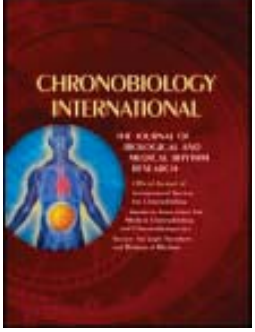

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The Relationship Between Breakfast Skipping, Chronotype, and Glycemic Control in Type 2 Diabetes

Sirimon Reutrakul[1,2], Megan M. Hood[3]*, Stephanie J. Crowley[3]*, Mary K. Morgan[1], Marsha Teodori[1], and Kristen L. Knutson[4]

[1]*Section of Endocrinology, Department of Internal Medicine, Rush University Medical Center, Chicago, Illinois, USA,* [2]*Division of Endocrinology and Metabolism, Ramathibodi Hospital, Mahidol University, Ratchathewi, Bangkok, Thailand,* [3]*Department of Behavioral Sciences, Rush University Medical Center, Chicago, Illinois, USA, and* [4]*Section of Pulmonary and Critical Care, Department of Medicine, University of Chicago, Chicago, Illinois, USA*

Breakfast skipping is associated with obesity and an increased risk of type 2 diabetes. Later chronotypes, individuals who have a preference for later bed and wake times, often skip breakfast. The aim of the study was to explore the relationships among breakfast skipping, chronotype, and glycemic control in type 2 diabetes patients. We collected sleep timing and 24-h dietary recall from 194 non-shift-working type 2 diabetes patients who were being followed in outpatient clinics. Mid-sleep time on free days (MSF) was used as an indicator of chronotype. Hemoglobin A1C (HbA_{1C}) values were obtained from medical records. Hierarchical linear regression analyses controlling for demographic, sleep, and dietary variables were computed to determine whether breakfast skipping was associated with HbA_{1C}. Additional regression analyses were performed to test if this association was mediated by chronotype. There were 22 participants (11.3%) who self-reported missing breakfast. Breakfast skippers had significantly higher HbA_{1C} levels, higher body mass indices (BMI), and later MSF than breakfast eaters. Breakfast skipping was significantly associated with higher HbA_{1C} values ($B = 0.108$, $p = 0.01$), even after adjusting for age, sex, race, BMI, number of diabetes complications, insulin use, depressive symptoms, perceived sleep debt, and percentage of daily caloric intake at dinner. The relationship between breakfast skipping and HbA_{1C} was partially mediated by chronotype. In summary, breakfast skipping is associated with a later chronotype. Later chronotype and breakfast skipping both contribute to poorer glycemic control, as indicated by higher HbA_{1C} levels. Future studies are needed to confirm these findings and determine whether behavioral interventions targeting breakfast eating or sleep timing may improve glycemic control in patients with type 2 diabetes.

Keywords: Breakfast skipping, chronotype, circadian, diabetes, glycemic control

INTRODUCTION

Diabetes mellitus was estimated to affect 22.3 million people in the United States in 2012, approximately 7% of the nation's population (American Diabetes Association, 2013). The economic costs of diabetes in 2012 was estimated at $245 billion, which was a 41% increase from the estimate in 2007 (American Diabetes Association, 2013). Poor glycemic control can lead to numerous complications, including microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (coronary artery disease and cerebrovascular disease), which contribute to increased health care costs. A number of behavioral factors, including sleep and eating patterns, can impact glycemic control and are therefore important to understand in order to improve diabetes management and decrease health care cost.

Breakfast skipping has been consistently associated with increased cardiometabolic risks in children and adults, both in cross-sectional and longitudinal studies (Alexander et al., 2009; Freitas Junior et al., 2012; Mekary et al., 2012; Rampersaud et al., 2005; Raynor et al., 2008; Smith et al., 2010). These include higher risks for overweight and obesity, increased visceral adiposity, insulin resistance, type 2 diabetes, and dyslipidemia. A longitudinal study of 2184 participants over 20 yrs found that those who skipped breakfast in both childhood and adulthood had significantly greater waist circumference and higher fasting insulin, total cholesterol, and low-density lipoprotein (LDL) cholesterol than

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*M.M.H. and S.J.C. contributed equally to this paper.

