Relationship between Resting Energy Expenditure and Sleep Parameters on Gestational Weight Gain and the Mediation Effect of Macronutrient Composition

by

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ABSTRACT

No studies have evaluated the impact of tracking resting energy expenditure (REE) and modifiable health behaviors on gestational weight gain (GWG). In this controlled trial, pregnant women aged >18 years (X=29.8±4.9 years) with a gestational age (GA) <17 weeks were randomized to Breezing™ (N=16) or control (N=12) for 13 weeks. The Breezing™ group used a real-time metabolism tracker to obtain REE. Anthropometrics, diet, and sleep data were collected every 2 weeks. Rate of GWG was calculated as weight gain divided by total duration. Early (GA weeks 14-21), late (GA weeks 21-28), and overall (GA week 14-28) changes in macronutrients, sleep, and GWG were calculated. Mediation models were constructed using SPSS PROCESS macro using a bootstrap estimation approach with 10,000 samples. The majority of women were non-Hispanic Caucasian (78.6%). A total of 35.7% (n=10), 35.7% (n=10), and 28.6% (n=8) were normal weight, overweight, and obese, respectively, with 83.3% (n=10) and 87.5% (n=14) of the Control and Breezing™ groups gaining above IOM GWG recommendations. At baseline, macronutrient consumption did not differ. Overall (Breezing™ vs. Control; M diff=-349.08±150.77, 95% CI: -660.26 to -37.90, p=0.029) and late (M diff=-379.90±143.89, 95% CI:-676.87 to -82.93, p=0.014) changes in energy consumption significantly differed between the groups. Overall (M diff=-22.45±11.03, 95% CI: -45.20 to 0.31, p=0.053), late (M diff=-23.16±11.23, 95% CI: -46.33 to 0.01, p=0.05), and early (M diff=20.3±10.19, 95% CI: -0.74 to 41.34, p=0.058) changes in protein differed by group. Nocturnal total sleep time differed by study group (Breezing vs. Control; M diff=-32.75, 95% CI: -68.34 to 2.84, p=0.069). There was a 11.5% increase in total REE throughout the study. Early changes in REE (72±211 kcals) were relatively small while late changes (128±294 kcals) nearly doubled. Interestingly, early changes in REE demonstrated a moderate, positive correlation with rates of GWG later in pregnancy (r=0.528, p=0.052), suggesting that REE assessment early in pregnancy may help predict changes in GWG. Changes in macronutrients did not mediate the relationship between the intervention and GWG, nor did sleep mediate relationships between dietary intake and GWG. Future research evaluating REE and dietary composition throughout pregnancy may provide insight for appropriate GWG recommendations.

DEDICATION

I would like to dedicate this dissertation to my extremely supportive husband, Craig. His support, love, and guidance are what allowed me to complete my doctoral education, without it I would not be where I am today. He reminded me that the day-to-day stress is only temporary and that it will all pay-off in the end. He pushed me to still enjoy life outside of school and work and always provided a listening ear. With his encouragement, we were still able to find time to do things we loved as he made me realize that work-life-balance is vital to success. His laid-back mentality to life made me see a different perspective, allowing me to realize that life is really not that difficult, despite the current challenges I might be experiencing. He picked me up after several failures and celebrated with me after each success. I am forever grateful for him – his love, his support, and his guidance.

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INTRODUCTION

Background and Significance

There are significant variations in gestational weight gain (GWG) among pregnant women in the United States. Although the Institute of Medicine (IOM) provides recommendations for appropriate GWG (**Table 1**), 47.2% of pregnant women gain more weight than is

Table 1. Institute of Medicine Recommendations for Total and Rate of Gestational Weight Gain by Pregravid Body Mass Index

Pregravid Weight Category	**BMI (kg/m^2)**	**Range of Total GWG (kgs)**	**Rates of GWG (kgs/wk)**
Underweight	Less than 18.5	12.5 to 13.0	0.5
Normal Weight	18.5 to 24.9	11.5 to 16.0	0.4
Overweight	25 to 29.9	7.0 to 11.5	0.3
Obese	30 or greater	5.0 to 9.0	0.2

Body Mass Index (BMI) is calculated as weight in kilograms divided by height in meters squared. Modified from the Institute of Medicine (US). Weight gain during pregnancy: reexamining the guidelines. Washington, DC. National Academies Press, 2009.

recommended for their pre-pregnancy body mass index (BMI).[1] Excessive gestational weight gain (EGWG) is associated with a multitude of complications that impact both maternal and neonatal health. These adverse short- and long-term health consequences include but are not limited to preeclampsia, gestational diabetes, postpartum weight retention, fetal macrosomia, neonatal hypoglycemia, and admittance to the neonatal intensive care unit.[2,3] Previous research has demonstrated that variations in GWG are associated with decreased physical activity, increased energy intake, higher pre-pregnancy BMI, race/ethnicity, and maternal education.[4,5] However, the majority of interventions have focused on diet modification and physical activity implementation in order to promote appropriate GWG. Recently, research efforts have shifted to evaluate the changes in resting energy expenditure (REE) across pregnancy as an alternative physiological variable that affects body composition changes.[6–10] However, there is a paucity of research investigating not only changes in REE during pregnancy but also how maternal awareness of REE impacts the total and rate of weight gain. Furthermore, there is a lack of research investigating how other behavioral factors (i.e. diet and sleep) impact GWG.

Resting Energy Expenditure

Tracking of REE allows pregnant women to assess actual caloric needs during pregnancy and achieve a healthy weight gain. Direct calorimetry is the gold standard method of estimating metabolic rate by measuring the heat exchange between the body and the environment; however, this measurement technique is expensive, time consuming, and requires highly specialized and rare equipment. Due to these limitations, indirect calorimetry is more readily used as it is more accurate than calculated estimates that must factor in weight status and self-reported physical activity. Indirect calorimetry provides a measure of metabolic rate by estimating heat production as a ratio of oxygen uptake and carbon dioxide production during respiration. Indirect calorimetry also requires equipment, typically a metabolic cart, that is bulky and too costly for in-home use. However, real-time, mobile tracking has become increasingly popular but few devices are capable of accurately estimating caloric needs. Furthermore, mobile health devices have primarily been used to track diet and physical activity as well as deliver health information[11] but have not been widely used during pregnancy as tools to track REE to promote appropriate weight gain.[12]

Currently, available accelerometer devices are not able to accurately measure REE as these devices rely on calculated predictions of caloric needs based on body mass index and captured physical activity data. A recent study that evaluated the accuracy of seven wrist-worn devices found that none of the devices had an error rate less than 20% for energy expenditure when compared to the gold standard of indirect caloriometry.[13] The most accurate of the devices had an error rate of 27% for energy expenditure whereas the least accurate had an error rate of 93%.[13] Recently, the Breezing™ device was developed as a user-friendly, accurate device for tracking REE. This portable, state-of-the-art, real-time metabolism tracker measures REE by indirect calorimetry, i.e. oxygen consumption rate (VO_2) and carbon dioxide production rate (VCO_2), using a hand-held, Bluetooth-enabled device. The Breezing™ device has been validated against the laboratory-based Douglas Bag Method which demonstrated a strong significant correlation for VO_2 (r^2=0.945, p<0.001), VCO_2 (r^2=0.976, p<0.001), and REE (r^2=0.960, p<0.001) between the two methods.[14] Additionally, the percentage error difference was within ±10% for REE values between 900-3500 kcal/day.[14]

Recent pilot data utilizing Breezing™ found very different resting energy needs and very distinctive changes in REE throughout pregnancy among four women.[15] The results of this case study demonstrate the high individual variation and the unique changes in REE during pregnancy but also that the device is safe and feasible for pregnant women to use.[15] The IOM pregnancy weight gain recommendations are based on pre-pregnancy BMI ranges and not actual caloric needs. Therefore, this device may be a beneficial tool for pregnant women to use to track energy needs during pregnancy to avoid EGWG.

