## Authors:

Molly C. Mulcahy, Allison C. Meyer, Erica Jansen, Dave Bridges

## Abstract

The timing of eating and duration of overnight fast are emerging components of the diet that are gaining popularity to manipulate for health reasons. In 102 parent-child dyads we find that later timing of first meal and midpoint of fasting, largely during the weekdays in tri XX, are associated with reductions in birth weight, but not parent mid-gestation oral glucose tolerance. These results warrant further examination

## Introduction

There are few times in life when nutritional intake matters as much as during the course of pregnancy. Modern science has demonstrated that pregnancy is a critical period of vulnerability that can impact trajectory toward health or disease, in both the birthing parent and the child. As such, much attention has been paid in scientific discourse on identifying modifiable behaviors that can improve the likelihood that results in a healthy pregnancy. The majority of the research in nutrition on this topic are focused on dietary quality, and nutrient adequacy. It is unsurprising that . However, recent evidence has pointed toward a previously under-considered modifiable component of the diet, the timing and duration of eating.

Initial evidence about the impact of the timing of eating on human health came from the field of sleep research. Routinely, researchers found that workers whose shifts are in opposition to the normal circadian rhythm have greater risks of ill health, including EXAMPLE, EXAMPLE, EXAMPLE.

New attention has been called to all health behaviors that impact or are impacted by one’s circadian rhythm. As such, modifying or compressing the timing of ones eating schedule is gaining popularity as a way to modulate health. One such modality is time-restricted eating. Evidence from human studies finds that condensing the eating window is effective for weight loss (Gabel et al., 2018; Hutchison et al., 2019; Lowe et al., 2020). There have also been studies that find that metabolic health markers, such as blood pressure and cholesterol can be improved from TRE without the reduction in body weight (Sutton et al., 2018). However, data from human pregnant populations remains scarce.

Timing data

Ramadan

Loy/Flanagan

Other groups have begun to disentangle the relationship between circadian eating and parental health during pregnancy. One such study found that the timing of meals was associated with maternal glycemia (directionality). Others have found that there is interest or openness to this behavior.   
  
Because pregnancy is a critical period of development with opportunity to impact health of the pregnant person and their child and because evidence surrounding the timing of eating in these populations is minimal, we sought to examine the association between the timing of eating and duration of fasting and mid-gestation glycemia and birth weight in a pregnancy cohort. We hypothesized that those who have earlier meal timing and longer duration of overnight fasts would have more favorable mid-gestation glucose tolerance test results without reductions in their infant’s birth weights.

## Methods

### Study population

The Pregnancy Related Eating Sleeping, and Stress (PRESS) cohort was developed as a longitudinal, survey-based, clinical research study. This study was designed to understand nutritional and behavioral contributors to perinatal health. Participants were recruited into PRESS in partnership the department of Obstetrics and Gynecology at Michigan Medicine. Those that were eligible based on their current OB status at Michigan Medicine reflecting pregnancy received an email with a public survey link. Individuals who were interested in the study were directed toward a public REDCap link that results in a screening questionnaire. Those who were 18 years old, currently pregnant, in weeks 1-30 of pregnancy, and were currently receiving care and planning to deliver at Michigan Medicine we deemed as eligible and were invited to join the study.

Because individuals were eligible to join the study between 1-30 weeks of gestation, participants joined the study at various timepoints. Gestational age at enrollment was self-identified by answering the question, “what week of your pregnancy are you currently in?” which was verified in the medical chart upon enrollment. There were three surveys that were sent to participants. One these were sent during the first trimester (1-13 weeks gestation), second trimester (14-28 weeks gestation, sent between 20-24 weeks), and third trimester (29-42+ weeks gestation, sent between 30-34 weeks). As participants could enroll in any trimester, they only received the surveys that were in line with target gestational weeks after enrollment. The bulk of the survey instruments sent in the surveys were repeated during all trimester data collection events, with the exceptions being an additional sociodemographic and lifestyle factor questionnaire and anticipated gestational weight gain instrument in trimester 1 and question about most recent body weight in pounds and ounces in trimester 3. Items in the questionnaires are listed in figure 1. At the time of this analysis, the majority of participants that had delivered had only completed survey information for trimester 2 and trimester 3. Therefore this analysis excludes data from trimester 1.