Correspondence: Sirimon Reutrakul, MD, Division of Endocrinology and Metabolism, Ramathibodi Hospital, Mahidol University, Rama VI Rd, Ratchathewi, Bangkok 10400, Thailand. E-mail: sreutrak10800@gmail.com

those who consumed breakfast at both time points (Smith et al., 2010). Another longitudinal study of 29 206 men with a follow-up at 16 yrs revealed that breakfast skipping was associated with a 21% increase in risk of developing type 2 diabetes, even after adjustment for body mass index (BMI) (Mekary et al., 2012). Despite this strong evidence for the association between breakfast consumption and metabolism in large population-based studies, very few data exist regarding the relationship between breakfast skipping and glycemic control in patients with type 2 diabetes. A cross-sectional study of 211 low-income Latino diabetic patients found that breakfast skipping, prevalent in approximately 25% of the participants, was associated with higher fasting plasma glucose levels, but not with hemoglobin A_{1C} (HbA_{1C}) values, which is the gold standard measurement of longer-term glycemic control (90 d) (Kollannoor-Samuel et al., 2011). Another study that examined the effect of dietary counseling on glycemic control over a 3-mo period in 50 participants with type 2 diabetes found that those who skipped breakfast during the study had poorer metabolic control, although the details of the changes in HbA_{1C} values were not provided (Schmidt et al., 1994).

The endogenous circadian (~24-h) timing system, controlled by the master circadian clock in the suprachiasmatic nuclei of the hypothalamus, plays a significant role in regulating a number of daily physiologic rhythms, including sleep/wake and feeding behavior, peripheral tissue metabolism, energy expenditure, and hormonal profiles (Arble et al., 2010; Huang et al., 2011). Many animal studies suggest the importance of the circadian system in body weight regulation as well as glucose and lipid metabolism (Arble et al., 2009; Turek et al., 2005). Laboratory studies in healthy volunteers have also demonstrated adverse metabolic consequences to circadian disruptions. Severe circadian misalignment, involving sleep/wake and meal schedules ~12 h out of phase from their habitual times resulted in increased postprandial glucose and insulin levels, elevated mean arterial pressure levels, as well as decreased leptin concentrations (Scheer et al., 2009). These data support the importance of the circadian timing system in metabolic regulation.

On an individual level, humans differ in their subjective rating of when they feel at their ''peak'' during the day, ranging from a ''morning lark'' to a ''night owl.'' This individual difference of ''chronotype'' can also be measured using self-reported sleep times. Roenneberg and colleagues quantify the construct by computing mid-sleep time (midpoint between self-reported sleep onset and wake time) on free (nonworking) days (MSF) (Roenneberg et al., 2003). A recent population-based study found that participants with an evening preference were 2.5 times more likely to have type 2 diabetes, suggesting that having a later chronotype may predispose individuals to type 2 diabetes (Merikanto et al., 2013). We recently reported that among type 2 diabetes patients, having a later chronotype was significantly associated with worse glycemic control, even after adjusting for sleep debt and demographic variables (Reutrakul et al., 2013), suggesting that endorsing a late chronotype may make it more difficult for a patient with type 2 diabetes to control their disease.

Available data suggest that chronotype may be associated with the timing and content of dietary intake as well. Late chronotypes tend to eat less after waking or skip breakfast (Meule et al., 2012; Nakade et al., 2009; Ostberg, 1973). In addition, endorsing a later chronotype has been associated with increased energy intake from alcohol, fat, and confections, as well as meal skipping (Sato-Mito et al., 2011). In our previous analysis of type 2 diabetes patients, participants with later chronotypes consumed a greater percentage of their daily calories at dinner compared with earlier chronotypes, which partially explained the association found between later chronotype and poorer glycemic control (Reutrakul et al., 2013). Yet, it is unclear if breakfast skipping plays an additional role in glycemic control beyond the contribution of caloric intake at dinner meals and whether this is related to chronotype in this group of type 2 diabetes patients.