Caloric Needs during Pregnancy

The American College of Obstetricians and Gynecologists (ACOG) guidelines for nutrition during pregnancy provide general recommendations regarding the five major food groups, oils and fats, vitamins and minerals, caffeine, and alcohol.[16] However, ACOG does not provide information on the increased caloric needs during pregnancy for different pre-pregnancy BMI categories. Differences in caloric needs are more individually assessed using ChooseMyPlate.gov or the Centers for Disease Control and Prevention websites.[17,18] These organizations provide information on caloric needs based on trimester, guidelines for weight gain, and specific food groups and/or nutrients to consume or avoid during pregnancy.[17,18] Although these organizations provide a more specific and individual assessment of energy needs during pregnancy, the calculation of caloric needs is based on BMI and not energy expenditure measurements. Recently, research has investigated energy expenditure during pregnancy as an alternative explanation to variations in GWG.[10] Before individually tailored nutrition and weight recommendations can be established a better understanding of the biological variation in physiological factors such as energy expenditure and their impact on pregnancy are needed.

Dietary counseling during pregnancy is challenging as proper nutrition is needed to support maternal and neonatal health. Historically, the belief that a woman was “eating for two” was believed to contribute to increased caloric consumption and excessive gestational weight gain. True caloric needs have been estimated to increase by approximately 340-400 kcal/d in the second and third trimesters during pregnancy with little change in the first trimester.[18] Recent research has indicated a 27% increase in resting energy expenditure among 51 pregnant women

which equates to 400±200 kcal/day.[10] This is similar to previously published studies reporting a 25-30% increase in REE among pregnant women.[19–21] Although similar increases in REE have been found, variation in REE may be due to a multitude of aspects including health status, physical activity and fitness level, genetics, biological variation, as well as other internal and external factors.[10] According to ChooseMyPlate.gov women with a normal or overweight pre-pregnancy BMI have the same daily caloric needs which are 2000, 2200, and 2400 kcal/day in the first, second, and third trimesters, respectively.[17] Whereas, an obese woman's caloric needs increase by an additional 200 kcal/day in each trimester when compared to normal or overweight women.[17] Although the differences in caloric needs among pre-pregnancy BMI categories and between trimesters are minimal, without individual assessment of energy expenditure, similar caloric recommendations are provided to the majority of pregnant women.

These simple and very general recommendations are easy to implement; however, they may lead to excessive gestational weight gain due to lack of consideration of individual variation among biological and behavioral factors that influence energy balance. Interventions that have targeted appropriate GWG have implemented diet modifications[22–24] and physical activity[25–27] programs with differing effects on GWG. However, a recent meta-analysis showed that there is only a small increase in energy intake during pregnancy which were not correlated with GWG.[28] Other studies that have focused on physical activity implementation have demonstrated a predictable decrease in physical activity throughout pregnancy.[29] Therefore, the variation in GWG is only partially explained by energy intake and physical activity changes. However, it has been reported that pregnant women with smaller increases in REE throughout pregnancy had greater gestational weight gain despite caloric intake only increasing by approximately 5%.[10] Therefore, it is crucial that alternative physiological variables such as REE are considered in order to better understand variations in GWG and individually tailor nutritional and weight gain recommendations.

Sleep during Pregnancy

Sleep is an important health behavior that has been associated with poor health outcomes. Particularly during pregnancy, insufficient sleep has been associated with a longer

labor, increased perceived pain, high incidence of cesarean sections, increased pro-inflammatory cytokines, and preterm labor.[30] The National Sleep Foundation recommends pregnant women obtain approximately 8 hours of sleep per night .[31] Common sleep problems that pregnant women experience include insomnia, restless leg syndrome, sleep apnea, and nocturnal gastroesophageal reflux (nighttime GERD).[31] However, research studies have found inconsistent results. One previous study demonstrated that greater perceived sleep deprivation was associated with increased odds of gaining the appropriate gestational weight.[32] On the other hand, another study found that poor sleep quality among pregnant women was associated with excess gestational weight gain.[33] Regardless of conflicting results, interrupted sleep patterns and increased sleep disturbances are experienced by the majority of women with 76% reporting poor sleep quality, 100% reporting increased nighttime awakenings, and 78% needing daytime naps.[34] These changes in sleep hygiene impact both maternal and neonatal health.

Overall, sleep has been associated with changes in basal metabolic rate among healthy adult populations.[35] Poor sleep quality or decreased sleep duration are associated with increased obesity/overweight, elevated fasting blood glucose, increased blood pressure, hypertriglyceridemia, and metabolic syndrome.[35] Among a cohort of healthy, non-pregnant adults, basal metabolic rate significantly decreased after a night of restricted sleep.[36] However, there is no study that has evaluated how sleep mediates the relationship between diet and weight gain among pregnant women. Previous research has found an increase in energy expenditure during pregnancy as compared to the postpartum state with the absolute change in REE positively correlated with corresponding changes in body weight; however, this study did not evaluate sleep parameters.[8] There needs to be a better understanding of how resting energy expenditure changes during pregnancy, the impact that sleep parameters have on GWG, and how this impacts not only weight gain but also other health outcomes.

Summary

Scientific and public health endeavors have strived to develop effective programs to improve maternal child health in the U.S. However, excessive gestational weight gain is a growing public health problem as women not only have a higher pre-pregnancy BMI but also are

retaining more postpartum weight. Both physiological and behavioral factors have been investigated in order to better understand weight gain variations among pregnant women. However, to date, there are no studies that have evaluated the impact of tracking REE among pregnant women, whether changes in REE associate with gestational weight gain, or if other health behaviors mediate gestational weight gain.

STATEMENT OF THE PROBLEM

The impact of obesity is one of serious concern when considering the impacts on women of reproductive age. Obesity not only influences the health of these women but also their offspring. Further, obesity during the perinatal period results in greater healthcare costs as a consequence of increased utilization of health care resources. Because more women are entering pregnancy at higher weights, greater efforts are needed to minimize weight gain during pregnancy so that the majority of women gain within the IOM recommendations.

Despite public health efforts, it is apparent that policy change may be ineffective in improving pregnancy outcomes (specifically GWG) unless coupled with tangible interventions. It is unclear what interventions provide both short- and long-term benefits to maternal child health with the majority of literature highlighting diet and physical activity as key predictors of GWG. Current recommendations for weight gain, diet, and sleep are inadequate, poorly communicated, and misunderstood. It is vital that women have a balanced, healthy lifestyle during pregnancy. There needs to be a better understanding of individual variations in the maternal health factors (i.e. diet and sleep) during specific trimesters among diverse populations

There is a surplus of research that has investigated the impact that poor diet and inadequate sleep have on maternal child health. Despite the growing literature, there are still many discrepancies in research findings. Research has shown that poor diet and inadequate sleep are associated with a range of pregnancy outcomes such as GDM, hypertension, fetal growth abnormalities, among others. The inconsistency among these studies indicate that there may be an alternative factor that has not been evaluated, such as resting energy expenditure. Assessing and tracking REE throughout pregnancy might provide better insight into maternal health. The consideration of REE in conjunction with behavioral factors (diet and sleep) may

result in a more comprehensive understanding of each independent behavior's impact on health. Behavioral factors tend to be modifiable allowing for individually tailored interventions for improvement of maternal child health. Without consideration of REE, recommendations for diet, sleep, and weight gain during pregnancy are based on inaccurate, non-specific predictive equations that may lead to under- or over-nutrition during a critical period of growth and development.