### Participant Exposures, Outcomes, and Covariates

#### Timing of first meal and last meal

The timing of eating during pregnancy was assessed during each trimester using a questionnaire that asked participants *“On a typical day during this trimester, when was the first time in the day you had something to eat? (This includes beverages that have calories; like coffee or tea with cream or sugar)”* to indicate the beginning of an eating window, and *“On a typical day during this trimester, when was the last you had something to eat before going to bed? (This includes beverages that have calories; like coffee with cream or sugar)”* to indicate the end of the eating window. We also collected timing of sleep onset and wake time. Participants provided answers to these questions with respect to both weekdays and weekends, for all eligible trimesters. Timing of eating data were inspected for overlapping eating and sleeping windows. Participants who did not report timing of eating or sleeping in military time were manually converted when necessary. Participant responses were evaluated for evidence of shift work, which was not apparent in the current sample.

#### Fasting duration and fasting midpoint

To determine fasting duration, we subtracted eating duration (the difference between the last eating occasion and first eating occasion, expressed hours and minutes) from 24 hours. The fasting midpoint was calculated as, time of last meal plus half the fasting duration.

#### Abstractions from medical chart data

Trained research staff accessed the participant’s medical charts to collect objective medical information about their current pregnancy. This included laboratory values, diagnoses of complications of pregnancy, parity, infant birth weight, sex of infant assigned at birth, and delivery method. Participants who did not have pre-existing diabetes underwent 1-hour oral glucose tolerance test (OGTT) during mid gestation (24-28 weeks’ gestation) according to Michigan Medicine guidelines. These labs were collected at a Michigan Medicine laboratory, where participants were instructed to consume a 50-gram liquid glucose drink in under 5 minutes. One hour later, blood was collected via venipuncture and glucose was determined by Michigan Medicine laboratory personnel. Primary outcomes of interest in this analysis were parent OGTT in mg/dL during mid-gestation and infant birth weight in grams.

#### Other Covariates

The data comprised in the PRESS study included validated instruments for repeated measures for dietary quality (DSQ paper here), perceived stress (PSS-4 paper here), nausea and vomiting of pregnancy (PUQ-24 Paper HERE), and disordered eating behavior (EDEQ-s paper here). Sociodemographic and baseline behavioral information was collected upon enrolling in the study. This included data about self-reported pre-pregnancy BMI, physical activity, relationship status, smoking exposure, as well as race/ethnicity, annual household income, and pregnant person’s level of education. Covariates were considered based on sociodemographic information available as well as *a priori* biological associations.

### Statistical Analyses

Univariate analysis was completed on all sociodemographic, eating exposure, and health outcome data were assessed for normality through histograms and residual plots. Measures that are normally distributed are expressed as mean ± standard deviation (SD) and those that were not normally distributed are expressed as median ± inter-quartile range (IQR). After initial investigation of variables, we assessed the associations between covariates of interest and primary exposures and outcomes identified in this study, grouped by weekday or weekend and trimester. When data were distributed normally, association was determined through ANOVA. When data was not normally distributed, associations were assessed through Kruskal-Wallis test. Associations with a P-value <0.10 were considered as covariates for later trimester and weekday/weekend specific models. Due to low subject numbers in some categories of covariate groups, we collapsed them into fewer categories; such as dichotomizing self-reported race and ethnicity, parent educational attainment, annual household income. Final models for OGTT were adjusted for pre-pregnancy BMI, physical activity, sleep duration, annual household income, and dichotomized race/ethnicity. Infant birth weight models were adjusted for gestational age at birth, infant sex assigned at birth, sleep duration, annual household income, dichotomized race/ethnicity, and physical activity.

Results:

#### Timing of eating during pregnancy differs based on sociodemographic factors

While recruiting for this study, we excluded individuals with pre-existing diabetes, inaccurate or missing timing data, loss to follow up, those who delivered multiples, and those without outcome data at the time of the analysis. This resulted in 102 unique individuals, 54 who had survey responses for trimesters 2 and 3 (Figure 2). PRESS participants tended to be older (32.1 ± 0.54 years), highly educated (78.4% had at least one college degree), wealthy (63.7% >$100,000 a year), and similar proportions of infant sex assigned at birth (56.9% male).