The goal of the present study was to investigate the association between breakfast skipping, a common behavior in individuals who endorse a late chronotype, and glycemic control in patients with type 2 diabetes. Thus, the aims of this analysis were (1) to describe differences in glycemic control, chronotype, and eating behaviors in breakfast skippers versus breakfast eaters; (2) to determine if breakfast skipping is independently associated with glycemic control after adjusting for relevant demographic, sleep, and dietary variables; and (3) to determine if the relationship between breakfast skipping and glycemic control is mediated by chronotype.

MATERIALS AND METHODS

Participants

Adults with type 2 diabetes who were being followed in endocrinology or primary care clinics at Rush University Medical Center were invited to participate. Exclusion criteria included pregnancy, inability to understand English or give informed consent, nursing home residents or institutionalized patients, presence of any neurologic or physical impairment that required the participants to depend on others for feeding, and patients receiving alternate routes of nutrition such as tube feeding or parenteral nutrition. All participants gave written informed consent. The protocol was approved by the Institutional Review Board, Rush University Medical Center, Chicago, Illinois.

After obtaining informed consent, self-reported age and race were recorded and weight was measured. Height, current medications, and most recent HbA_{1C} values were extracted from patient medical records.

Body mass index (BMI) was calculated using the standard formula [weight (kg)/height (meter)^2]. Research personnel interviewed participants about their diabetes history and management using the University of Chicago Diabetes/Quality of Life Survey (Meltzer & Egleston, 2000). Depressive symptoms were assessed using The Center for Epidemiologic Studies—Depression (CES-D) Scale (Netzer et al., 1999). Additional validated measures as described below were also collected (total assessment time ranged between 30 and 45 min). Further details of the research design and methodology were previously described (Reutrakul et al., 2013).

Subjective Sleep and Chronotype

Self-reported usual bedtime, wake-up time, sleep onset latency, and actual sleep duration on weekdays and weekends over the previous month were recorded. From these, we calculated mid-sleep time as the midpoint between sleep onset (bedtime plus sleep latency) and wake time. The metric of chronotype, *mid-sleep time on free days* (MSF), was derived from mid-sleep time on weekend nights with further adjustment for the sleep duration on weekend nights and its weekly average as follows: MSF = mid-sleep time on free days (weekend) $- 0.5 \times (SD_F - (5 \times SD_W + 2 \times SD_F)/7)$, where SD_F is calculated sleep duration on weekend nights and SD_w is calculated sleep duration on weekday nights (Roenneberg et al., 2004).

Participants self-reported their perceived actual sleep duration and their preferred sleep duration on weekdays (i.e., how many hours they would choose to sleep if their job, family, or other responsibilities did not limit the number of hours they slept). *Perceived sleep debt* was then calculated using the difference between perceived actual sleep duration and preferred sleep duration on weekdays. Perceived sleep debt is a subjective perception of not getting enough sleep, which could be a result of insufficient sleep, poor sleep quality or other factors such as sleeping more for pleasure. This variable has been shown to be more strongly correlated with HbA_{1C} than the reported sleep duration itself (Knutson et al., 2006).

Caloric Intake Measures

Participants completed a 24-h dietary recall by interview to determine the content and timing of their meals over the previous day. Specific details (e.g., portion sizes, brand names, cooking methods, additives such as sauces and dressings, etc.) were clarified by the interviewer. Interviewers included a registered dietician, an endocrinologist, a certified diabetes educator, and a medical resident and all followed the same interview format. Participants categorized each entry as breakfast, lunch, dinner, or snack. Entries that consisted of drinks only (e.g., coffee with cream) were not counted as completed meals unless food items were also consumed. Calorie consumption for each meal was calculated using an online dietary database (www.livestrong.com). Breakfast skipping was defined as having no entry or a liquid-only entry for breakfast on the 24-h dietary recall. Percentage of total daily calories consumed at each meal was calculated and used as an indicator of daily caloric distribution. Morning appetite was assessed using the question ''How hungry are you usually in the morning?'' The responses included ''not at all,'' ''a little,'' ''somewhat,'' ''moderately,'' and ''very.''