STUDY PURPOSE AND RATIONALE

The purpose of this randomized controlled observational trial was to investigate gestational weight gain among pregnant women that used the Breezing™ device over a 13-week time period compared to pregnant women who did not use the device (**Figure 1**). Additionally, we analyzed how REE changes throughout pregnancy and its relationship to gestational weight gain among the study cohort (**Figure 2**). Furthermore, we explored the mediating effect of dietary composition on the relationship between the intervention (i.e. use of the Breezing™) and rate of GWG (**Figure 3**). Lastly, we investigated the relationship between maternal dietary macronutrient composition and gestational weight gain and the potential mediating effect of various sleep parameters (**Figure 4**). The rationale for the proposed study is that with a better understanding of individual variation in REE during pregnancy, nutrition interventions can be individually tailored to true energy needs in order to develop evidence-based nutritional recommendations for clinical providers that minimize the risk of excessive weight gain.

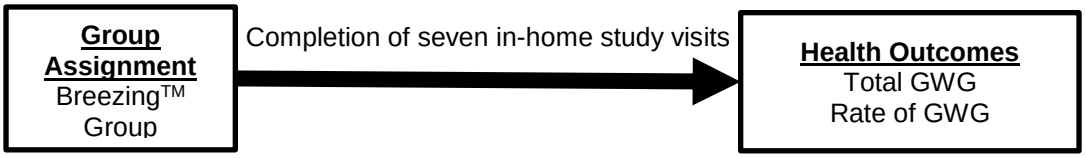
SPECIFIC AIMS & HYPOTHESES

We tested our central hypotheses by pursuing the following specific aims:

Aim 1: Evaluated the impact of a mobile, real-time metabolism tracking device on rate of gestational weight gain in pregnant women (**Figure 1**).

Hypothesis 1: We postulated that the Breezing™ group would have a higher proportion of women who gained the appropriate rate of weight per IOM recommendations as compared to the control group.

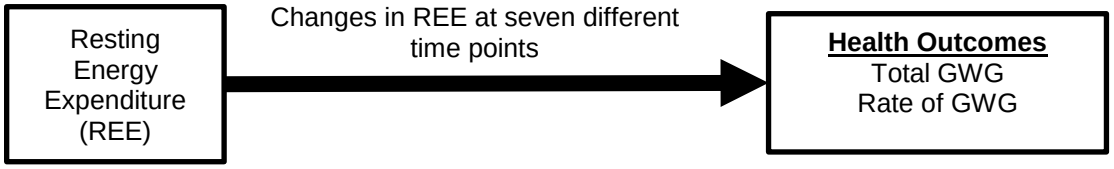
Figure 1. Primary Objective to Assess the Impact of the Intervention on Health Outcomes



Aim 2: Investigated how resting energy expenditure changed throughout pregnancy and whether REE was associated with rate of GWG among the study cohort (**Figure 2**).

Hypothesis 2: We expected that lower and decreased resting energy expenditure throughout the 13-week study period was associated with higher rates of weight gain.

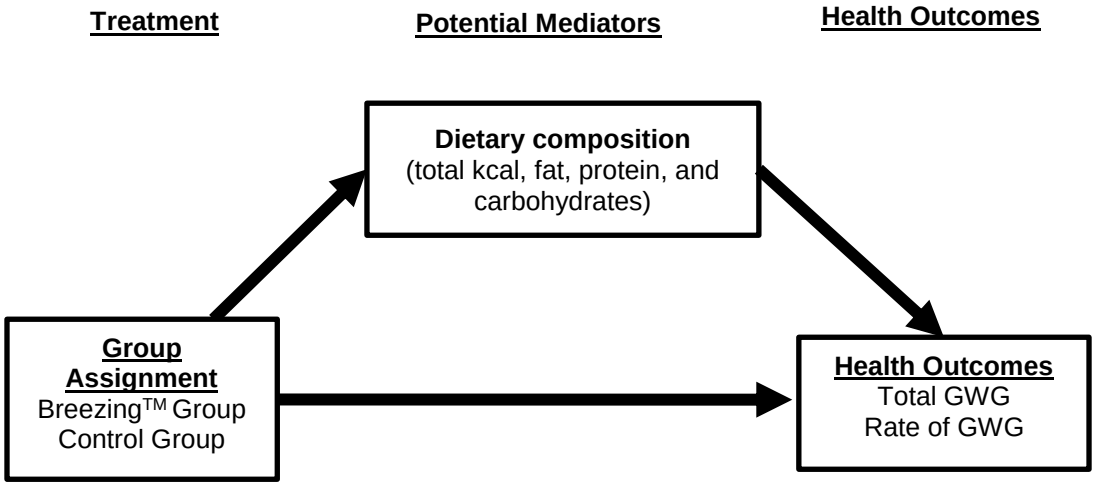
Figure 2. Evaluation of Changes in REE Impact on Health Outcomes



Aim 3: Determined whether dietary composition (total energy, carbohydrate, fat, and protein) mediated the intervention effect on rate of GWG within the Breezing™ and control groups through simple mediation models (**Figure 3**) and multiple mediation models.

Hypothesis 3: We hypothesized that changes (early, late, and overall) in dietary composition would mediate the intervention effect on rate of GWG. Specifically, that women in the Breezing™ group would have a lower rate of GWG through alterations in energy and macronutrient consumption.

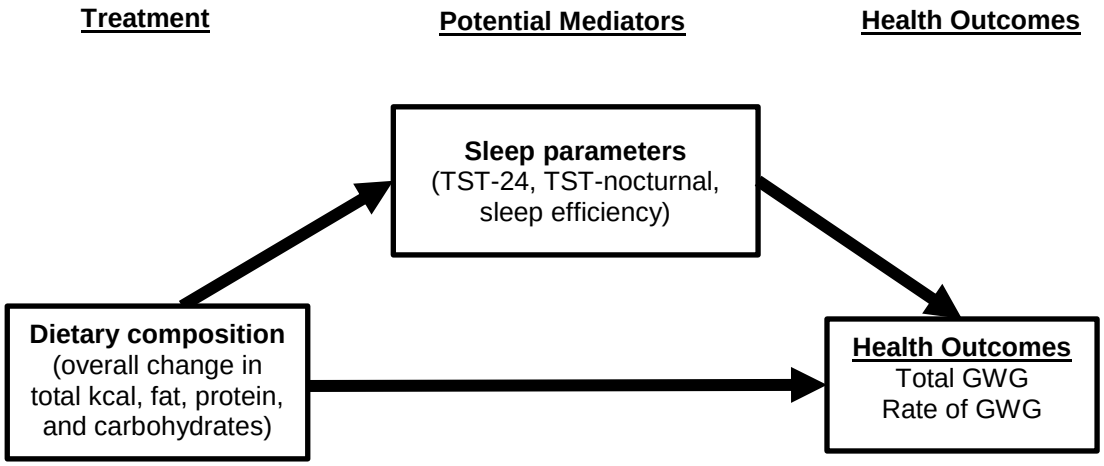
Figure 3. Simple Mediation Model where Each Diet Variable (M) was Tested for Mediation Effects on the Relationship between Group Assignment (X) and Gestational Weight Gain (Y)



Exploratory Aim: Evaluated whether objective sleep parameters (actigraphic total 24-hour sleep time, total nocturnal sleep time, or sleep efficiency) mediated the relationship between dietary composition (total energy, carbohydrates, fats, and protein) and rate of GWG (**Figure 3**).

Exploratory Hypothesis: We hypothesized that changes (early, late, and overall) in sleep variables would mediate the relationship between overall changes in dietary composition and rate of GWG. Specifically, we hoped to observe that late changes in sleep would mediate the relationship between energy and macronutrient intake parameters and rate of GWG.