In this population the timing of the first eating occasion on weekdays during the second trimester was associated with parent-reported race and ethnicity, maternal education, sleep duration, and marital status. Participants from historically excluded groups tended to eat their first and last meal later in the day, as well as have a later fasting midpoint (Table1). This was also true with respect to measures of socioeconomic status like household income and maternal education, where those who were wealthier and more highly educated tended to begin and finish eating earlier in the day than those with fewer resources. Participants who were married or in a partnership tended to consume meals earlier, begin fasts earlier and have earlier fating midpoints. Sleep duration greater than 8 hours was significantly associated timing of the first and last meal, as well as longer fasting durations, but not fasting midpoint. Similar associations were seen for weekend values during trimester 2. However, delivering before 37 weeks gestation was associated with later timing of first meal on weekend, and the timing of eating for both first and last meals tended to be later than on weekdays (Table 2).

The timing of eating in trimester 3 on weekdays had fewer significant associations than did trimester 2 (Table 3). Later sleeping midpoint was associated with higher self-reported stress levels, which was driven by first meal. There were also more associations with gestational factors, such as earlier timing of first meal and vaginal delivery, and longer fasting duration occurring more in pregnancies that resulted in children assigned male sex at birth. Timing of eating variables in trimester 3 on weekends were also later than weekday, and with fewer associations (Table 4). Timing of first and last meal was again associated with parent race/ethnicity. Having greater amounts of physical activity during pregnancy was associated with lower oral glucose tolerance test in mid-gestation (Table 5). Whereas infant birth weight positively associated with gestational age at delivery.

#### Infant birth weight is inversely associated with the timing of eating during pregnancy

During trimester 2 on weekdays, There was a significant association between the first meal of the day and infant birth weight. One hour later initiation of eating was related to a 88.56 gram reduction in infant birth weight (Table 6; P=0.00018). This was robust to adjustment for XXXX. This was similar to relationships on weekends. During trimester 2, both later timing of first meal and fasting midpoint was associated with reductions in infant birthweight (Table 7; P values).There were less robust associations on weekdays during trimester 3. Where each hour later the fasting midpoint was on weekdays during the second trimester, there was a 104.7-gram reduction in infant birth weight (Table 6, P=0.0001). This directionality was consistent with fasting duration, where each hour longer spent fasting in trimester 2 was related to an 82.3-gram reduction in birthweight (P=0.022). Neither of these associations remained after adjustment for gestational age XXXXXX.

#### Parent glycemia during pregnancy is not related to the timing of eating during pregnancy

The association between timing of eating variables on weekdays was small in magnitude and only met statistical significance in unadjusted model for timing of the first meal in trimester 3 in which each hour later meal initiation was related to a 6.67 mg/dL increase in 1-hour OGTT (Table 8; P=0.045). After adjustment for XXX this was fully attenuated. There were no significant associations in trimester 3 on weekends, and timing of first meal on weekends during trimester 2 was also positively related to OGTT (Table 9;P=0.032).

### Discussion

This work demonstrates that even in small populations, there is sufficient evidence to

* In relation to ramadan, this differs
* Despite associations of eaitng timing in Loy and the case study, timing of eating and duration of fasting isn’t associated with maternal glycemia.
  + This suggest that this may not be a dietary regimen that merits practice in pregnant populations. This is because it appears to be deleterious for infant size. It also might not be a great intervention for maternal diabetes – as this shows it might not improve glycemia at all, but might be warranted for those who are at risk of delivering macrosomic infants.
* Limitations:
  + Small sample size
  + Residual confounding
  + Only analyzed in women who didn’t have diabetes – might not be the right population where we’d see an effect.
  + Non-diverse, very privileged sample – these bivariate associations suggest that timing of eating has strong association to the sociodemographic context to one’s life, such as partner status and - which could result in failing to capture the true biological or psychosocial contributor of the phenotype.
* Strengths:
  + Trimester specific design/ weekday and weekends
  + Comprehensive analysis of not just duration of fast, but impact on timing of eating window in a way that hasn’t been done before

### Conclusions

The timing of eating during the second and third trimester of pregnancy has the ability to impact infant birth weight, but not parent mid gestation glucose tolerance. As such, this should be considered as both an area of further research and a factor to counsel patients if one is anticipating have a particularly large or small child. These results need to be replicated in diverse samples and in larger populations to confirm these results before recommendations to clinical practitioners who might intervene on the circadian health of pregnant populations.