Statistical Analysis

Prior to completing analyses, study data were checked for normality and presence of potential violations of statistical assumptions. HbA_{1C} values and diabetes duration were not normally distributed and were expressed as median (interquartile range). Number of diabetes complications was categorized as none or $\geq$1. Morning appetite was categorized as having appetite in the morning, ranging from ''a little'' to ''very'' hungry, or none (i.e., ''not at all''). In addition, the natural logarithm transformation of HbA_{1C} was used as the outcome variable in the regression analyses. Preliminary analyses demonstrated no collinearity among the variables.

To compare continuous demographic and metabolic data of breakfast eaters and breakfast skippers, independent sample Student's *t* tests were used for variables that were normally distributed, and Mann–Whitney *U* tests were used for variables that were not normally distributed (HbA_{1C} and diabetes duration). Chi-square tests were used to compare categorical variables.

To determine whether breakfast skipping was significantly associated with glycemic control beyond the role of other potential contributing factors, we used hierarchical regression modeling. Thus, age, sex (reference: male), race (reference: nonwhite), BMI, diabetes complications, insulin use (yes/no), depression score, perceived sleep debt, and percentage of daily caloric intake at dinner were entered in the first step. Breakfast skipping was then entered in the second step and change in R^2 was obtained to determine whether breakfast skipping explained significant variance in HbA_{1C} beyond the role of the variables entered in step 1.

To determine if chronotype mediated the association between breakfast skipping and glycemic control, four multiple regression analyses were completed according to the Baron and Kenny test for mediation (Baron & Kenny, 1986). Demographic and sleep variables (age, sex [reference: male], race [reference: nonwhite], BMI, diabetes duration, insulin use, depression score, and perceived sleep debt) were controlled for in each step. The first step regressed breakfast skipping on HbA_{1C}, where HbA_{1C} was the dependent variable. In steps 2 and 3, additional regression analyses were performed to assess the association between (1) breakfast skipping and MSF, with MSF as the dependent variable; and (2) MSF and HbA_{1C}, with HbA_{1C} as the dependent

variable. In the final step, both MSF and breakfast skipping were entered as independent variables in a multiple regression analysis to assess their associations with HbA_{1C}.

RESULTS

Statistical comparisons between breakfast eaters ($n = 172$) and breakfast skippers ($n = 22$) on demographic, sleep, and dietary variables are shown in Table 1. Compared with breakfast eaters, breakfast skippers were significantly younger, and had significantly higher HbA_{1C} levels and significantly higher BMI. There were no differences between groups in the median diabetes duration, insulin use, or number of diabetes complications.

Breakfast skippers reported a significantly later chronotype, as indicated by later MSF. Their usual bedtime on weekdays and weekends was later than those of breakfast eaters. Weekend wake time was later for breakfast skippers compared with breakfast eaters, and a trend emerged for later weekday wake time. There were no differences between the groups in perceived sleep debt.

Significantly more breakfast skippers reported having no appetite in the morning than breakfast eaters. In addition, breakfast skippers reported consuming fewer total calories during the previous day (see Table 1 and Figure 1). Total lunch calories and dinner calories did not differ between groups; however, the daily distribution of calories differed between groups. As expected, breakfast skippers consumed a greater