Figure 4. Simple Mediation Model where Each Sleep Variable (M) was Tested for Mediation Effects on the Relationship between Diet Composition (X) and Gestational Weight Gain (Y)



REVIEW OF THE LITERATURE

Maternal Obesity

The overweight and obesity epidemic has grown to drastic proportions among women of reproductive age. This public health issue affects both developed and developing countries with the greatest burden of overweight and obesity among lower-middle and low income countries.[37] In the United States (US), sixty and thirty-five percent of women aged 20-34 years old were overweight or obese in 2013-2016, respectively, which is almost a two-fold increase (37% vs. 18.5%) from 1988-1994.[38] Furthermore, overweight (>80%) and obesity (>50%) disproportionately impact reproductive-aged Non-Hispanic Black[39,40] and Hispanic/Latino White women.[38,40] Over the last decade obesity has somewhat leveled off in the United States;[41] however, there were still over a million obese pregnant women in the US in 2014.[37] Despite declines, there has been a steady increase in the prevalence of women with obesity class II (BMI of 35-39.9 kg/m^2) and III (BMI>40 kg/m^2).[41] Extreme obesity (BMI>40 kg/m^2) has almost tripled (3.9% vs. 9.9%) from 1988-1994 to 2013-14 among women aged 20 years or older.[42] During this same time period, obesity among adolescent females aged 12-19 years old increased from 9.7% to 21.4% with Non-Hispanic Black (20.9%), Hispanic White (22.1%), and Mexican American (24.2%) adolescents disproportionately affected compared to Non-Hispanic Whites (14.6%).[42]

The magnitude of the growing obesity epidemic among women of reproductive age impacts health across generations, burdens the individual and healthcare system, and shifts the focus away from prevention to intervention.

Several studies have evaluated the increased health care costs associated with maternal overweight and obesity and found a 37-57% increase in pregnancy and labor/delivery costs for overweight women and women of varying obesity statuses.[43,44] According to a health economic study, an overweight woman incurs $10,500 more in health care costs as compared to her normal-weight counterpart after adjusting for comorbidities.[44] This increased utilization of health care services[43,45] is due to an increased frequency of fetal tests,[45] provider prenatal visits,[43,45] and telephone calls to the provider office.[45] Women with obesity also have a significantly greater length of stay in the hospital[43] compared to normal-weight women after adjustment for delivery mode and high-risk conditions.[45] Research has also shown that children of overweight or obese mothers have higher health care utilization and costs during the first 18 years of life as evidenced by more hospital admissions, longer hospital stays, and more frequent physician visits.[46] This equates to an additional $1,770 of direct health care costs among offspring of women with obesity compared to normal-weight women.[46] The increased utilization of health care resources and personnel time demonstrates that the disease burden of maternal overweight and obesity not only impacts maternal health but also offspring outcomes and public health for decades.

Obesity is a low-grade inflammatory state that causes metabolic dysfunction characterized by hypercholesterolemia, hyperglycemia, and insulin resistance.[47,48] When this dysfunction is coupled with pregnancy, the adverse health outcomes are exemplified. Maternal overweight and obesity is associated with a multitude of health consequences such as decreased fertility,[47,49,50] increased risk of diabetes[44,47,49,50] and hypertensive disorders,[47,49,50] increased rate of induction of labor,[50,51] higher incidence of cesarean sections and preterm birth,[50,51] and increased risk for stillbirth.[49,50] Fertility is affected as a result of obesity-associated endocrine dysfunction, which can further increase the risk for polycystic ovarian syndrome and oxidative stress.[47] Previous studies have found that the likelihood of conception is reduced by 5% for each unit increase in BMI among women with obesity.[47] Furthermore, obese women are far less likely

to initiate breastfeeding due to reduced milk production, poor latching onto the breast, and difficulties with proper feeding position.[50] Breastfeeding has been shown to help with postpartum weight loss, increased bonding between mother and baby, and greater time between gestations[50] while simultaneously providing all of the necessary nutrients and energy needs to the developing infant. Pregnancy is a state of delicate metabolic balance resulting in enhanced inflammation due to the drive of necessary nutrients to the developing fetus. This increased inflammation is associated with a multitude of potential negative health consequences for maternal and infant health which are only intensified during this time period among overweight and obese women.

The long-term health consequences of overweight and obesity are not limited to maternal health as they also adversely affect fetal and neonatal health. It has been reported that maternal obesity is associated with fetal growth abnormalities (i.e. fetal macrosomia, large-for-gestational-age, and small-for-gestational-age infants),[47,52] congenital anomalies (i.e. neural tube, cardiac, and limb defects), neurological outcomes (i.e. emotional symptoms, conduct and peer-interaction problems),[53,54] attention deficit disorder and autism,[53] and greater admissions to the neonatal intensive care unit (NICU).[51,55] Approximately 20% of women with obesity deliver an infant with fetal macrosomia,[47,56] which is primarily due to increased fetal fat mass.[56,57] This risk for the infant increases as maternal BMI[47] and gestational weight gain increase.[55] The cost of fetal and neonatal complications is substantial, ranging from $1,757 to $15,065 for treatment for mild cases such as shoulder dystocia and more severe complications that require admission to the NICU.[44] Furthermore, the state of chronic oxidative stress caused by obesity may impact fetal gene expression and cellular growth patterns.[47] When coupled with environmental factors, fetal pathophysiology may be irreversibly modified thereby increasing the risk for metabolic disease later in life.[47] A longitudinal birth cohort study found that children born to overweight or obese women had 1.42 and 2.74 increased odds of being overweight or obese by age four.[58] This study demonstrates the substantial impact that maternal overweight and obesity has on child health outcomes from birth through adolescence. Therefore, it is vital that women are healthy before, during, and after pregnancy to promote the health of their children.

Due to the increased risk for negative health outcomes and associated costs, numerous organizations, including the Academy of Nutrition and Dietetics and American Society for Nutrition, recommend that all overweight and obese women of reproductive age be counseled regarding a healthy diet and physical activity before, during, and after pregnancy.[50] Furthermore, the ACOG recommends that providers counsel women of reproductive age on the importance of conceiving at a normal BMI and that all women's health providers should offer pre-conceptional counseling on nutrition and physical activity.[2] Nonetheless, provider counseling is challenging due to time constraints, lack of comfort addressing weight, and insufficient training in behavior modification coaching. These challenges are made more difficult due to women having distorted views of a healthy body weight[59,60] and lack of knowledge of appropriate gestational weight gain[59] which further increases the odds of excessive gestational weight gain by sevenfold.[61] Despite these barriers, providers are presented with a unique opportunity to advise women on a healthy diet and lifestyle that will ultimately impact their health, the health of their unborn child, and the health of future generations.

Gestational Weight Gain Recommendations & Interventions

Gestational weight gain (GWG) is a normal part of pregnancy due to increases in maternal fat and fluid stores, fetal and placental development, and amniotic fluid requirements; however, appropriate GWG is seldom achieved with over 47% of women gaining more than the recommended amount of weight.[1] The recommendations provided by the Institute of Medicine (IOM) were originally developed in 1990 and revised in 2009. Revisions to these recommendations expanded the guidelines to include obese women and anchored recommendations to pre-pregnancy weight status.[62,63] Despite revisions to the previous recommendations, it is noteworthy that the revised recommendations for the amount and rate of weight gain for obese women was primarily based on data from women with a BMI between 30-35 kg/m^2.[62] The updated 2009 IOM guidelines demonstrated disparities among the BMI weight categories after an evaluation of GWG among pregnant women found that overweight and obese women had a median weight gain that exceeded the midpoint of the 2009 IOM recommendations by 10 lbs and 9 lbs, respectively.[57] A decade after implementation of the 2009 IOM

recommendations, a quasi-experimental study that assessed changes in GWG found there were no differences in total weight gain across pre-pregnancy BMI categories.[63] It has been reported that overweight and obese women are more likely to gain more than the recommended amount of weight compared to normal or underweight women and that the greatest proportion of women with excessive gestational weight gain were overweight[62,64,65] or obese[64–67] prior to conception. Unfortunately, despite public health efforts, it is apparent that policy change may be ineffective at improving GWG outcomes unless coupled with tangible interventions.

