alternate day fasting for weight loss in normal weight and overweight subjects: a randomized controlled trial. *Nutr J* **12**, 146.
61. Halberg N, Henriksen M, Söderhamn N, *et al.* (2005) Effect of intermittent fasting and refeeding on insulin action in healthy men. *J Appl Physiol* **99**, 2128–2136.
62. Froy O, Chapnik N & Miskin R (2009) Effect of intermittent fasting on circadian rhythms in mice depends on feeding time. *Mech Ageing Dev* **130**, 154–160.
63. Parr EB, Devlin BL, Radford BE, *et al.* (2020) A delayed morning and earlier evening time-restricted feeding protocol for improving glycemic control and dietary adherence in men with overweight/obesity: a randomized controlled trial. *Nutrients* **12**, 505.
64. Jamshed H, Beyl RA, Della Manna DL, *et al.* (2019) Early time-restricted feeding improves 24-hour glucose levels and affects markers of the circadian clock, aging, and autophagy in humans. *Nutrients* **11**, 1234.
65. Gabel K, Hoddy KK, Haggerty N, *et al.* (2018) Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: a pilot study. *Nutr Healthy Aging* **4**, 345–353.
66. Sutton EF, Beyl R, Early KS, *et al.* (2018) Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. *Cell Metab* **27**, 1212–1221e3.
67. Hutchison AT, Regmi P, Manoogian EN, *et al.* (2019) Time-restricted feeding improves glucose tolerance in men at risk for type 2 diabetes: a randomized crossover trial. *Obesity* **27**, 724–732.
68. Ravussin E, Beyl RA, Poggiogalle E, *et al.* (2019) Early time-restricted feeding reduces appetite and increases fat oxidation but does not affect energy expenditure in humans. *Obesity* **27**, 1244–1254.
69. Gabel K, Marcell J, Cares K, *et al.* (2020) Effect of time restricted feeding on the gut microbiome in adults with obesity: a pilot study. *Nutr Health* **26**, 79–85.
70. Moro T, Tinsley G, Bianco A, *et al.* (2016) Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. *J Transl Med* **14**, 290.
71. Kahleova H, Lloren JI, Mashchak A, *et al.* (2017) Meal frequency and timing are associated with changes in body mass index in adventist health study 2. *J Nutr* **147**, 1722–1728.

British Journal of Nutrition