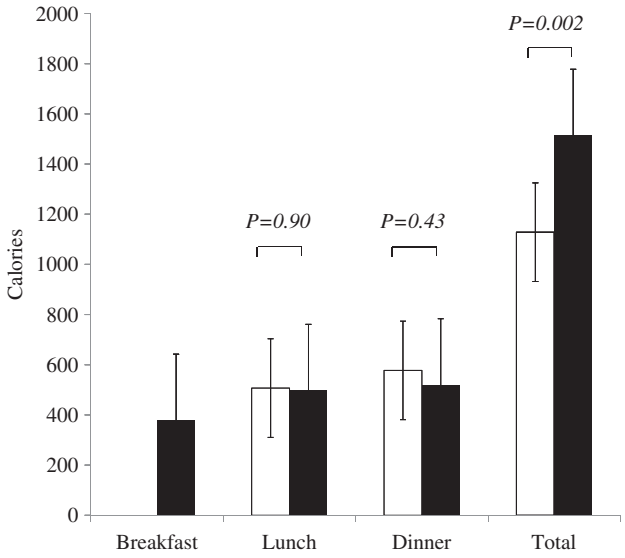

FIGURE 1. Caloric intake at each meal and total daily consumption in breakfast skippers (open bars) and breakfast eaters (black bars).

TABLE 1. Descriptive demographic, circadian, sleep, and dietary data ($n = 194$ unless otherwise noted).

Variable	Breakfast eaters ($n = 172$)	Breakfast skippers ($n = 22$)	p Value‡
Demographic and metabolic variables			
Age (yr)	59.5 ± 12.4	49.6 ± 14.6	0.001
Female, *n* (%)	119 (69.1)	16 (72.7)	0.73
White, *n* (%)	48 (27.9)	7 (31.8)	0.70
HbA_{1C} (%)	7.4 (6.6–8.7)	9.0 (7.1–10.6)	0.002¶
BMI (kg/m^2)	35.1 ± 8.2	40.0 ± 7.2	0.008
DM duration* (yr)	12.0 (5.0–20.0)	10.0 (2.0–16.8)	0.18¶
DM complications ≥1, *n* (%)	121 (63.9)	17 (77.2)	0.50
Insulin use, *n* (%)	97 (56.4)	11 (50.0)	0.57
Depression score	13.5 ± 9.07	13.9 ± 8.7	0.84
Sleep and circadian variables			
Perceived sleep debt (h)	1.5 ± 1.9	2.0 ± 1.7	0.23
MSF†	3:21 ± 1:39	4:34 ± 2:18	0.002
Bedtime weekday†	22:39 ± 1:29	23:54 ± 2:47	0.05
Bedtime weekend†	23:00 ± 1:42	0:22 ± 2:38	0.001
Wake time weekday†	6:47 ± 1:48	7:47 ± 2:43	0.10
Wake time weekend†	7:21 ± 2:01	8:35 ± 2:23	0.009
Dietary variables			
Lack of morning appetite, *n* (%)	32 (18.6)	13 (59.1)	<0.001
Total daily calorie	1514 ± 560	1128 ± 386	0.002
Breakfast calorie (% of daily total)	27 ± 13	N/A	
Lunch calorie§ (% of daily total)	26 ± 19	36 ± 23	0.024
Dinner calorie‖ (% of daily total)	35 ± 19	53 ± 22	<0.001

Data are presented as mean ± SD, or median (interquartile range) unless otherwise noted.
*$n = 193$.
†Time is presented in 24-h clock time.
‡p Values are from unpaired t test for continuous variables and chi-square for categorical variables, unless otherwise noted.
¶Mann–Whitney U test.
§$n = 140$ for breakfast eaters and $n = 18$ for breakfast skippers.
‖$n = 158$ for breakfast eaters.

percentage of their daily caloric intake at lunch and dinner compared with breakfast eaters.

Figure 2 depicts average sleep/wake and meal timing among breakfast skippers and breakfast eaters. Despite having later wake time and bedtime, breakfast skippers consumed lunch and dinner at similar times to breakfast eaters (lunch 13:21 ± 1:30 versus 13:23 ± 1:21 h, $p = 0.89$; dinner 18:43 ± 1:29 versus 18:48 ± 1:26 h, $p = 0.84$).