Interventions aimed at improving maternal health can target three time periods – antepartum, intrapartum, and postpartum – of reproductive health. Since weight loss is not recommended during pregnancy,[62] the majority of interventional studies have targeted the preconception period[57] to increase the number of women entering pregnancy at a healthy weight or the postpartum period to reduce the number of women that retain weight gained during pregnancy.[68] Interventions during pregnancy have focused on women gaining within the IOM recommendations which have primarily consisted of lifestyle interventions, either in-person or technology-delivered, that have focused on improved dietary habits, increased physical activity, or a combination of the two. A recent systematic review of 44 studies concluded that diet, exercise, or a combination of both was effective for reducing weight gain during pregnancy with the most successful interventions being diet-only.[69] Bogaerts et al. developed a lifestyle intervention that provided pregnant women with an informational brochure or educational group sessions addressing healthy diet and physical activity information (lifestyle group) and found significant differences in GWG between the groups (9.5 kgs in brochure vs. 10.6 kgs in lifestyle vs. 13.5 kgs in control).[25] However, another lifestyle intervention delivering dietary and exercise components did not influence overall GWG.[70] Another systematic review found that regardless of pregravid BMI, diet and physical activity interventions were successful in reducing GWG, achieving GWG within IOM recommendations, and decreasing postpartum weight retention without adverse neonatal/fetal outcomes.[71] While several studies have demonstrated a beneficial impact on weight among women of reproductive age,[23–27,69,71–77] other studies have shown little to

no effect.[22,70,78–80] These findings, highlight the inconsistent results among lifestyle or behavioral interventions targeted at pregnant, typically overweight or obese women.

Exercise interventions have been effective in reducing the total or rate of weight gain among pregnant women.[26,27,75–77] Bisson et al. reported that the exercise group gained significantly less weight per week than the control group (0.35 vs 0.46 kg per week) despite similar caloric intakes; however, the intervention did not demonstrate a lasting effect as the total weekly weight gain was not significantly different between groups (0.47 vs 0.45 kgs per week for exercise vs control) at the last follow-up visit.[26] Similarly, Wang et al. found women in an exercise group had significantly less GWG at 25 weeks gestation and at the end of pregnancy.[27] A systematic review and meta-analysis reported a mean difference of -1.1 kgs in GWG among women who participated in an exercise intervention as compared to those that did not.[76] Likewise, among the included cohort studies, active women had a 18% lower risk of exceeding the IOM GWG recommendations compared to inactive women.[76] Antenatal exercise interventions have also been effective in reducing gestational weight gain among overweight and obese pregnant women with a standard mean difference of -0.36 kgs (CI: -0.64, -0.09).[77] However, Nitert et al. found that despite increases in overall physical activity levels, there were no differences in total GWG or rate of GWG between exercise and control study groups.[78] Clearly, exercise plays an important role in appropriate weight gain during pregnancy. Despite some contradictory results, exercise interventions targeted at pregnant women suggest promise for mitigating excessive gestational weight gain.

Intervention studies that have primarily focused on the delivery of a nutrition or diet program have had varying effects on GWG, possibly due to the heterogeneity among study designs and interventions being delivered. A systematic review found that the majority (69%) of the included studies reported a significant difference in GWG with the intervention groups gaining 5.0-10.6 kgs as compared to the control groups that gained 6.7-14.1 kgs.[72] However, a behavioral nutrition intervention program designed for obese pregnant women demonstrated improved diet quality but did not significantly impact GWG (mean weight gain of 10.0 kgs vs 9.7 kgs) or postpartum weight loss at six-months follow-up (72.2% diet group vs 83.3% control group had

returned to or were below their pre-pregnancy body weight).[22] Lack of differences in postpartum weight retention were also found in the Fit for Delivery study, which evaluated the effectiveness of a telephone-based intervention that targeted healthy eating, exercise, and gestational weight gain.[81] On the other hand, pregnant women enrolled in a medical nutrition program that reduced fat and carbohydrate and increased protein consumption, gained significantly less weight throughout pregnancy.[23] Previous research has also found that pregnant women randomized to a low glycemic index diet were less likely to exceed the IOM GWG recommendations.[24] The drastic differences in the objectives of these studies and the inconsistent findings make the synthesis of study results impossible and increases confusion regarding the true role of diet in prenatal weight gain.

Recently, intervention studies have been utilizing technology, e.g. mobile text messaging, educational DVDs, or telehealth delivered visits, to provide healthy lifestyle, diet, and exercise regimens during pregnancy. One study that used mobile text messaging combined with four midwifery visits that provided information on a healthy diet and lifestyle found that women in the intervention group had significantly less GWG (5.6 vs 7.2) and were more likely to gain within the IOM recommendations.[73] A similar text messaging study found significant reductions in GWG (7.8 vs 9.7 kgs) and maintenance of physical activity but did not impact diet quality.[74] However, a study that used an educational DVD to deliver healthy diet and exercise information to pregnant women reported no significant difference in GWG or physical activity level between the groups.[79] Similarly, a mobile health intervention among low-income WIC participants did not find differences in body weight, body fat, or waist/hip ratio; however, this study was limited due to large variations in intervention adherence.[80] When adherence to intervention was controlled for, significant reductions in body weight and percent body fat among the high adherers were reported.[80] Overall, technology may provide a convenient and affordable method to target pregnant women and improve health outcomes.

The effect of interventions studies on other pregnancy-related health outcomes beyond excessive GWG have had contradictory findings regarding their impact on short- and long-term perinatal outcomes. This is evidenced by a lifestyle intervention consisting of dietary consults and

twice-weekly exercise sessions that had no impact on glucose levels or rate of gestational diabetes mellitus (GDM) among study participants.[82] Similarly, a large longitudinal study found no difference in the rate of GDM or LGA despite reductions in GWG and increases in physical activity among intervention participants.[83] However, a medical nutrition program specifically tailored to the dietary needs of the pregnant women successfully reduced the incidence of GDM, preeclampsia, and macrosomia.[23] Furthermore, an exercise intervention among obese pregnant women had no effect on maternal blood glucose, insulin, triglycerides, or total, HDL, LDL cholesterol levels at any stage of pregnancy.[78] However, an exercise intervention reported lower incidence of preterm birth, macrosomia, and LGA infants among intervention and control participants, but these differences were not significant.[27] Better understanding of the longitudinal effect that interventions during key periods of reproductive health have on maternal and fetal health is needed.

Excessive gestational weight gain has been shown to have substantial and lasting effects on the offspring with long term health consequences. Several studies have reported that when GWG exceeded recommendations, there were increase odds of higher birth weight,[84] LGA infants,[84–86] gestational hypertension,[85] preeclampsia,[85] and emergency cesarean sections,[85] regardless of pre-pregnancy BMI category. The opposite has been reported among women who exceeded GWG recommendations demonstrating increased neonatal fat mass and fat-free mass.[57] Additionally, a case-control study found that women with obesity class III who lost or maintained weight while pregnant resulted in an increase in appropriate-for-gestational-age infants compared to women in the same obesity class who gained weight.[43] However, in a follow-up study of a large prospective birth cohort, there were no differences in BMI or weight- and height-for-age at five years of age among children whose mothers received a weight restriction intervention during pregnancy as compared to controls.[87] These findings demonstrate that maternal weight gain during pregnancy has lasting impacts on infant health but longitudinal assessment of these effects on child health later in life are needed. Despite this, it is vital that healthcare providers counsel pregnant patients regarding GWG in order to minimize the impact on maternal and infant health.

Only 31% to 55% of pregnant women report receiving advice from their healthcare providers regarding appropriate GWG[60,88,89] with 79% of this advice specifically addressing IOM recommendations.[88] Interestingly, approximately two-thirds of obese pregnant women underestimate their pre-pregnancy weight[60] potentially increasing their risk for excessive gestational weight gain after being categorized into the wrong IOM weight gain category. Although healthcare providers regularly check weight gain at prenatal care visits, seldom do they review weight gain progress with pregnant patients; ultimately, this may portray a lack of concern for GWG and related health consequences.[90] Patient-provider communication regarding pre-pregnancy weight status and GWG needs to drastically improve. One study found that women who were counseled using two or more of the 5 A's (i.e. assess, advise, agree, assist, and arrange) gained significantly less weight.[89] Similarly, studies have used the person-centered care (i.e. a model of care that focuses on the individual not the patient by allowing the individual to identify the problem, share in the decision making, and participate in documentation) model to address weight gain during pregnancy and found that women who received this type of care at prenatal visits gained less weight.[91] Given the success of such models of care, further work is needed to identify what information should be shared to minimize the risk for excessive gestational weight gain.

Caloric and Nutritional Needs During Pregnancy

Despite knowledge that dietary habits and overall nutrition are vitally important for proper fetal development and overall health of the mother, culturally, non-scientific dietary advice (e.g 'eating for two') persists among women of childbearing age.[92–94] Such beliefs have been implicated in excess energy consumption and gaining inappropriate amounts of weight during pregnancy.[94] Guidelines regarding proper nutrition during pregnancy have been developed by the American College of Obstetricians and Gynecologists (ACOG), the Centers for Disease Control and Prevention (CDC), the United States Department of Agriculture (USDA), and the IOM.[16–18,95]

ACOG and CDC recommendations briefly mention five food groups (i.e. grains, fruits, vegetables, protein foods, and diary) and recommend utilizing USDA's ChooseMyPlate for specific amounts of each food group and methods of incorporating these foods into the diet.[16]

Both of these guidelines provide more detailed information for specific nutrients including increasing folic acid and iron, limiting caffeine intake, avoiding alcohol consumption, increasing omega-3 fatty acid ingestion, and avoidance of certain deli meats and fish.[16,18] The USDA ChooseMyPlate website utilizes the Dietary Guidelines for Americans[96] to guide their recommendations with an interactive, user-friendly tool that provides evidence-based recommendations personalized for individual characteristics (i.e. age, height, weight, physical activity level, and stage of pregnancy).[17] Although ChooseMyPlate guidance relies on pre-pregnancy weight status for identifying caloric needs, recommendations are identical for both normal- and overweight women and increase only for obese women. While these general recommendations may be easy to implement, they only provide advice on total daily energy needs and consumption of specific food groups. In contrast to ChooseMyPlate guidance, the IOM recommends caloric macronutrient proportions in the ranges of 45-65%, 20-35%, and 10-35% for carbohydrates, fat, and protein, respectively, for pregnant women.[95] This equates to 71 and 175 grams of protein and carbohydrates per day, respectively, for a typical 2000 kcal diet.[95]

Total energy intake during pregnancy has been reported to range from approximately 1860 to 2550 kcal/day.[97–101] It is not well-understand how energy requirements change during pregnancy with studies reporting an increased caloric need of approximately 340-450 kcal/day in the second and third trimesters of pregnancy.[18] Rad et al. found that total energy, carbohydrate, fat and protein intake did not substantial change throughout pregnancy;[102] however, a meta-analysis reported that total energy, protein, fat, and carbohydrate increased by 184±86 kcal/day, 5.9 gms/day, 10.1 gms/day, and 17.8 gms/day from the first to the third trimesters.[101] Macronutrient composition during pregnancy ranges from 15-16% for protein, 31%-33% for fat, and 47.8-51.8% for carbohydrates with the majority of studies finding similar distributions.[98–100,103] However, 51% of pregnant women have total energy intakes above the recommended daily intakes with 19% not meeting carbohydrate and 38% exceeding fat recommendations.[104] It has been reported that highly processed foods are readily consumed during pregnancy comprising an estimated 63.2% of daily energy intake[105] which might explain reported overconsumption of energy and fat. On the other hand, a systematic review of 23 studies found that maternal dietary

changes during pregnancy include significant increases in fruit and vegetable consumption, decreased egg intake, higher ingestion of milk and dairy products, and decreased consumption of fried and fast foods when compared to preconception.[106]

Inadequate or excessive nutrient intake and poor diet quality are associated with various risk factors. Previous research has demonstrated that diet quality is reduced with higher BMI,[107] less education,[107,108] cigarette use,[108] and increased parity.[107] Socioeconomic status has been found to be an independent risk factor for poor dietary intake,[108,109] specifically protein and fat intakes have been associated with higher and lower SES, respectively.[109] Poor diet quality during pregnancy has been associated with higher maternal age, less education, and increased rate of unintended pregnancy.[106] Previous research has shown that Healthy Eating Index scores significantly decreased (56.7±10.1 early pregnancy to 53.3±12.7 4 mos postpartum) among overweight and obese women due to reductions in milk, meat, bean, and oil consumption.[110] Unfortunately, the majority of these risk factors are not modifiable, further complicating appropriate dietary recommendations for pregnant women.

Maternal nutrient availability and placental nutrient transport are the primary factors that impact fetal growth and development.[111] Placenta size and weight (i.e. fetal to placenta weight ratio) is a direct predictor of placental nutrient transport efficiency with a higher ratio indicating higher efficiency.[111] It is believed that the fetal growth rate is matched with the availability of maternal nutrients such that excess nutrients will accelerate fetal growth.[111] The fetal nutrient environment depends on maternal health and nutrient consumption which impact metabolic programming and the etiology of offspring diseases later in life.[112] The pathophysiology of adipose tissue development begins in utero which is necessary for exposure to the cold extrauterine environment during delivery.[112] However, when maternal levels of glucose and lipids are high such as in GDM and obesity, the placenta compensates through increased placental transport of nutrients which ultimately increase fetal growth.[111] On the other hand, maternal nutrient restriction is correlated with a multitude of long term effects on the neonate including higher blood pressure, increased incidence of adult hypertension and coronary heart disease, and increased fat mass accompanied with glucose intolerance and insulin resistance.[112] The fetal

environment is drastically impacted by maternal health and nutrient availability; therefore, it is important that women have a balanced, healthy diet during pregnancy.

The maternal diet is pivotal for appropriate fetal growth and development and overall pregnancy outcomes. There is a multitude of research that has evaluated the impact of maternal diet on maternal and child health. It is well known that a high quality diet during pregnancy is related to better pregnancy outcomes such as lower blood glucose,[107,113] reduced risk for preeclampsia,[107] increased fertility,[114] and lower incidence of GDM.[115] However, there are contradictory findings pertaining to specific diets (i.e. DASH diet, macronutrient distributions, Mediterranean diet) on health outcomes. Surprisingly, no associations have been observed between higher DASH diet scores and maternal blood pressure, GDM, preterm delivery, or birth weight.[116] However, the DASH diet has been correlated with decreased fasting glucose levels in pregnant women.[117] Interestingly, greater adherence to the DASH diet has been associated with increased GWG such that a one-unit increase in the DASH diet score was associated with a 0.19 kg increase in GWG, but only among women with obesity prior to conception.[116] On the other hand, better adherence to the Mediterranean diet demonstrated a decreased risk of GDM.[115] Consumption of ultra-processed foods are associated with poor pregnancy outcomes such as higher GWG[105] and increased neonatal skinfold thickness and body fat percent.[105] Macronutrient distribution seems to play a role in various maternal and neonatal health outcomes. A low-glycemic index (GI), high-fiber diet was found to be the most effective diet to reduce maternal fasting blood glucose[117] whereas a low carbohydrate, high fat diet increased the risk of GDM.[113,114] Conversely, increased maternal carbohydrate intake has been reported to be associated with lower infant fat-free mass index,[118] neonatal fat mass,[103] increased birth length,[98] and higher child BMI z-scores at 2-4 years of age.[100] Additionally, higher maternal intake of protein during pregnancy was found to be correlated with increased risk of GDM,[119] lower neonatal abdominal adipose tissue,[120] higher child lean mass at 10 years of age,[109] higher blood pressure in offspring at 20 years of age,[99] and higher mean BMI and incidence of overweight among female offspring at age 19-21 years.[121] Maternal fat intake has been associated with higher GWG,[122] infant[103,118] and childhood[97,109] fat mass and fat-free mass index.[118] The lack of

consensus in study findings demonstrates the complexity of maternal nutrition and its association with both short- and long-term health outcomes for mothers and infants.