Breakfast Skipping and Glycemic Control

Table 2 presents the results from the hierarchical multiple regression analysis. Since breakfast skippers had a significantly higher percentage of daily caloric intake at dinner that was previously reported to be associated with poorer glycemic control (Reutrakul et al., 2013), we controlled for this variable in the regression model. In addition, since perceived sleep debt in this cohort was shown to be positively correlated with HbA_{1C} level (correlation coefficient 0.15, $p = 0.04$) (Reutrakul et al., 2013), this variable was included in the regression model. Self-reported actual sleep duration in this cohort was not correlated with glycemic control (data not shown) and therefore was not analyzed further.

The first step, which included age, sex, race, BMI, insulin use, number of diabetes complications, depression score, perceived sleep debt, and percentage of daily caloric intake at dinner, explained 23% of the variance in HbA_{1C}. In the second step, breakfast skipping was entered, explaining an additional 3% of the variance in HbA_{1C} ($\Delta R^2 = 0.03$, $p = 0.01$, total adjusted $R^2 = 0.25$), which indicated that breakfast skipping contributed significantly to the model's explanation of the variance of HbA_{1C} above and beyond demographic and sleep variables as well as percentage of caloric intake at dinner. Breakfast skipping was significantly associated with HbA_{1C} ($B = 0.108$, $p = 0.01$) such that skipping breakfast was associated with a 10.8% increase in HbA_{1C} of its original value.

Thirty-one participants (two breakfast skippers) were interviewed on Mondays, yielding a food recall based on a Sunday. Therefore, we performed additional analyses to determine whether a weekend day food log impacted the results. When food recalls from a Sunday were omitted from the analysis, breakfast skipping remained significantly associated with HbA_{1C} ($p = 0.01$), suggesting that the results were not affected by the interview days.

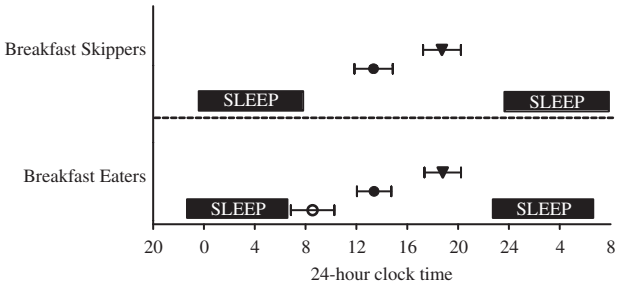

FIGURE 2. Mean (± SD) self-reported meal times during the previous day for breakfast skippers and breakfast eaters (breakfast ○, lunch •, dinner ▼). Mean self-reported sleep times for the same day are double-plotted.

Chronotype as a Mediator Between Breakfast Skipping and Glycemic Control

To determine if chronotype mediated the relationship between breakfast skipping and glycemic control, a series of regression models was performed. In the first regression, breakfast skipping was significantly associated with higher HbA_{1C} ($B = 0.13$, $p = 0.002$). In the second regression, breakfast skipping was significantly associated with later MSF ($B = 0.98$, $p = 0.014$). In the third model, as previously reported with this sample (Reutrakul et al., 2013), MSF was significantly associated with HbA_{1C} ($B = 0.025$, $p = 0.001$). Given that the first three steps were significant, the fourth regression model examined MSF and breakfast skipping together. Both MSF ($B = 0.021$, $p = 0.005$) and breakfast skipping ($B = 0.112$, $p = 0.007$) were significantly associated with higher HbA_{1C}. This mediation analysis indicates that chronotype did not completely mediate the relationship

TABLE 2. Multiple regression analysis predicting natural log of HbA_{1C} ($n = 194$).