Maternal diet is associated with a multitude of maternal and neonatal outcomes; however, there is a lack of agreement among the current literature on what constitutes the healthiest maternal diet and how modifying specific nutrients impacts perinatal health. Regardless of inconsistencies it is still vital that healthcare providers counsel pregnant women on a healthy, well-balanced diet. Unfortunately, there is great variation in the percentage of healthcare providers who provide nutrition counseling during pregnancy, ranging from 17.9-69.3%.[123–125] Nutrition counseling during prenatal visits has been shown to improve GWG, reduce risk of anemia, increase birthweight, and decrease the risk of preterm delivery.[126] However, prenatal nutrition counseling is challenging due to inadequate knowledge of recommendations and provider time constraints. Without more consistency regarding maternal diet and its association with maternal child health, prenatal nutrition counseling may be confusing and ineffective for women.

Resting Energy Expenditure

Resting energy expenditure (REE) is the amount of energy expended at rest to maintain basic organ function, respiration, circulation, and other functions for survival. It is the largest component of energy expenditure accounting for 60-70% of total daily energy expenditure. Tracking of energy expenditure is primarily obtained using direct or indirect calorimetry or predictive equations. Direct calorimetry estimates metabolic rate by measuring the exchange of heat between the body and the environment. Typically, this measurement is done over a 24-hour time period in an isolation chamber; therefore, it is expensive and time consuming. On the other hand, indirect calorimetry estimates metabolic rate by measuring heat production through determination of oxygen uptake and carbon dioxide production during respiration. This measurement requires equipment, usually a metabolic cart, with a plastic hood that is placed over the individual's entire head that is connected to a computer via a tube. Although these measurements are more accurate and precise, they are seldom used in a free-living setting due to the need for expensive, bulky equipment, and time constraints. Measurements of energy

expenditure, therefore, have primarily been obtained through the use of predictive equations. The two most widely used equations for predictive estimates of REE are Harris Benedict and Mifflin-St. Joer equations. Both of these equations use height, weight, and age as part of the calculation for resting metabolic rate (RMR). They have been compared against each other with strong agreement; however, Harris-Benedict equation measurements were more strongly correlated with indirect calorimetry.[127] These equations do have limitations, mainly that they were designed for healthy, non-diseased adults. Therefore, their utility during pregnancy is questionable. RMR measured by indirect calorimetry has been significantly correlated with predicted energy values in the early part of pregnancy but not after 30 weeks gestation.[128] In 2009, a new equation derived from the Harris-Benedict equation was proposed for pregnant women which yielded high concordance with indirect calorimetry measures of REE.[129] Regardless, the method of measuring or calculating REE is typically determined by access to resources, cost, and time.

Recently, real-time, mobile tracking of REE has become increasingly popular but few devices are able to accurately estimate caloric needs; further, they have rarely been evaluated in a pregnant population.[11,12] A recent study that evaluated the accuracy of seven wrist-worn devices found that none of the devices had an error rate less than 20% for energy expenditure.[13] This study reported that the most accurate of the devices had an error rate of 27% whereas the least accurate had an error rate of 93% for energy expenditure.[13] The Breezing™ device, a user-friendly, portable, real-time metabolism tracker, uses indirect calorimetry to assess REE. Indirect calorimetry calculates REE by measuring the oxygen consumption rate (VO_2) and the carbon dioxide production rate (VCO_2). A validation study that compared the Breezing™ device against the laboratory-based Douglas Bag Method (indirect calorimetry) demonstrated a strong significant correlation for VO_2 (r^2=0.945, p<0.001), VCO_2 (r^2=0.976, p<0.001), and REE (r^2=0.960, p<0.001) between the two methods.[14] Furthermore, it has been demonstrated that the percent error difference was within ±10% for REE values between 900-3500 kcal/day,[14] demonstrating the utility of this device for diverse populations. Although the Breezing device has not be validated in a cohort of pregnant women, indirect calorimetry has been widely used during pregnancy.[130–134] Additionally, the Breezing™ device has been used in a pilot study of pregnant women which

demonstrated drastic variations in REE throughout pregnancy that did not correlate with predictive equation estimates.[15] These studies further demonstrate the efficacy and safety of the Breezing™ device[14,15,135] and provide evidence to suggest that indirect calorimetry may be a more accurate measurement of REE during pregnancy than equations.[15]

The majority of previous studies that have evaluated variations in REE during pregnancy have demonstrated an overall increase; however, several of these studies reported trimester-specific changes. Chihara et al. found nonsignificant increases in REE of approximately 344 kcal during pregnancy but only found these non-significant increases in REE after 32 weeks gestation.[7] Conversely, Byrne et al. demonstrated that REE significantly increased by 177±176 kcal/day during pregnancy between 15 and 30 weeks gestation.[128] On the other hand, a multitude of studies have found drastic changes in REE as pregnancy progresses.[10,15,136,137] Catalano et al. reported that REE increased approximately 25-35% during gestation with average caloric needs of 1402±187 kcal/day in the pregravid period, 1513±233 kcal/day in early pregnancy, and 1886±372 kcal/day during late pregnancy.[138] Similarly, Willommet et al. found that REE increased as gestation progressed with a difference of 72 and 100 kcal/day between the first and second and the second and third trimesters, respectively.[137] After accounting for fat-free mass, Berggren et al. reported an average increase in REE of 13% (1428±172 vs 1820±283 kcal/day).[10] Clearly, there are changes in REE whether they are during specific trimesters or throughout the duration of pregnancy. This is further evidenced by a case study of four pregnant women that used the Breezing™ device which found unique changes in REE with no consistent changes across the participants.[15] It is apparent that REE is a highly variable measure that is impacted by numerous biological and behavioral factors. Without consideration of REE, nutrient and GWG recommendations are based on inaccurate, non-specific predictive equations that may lead to under- or over-nutrition during a critical period of growth and development.

There are various biological factors that have been found to contribute to variations in REE including disease status (i.e. GDM and pregnancy) and adiposity (i.e. body weight, fat mass, and fat-free mass). Disease states such as GDM, obesity, or pregnancy have inconsistent outcomes pertaining to their effects on REE. This was apparent in a study that compared

differences in REE among women with normal glucose tolerance and those with GDM. This study found no changes during the first, second, and third trimesters among women with GDM.[139] However, this same study showed that pregnant overweight women with normal glucose tolerance or GDM had significantly higher REE at all periods when compared to normal- and under- weight women with and without glucose intolerance.[139] Historically, it was believed that women with obesity were thought to have lower REE and total energy expenditure; however, recent literature has reported the opposite.[140] A narrative review found that 91% (19/21) of studies that assessed differences in REE between obese and non-obese individuals reported higher REE in obese individuals with a mean difference ranging from 49-826 kcal/day.[140] Furthermore, a comparison of REE between pregnant (1673±203 kcal/day) and non-pregnant (1413±172 kcal/day) women revealed a significantly higher REE during pregnancy.[141] This increase in REE as a result of pregnancy has been reported in several other studies as well.[67,142,143] These findings indicate that variations in REE during pregnancy may play a vital role in health outcomes for both mom and baby.

Investigation of the relationship between adiposity and REE reveals inconsistent findings. Previous research has found that increases in RMR in early pregnancy were not correlated with body weight, BMI, or weight gain in a cohort of obese pregnant women.[128] This is in contrast to other study results that demonstrated that changes in RMR/REE were positively correlated with changes in body weight, primarily due to the metabolically active portion of body fat.[8,10,136,139,140,144] Biological variation in REE appears to be influenced by an array of factors. How these factors impact maternal and child health remains an area for further investigation.