	Model 1		Model 2	
Variable	*B*	*p* Value	*B*	*p* Value
Age	−0.003	0.002	−0.003	0.009
Sex (reference: male)	0.013	0.655	0.015	0.610
Race (reference: nonwhite)	−0.019	0.528	−0.024	0.423
BMI	−0.001	0.714	−0.001	0.466
Number of DM complications	0.038	0.196	0.031	0.299
Insulin use (reference: yes)	0.137	<0.001	0.144	<0.001
Depression score	0.0001	0.936	0.0004	0.786
Perceived sleep debt	0.001	0.849	−0.0001	0.994
Percentage of daily caloric intake at dinner	0.0018	0.005	0.0014	0.038
Breakfast skipping			0.108	0.012
Adjusted R^2	0.23		0.25	
ΔR^2	–		0.03	0.012

B = unstandardized coefficient.

between breakfast skipping and HbA_{1C}, and that both chronotype and breakfast skipping remained independently associated with poor glycemic control.

DISCUSSION

Our results demonstrated that both breakfast skipping and having a later chronotype are associated with poorer glycemic control in patients with type 2 diabetes. Breakfast skipping was associated with a 10.8% increase in HbA_{1C} of its original value. For example, given similar demographics, a breakfast eater may be expected to have an HbA_{1C} level of 7%, whereas a breakfast skipper would have an HbA_{1C} level of 7.8%. This difference approximates the potency of several available antidiabetic medications (Ismail-Beigi, 2012). A reduction in HbA_{1C} by 0.9% in patients with type 2 diabetes has been shown to reduce progressions of microvascular complications; 21% for retinopathy and 34% for albuminuria, a marker for nephropathy (UK Prospective Diabetes Study [UKPDS] Group, 1998). Our study is the first to report the differences in HbA_{1C} levels between breakfast skippers and breakfast eaters in patients with type 2 diabetes, and highlights the potential impact of the eating behavior on the course of the disease. Future research is warranted to examine whether behavioral interventions targeting breakfast-eating behavior will have a similar impact on HbA_{1C} levels within patients who report skipping breakfast.

We found that participants who skipped breakfast had significantly later chronotypes than those who consumed breakfast, with significantly later bedtimes and wake times, which is in agreement with previous studies (Meule et al., 2012; Nakade et al., 2009; Ostberg, 1973). Defining breakfast skipping in late chronotypes may be challenging given their late wake times. For example, studies that categorize breakfast skippers by the time when the meal is consumed, (i.e., 05:00 to 10:00 h, 06:00 to 09:00 h) may inadvertently define late chronotypes as breakfast skippers because they are likely sleeping during these periods (Alexander et al., 2009; Smith et al., 2010). In our study, breakfast was determined by participant self-report and not by clock time, consistent with some other studies of breakfast skipping (Kollannoor-Samuel et al., 2011; Mekary et al., 2012). Therefore, participants with later chronotypes could still be categorized as breakfast eaters depending on their personal definition of breakfast. The need to adjust to typical early social schedules (i.e., work, family, or school schedules) despite a drive for later wake times may partially explain our findings of the association between later chronotype and breakfast skipping. In addition, significantly more breakfast skippers reported having no appetite in the morning compared with breakfast eaters, suggesting that circadian regulation of appetite may play a role in skipping breakfast in addition to factors related to social schedules. Genetic factors may also explain the link between breakfast skipping and chronotype, as one previous study reported specific polymorphisms on the *Per2* gene were associated with adverse diet-related behaviors, including breakfast skipping (Garaulet et al., 2010). Despite this association between breakfast skipping and chronotype, chronotype did not completely mediate the association between breakfast skipping and glycemic control, suggesting that later chronotype and breakfast skipping maintained independent associations with higher HbA_{1C} levels.

There are a number of possible reasons why breakfast skipping may be associated with alterations in metabolic regulation. These include increased BMI, increased insulin resistance, and alterations of meal timing. First, breakfast skipping has been associated with increased BMI and waist circumference (Raynor et al., 2008; Smith et al., 2010). Our participants who skipped breakfast had significantly higher BMIs than those who consumed breakfast, despite having less total daily caloric intake from the 24-h food recall, which is supported by findings from many previous studies (Nicklas et al., 2000; Rampersaud et al., 2005; Skinner et al., 1985). Second, breakfast skipping was shown to be associated with increased insulin resistance and diabetes risk independently of BMI. An increased risk of type 2 diabetes in a large cohort study persisted in breakfast skippers even after stratification by BMI or diet quality (Mekary et al., 2012). In a study of obese children and adolescents, frequency of eating breakfast was negatively correlated with fasting glucose levels, independent of age, sex, and trunk fatness (Freitas Junior et al., 2012). Similarly, breakfast skipping in our participants was associated with worse glycemic control even after adjusting for BMI, suggesting that mechanisms beyond increased weight likely play a role in the relationship between breakfast skipping and glucose metabolism.

Third, timing of meal consumption may explain the relationship between breakfast skipping and metabolism. In this study, skipping breakfast was associated with consumption of a higher percentage of the daily caloric intake later in the day. In humans, glucose tolerance has been shown to be reduced in the evening, from a combination of reduced glucose utilization, decreased insulin sensitivity, and inappropriately low insulin secretion (Van Cauter et al., 1997), which highlights the importance of meal timing in glucose metabolism. The association between breakfast skipping and glycemic control in our study, however, remained significant after adjusting for percentage of daily calories consumed at dinner. Recently, a 20-wk weight-loss treatment study in Spain revealed that participants who ate their main meal of the day later (after 15:00 h) lost less weight despite having similar energy intake, dietary composition, estimated energy expenditure, appetite hormones, and sleep duration than participants who ate before 15:00 h (Garaulet et al., 2013). Another randomized weight loss study found that breakfast

skippers who were randomized to eating breakfast lost more weight than those randomized to continue skipping breakfast, despite being on a similar 1200 calorie per day diet plan (Schlundt et al., 1992). These data suggest that timing of food consumption, particularly early in the day, may play a role in body weight regulation and energy metabolism in humans. The molecular mechanisms of breakfast skipping may be partially explained by a recent study in mice that revealed that fasting early in their active periods (early nocturnal fasting), a proxy for breakfast skipping in humans, was associated with increased lipid synthesis and alteration in the expressional pattern of clock genes such as *Clock*, *Bmal1*, *Cry1*, and *Per2* in the liver and fat cells. These changes resulted in a predisposition to obesity (Yoshida et al., 2012).

We found that breakfast skipping was associated with later chronotype, which was previously reported to be associated with worse glycemic control (Reutrakul et al., 2013). Late chronotypes are at greater risk for experiencing chronic mild circadian misalignment, such that feeding and sleeping behaviors are more likely to occur at inappropriate times according to the circadian system. This may be due to the need to adapt to typical social schedules. Neurohormonal and metabolic dysregulations due to experimentally induced circadian misalignment have been demonstrated in laboratory studies of healthy volunteers. These resulted in impaired glucose tolerance and elevated mean arterial pressure levels (Buxton et al., 2012; Scheer et al., 2009). In addition, epidemiologic data have revealed that shiftwork, an example of severe circadian misalignment, is associated with increased risk of metabolic syndrome and cardiovascular disease (Boivin et al., 2007). These findings could help explain the association between chronotype and poor metabolic control in our participants.

The current study had some limitations. The number of participants who skipped breakfast was relatively small, though the prevalence was consistent with other studies (Mekary et al., 2012; Rampersaud et al., 2005). The food recall was completed for only 24 h and it was unknown if they were habitual breakfast skippers. The majority of our participants were female, with only six male breakfast skippers; therefore, it is possible that the results may not generalize to male patients. In addition, our participants reported relatively low daily caloric intake, which could reflect either underreporting or calorie-restricted diets, but we do not have this information. Future research directions include confirming the findings from this study in a larger population of patients with type 2 diabetes.

In summary, type 2 diabetes patients who skipped breakfast had later chronotype and poorer glycemic control than those who consumed breakfast. Later chronotype and breakfast skipping were independently associated with poorer glycemic control. These data suggest that both daily timing of meals and sleep may be important factors in disease management of type 2 diabetes. Behavioral interventions such as eating breakfast or modifying sleep timing could be considered as strategies to improve glycemic control in this group of patients.

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DECLARATION OF INTEREST

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