There are several behavioral factors such as activity level, nutrition, and sleep that have been evaluated for their association with REE. It has been argued that GWG is related to increased energy consumption and decreased physical activity[8,10,141] during pregnancy. One study compared the activity energy expenditure among healthy pregnant and non-pregnant women and found that pregnant women spent 92 more mins/day sitting, lying down, reclining, and sleeping and 21 mins/day less walking and using stairs when compared to non-pregnant women; however, they did not assess changes in REE.[141] Approximately 70% of pregnant

women compared to 89% of postpartum women spent 30 minutes or more on moderate intensity physical activity, which was coupled with a 21.4% increase in RMR.[8] Unfortunately, the belief that energy intake substantially increases during pregnancy has little validity. The majority of studies have reported little or no difference in caloric intake with an approximate 5-9% increase in caloric consumption during pregnancy.[10,144] However, energy expenditure does considerably vary between women with higher BMI[67] and who gain weight in excess.[6,136] Previous research has found that REE had a strong, positive correlation with specific nutrients such as total energy, protein, fat, carbohydrates, cholesterol, sugar, and fiber.[9] Finally, sleep restriction has demonstrated detrimental effects on metabolism representing a 2.6% (-42 kcal/day) reduction in RMR.[36] This change in RMR rebounded after one day of sleep recovery above the RMR at baseline (+60 kcal/day).[36] These behavioral factors are modifiable which provides an opportunity for individually tailored interventions to adjust specific behaviors to improve health by changing REE.

REE accounts for 60-70% of total daily energy expenditure and has a substantial impact on human health. There are various biological and behavioral factors that impact an individual's REE. Variations in REE during pregnancy are not well understood and available results are heterogeneous. However, it is still important to understand these changes and the impact they have on maternal child health, particularly on the developing fetus. A previously conducted case series of pregnant women that utilized the Breezing™ to track REE demonstrated that the use of this device increased the knowledge of metabolism, weight gain, and caloric intake during pregnancy as well as improved their awareness of energy expenditure.[15] Furthermore, awareness of REE measured using the Breezing™ device resulted in significantly greater weight loss than the control group among overweight and obese adults with Type II diabetes.[135] Therefore, awareness of REE might improve weight gain during pregnancy. Variations in GWG are only partially explained by energy intake and physical activity changes; therefore, evaluating these and other behavior factors in relation to REE changes across pregnancy may clarify differences in GWG outcomes when other factors remain constant. Furthermore, findings may result in clinical

interventions that individualize behavior recommendations during pregnancy to improve adherence to the IOM weight gain guidelines.

Sleep Habits and Hygiene

Sleep is an important health behavior that has drastic implications for maternal child health if inefficient or inadequate. There are no formal recommendations regarding sleep during pregnancy; however, the National Sleep Foundation encourages pregnant women to obtain the recommended sleep for adults, approximately 8 hours per night, and increase the number of daytime naps required to combat increased fatigue commonly experienced by pregnant women.[31] Pregnant women are at risk for a multitude of sleep problems such as insomnia, restless leg syndrome, sleep apnea, and nocturnal gastroesophageal reflux,[31] which can manifest as early as 10 weeks of gestation.[145] A survey of over 2400 pregnant women reported poor sleep quality (76%), insufficient sleep (38%), and significant daytime sleepiness (49%) as common sleep complaints with later bedtimes, increased number and duration of night awakenings, and decreased total sleep duration worsening as pregnancy progressed.[34] Racial and ethnic differences have indicated that Non-Hispanic White women are more likely to report troubled sleep despite being more likely to achieve adequate sleep duration when compared to their Black and Hispanic counterparts.[146] Insufficient sleep, insomnia, short sleep duration, and poorer sleep quality among pregnant women have been found in numerous studies.[147–150] Previous research has found that the average nightly sleep during pregnancy ranges from 6.44 to 8.39 hours.[33,34,147,151–155] Additionally, sleep efficiency (total nocturnal sleep time divided by total time spent in bed multiplied by 100) among pregnant women averages 80% indicating poor sleep efficiency,[156,157] and this decreases as pregnancy progresses.[157] Regardless, approximately 62% of pregnant women inaccurately estimate their average nocturnal sleep duration with 39% overestimating and 23% underestimating.[155] Gaining a better understanding of sleep health and hygiene among pregnant women will allow for the identification of at-risk groups and the development of targeted interventions to minimize detrimental outcomes.

Several factors have been identified for their associations with sleep (duration, quality, efficiency, and disturbance) during pregnancy, including month of pregnancy,[34,158–160]

siblings,[34,159] employment status,[34,148,152] education level,[34,156] maternal age,[148,152,160,161] dietary composition, [152,162] income level,[34,159,163] and physical activity.[152,162,164] As pregnancy progresses, the risk of poor sleep quality increases, with a 2.11-fold and 1.86-fold increase in the second and third trimesters, respectively.[158] Employment status (employed vs. unemployed) is strongly correlated with sleep during pregnancy.[148,152] Duke et al. reported that pregnant women who had a job were more likely to meet or exceed sleep recommendations for adults (i.e. 7-9 hours per night) compared to their unemployed counterparts.[152] On the other hand, Signal and colleagues reported that pregnant women who were not currently employed had longer sleep duration.[148] Conversely, it has been reported that pregnant women with fewer employment hours had poorer sleep quality.[156] One study found that a household income <$50,000 was correlated with poorer sleep quality, reduced sleep duration, and increased sleep fragmentation.[163] As previously indicated, maternal diet is a major factor for overall health, appropriate fetal growth and development, and better pregnancy outcomes. Diet quality, such as increased fruit and vegetable consumption, among pregnant women is positively associated with the number of women who meet or exceed sleep recommendations (i.e. 7 to 9 hours)[152] for adults and achieve better sleep quality[162] but not total sleep duration.[152,162] Among non-pregnant adult women and men, it has been reported that short sleep duration is associated with reduced circulating leptin and increased adiposity[165] which may impact appetite. Furthermore, sleep restriction has been shown to increase caloric consumption from snacks that consisted of higher carbohydrate intake.[166] Exercise during pregnancy within the last 30 days equated to 20 minutes of additional sleep among pregnant women.[152] Additionally, women who were physically active during pregnancy were more likely to be good sleepers (Pittsburgh Sleep Quality Index<5 indicates good sleep; 32.7% vs 22.5%).[162] Taken together, this demonstrates that sleep health is multifactorial with a wide range of aspects that affect the duration, quality, and efficiency of sleep achieved. These factors tend to be more prominent during pregnancy as pregnancy-related physical changes influence overall health. It is vital that sleep-related health be evaluated during pregnancy and that pregnant women are counseled on adequate sleep for better health and pregnancy outcomes.

Sleep loss and changes in sleep patterns that occur during pregnancy may play a role in adverse pregnancy outcomes. Several studies and review articles have found that sleep loss (i.e. decreased total sleep duration, reduced sleep efficiency, or increased sleep disturbance) was associated with increased prevalence of prenatal and postpartum despression,[149,153,167,168] higher risk of gestational diabetes,[149,169–171] abnormal glucose tolerance,[170,172,173] increased hypertension,[149,174] more incidence of preeclampsia,[174,175] longer labor and delivery,[149] higher incidence of preterm birth,[149] and increased risk of placenta abruption.[154] However, these results are inconsistent across studies. Perceived severity of morning fatigue and sleep quality during pregnancy are strongly associated with depressive symptoms.[153,167] One study reported that women who slept less than 4 hours early in pregnancy had a 5.56-fold increased risk of GDM when compared to women who slept >9 hours.[169] This study also found that with every hour increase in nighttime sleep duration there was a 15% reduction in GDM risk.[169] Worse sleep efficiency is associated with increased postpartum weight retention of >5 kgs of pre-pregnancy weight.[176] Risk of placenta abruption demonstrated a U-shaped relationship with maternal sleep duration indicating both short (OR=2.01) and long (OR=2.11) duration sleepers were at increased risk.[154] Women with more sleep-disordered breathing symptoms and total nap duration had a 3.37 and 1.64 increased risk of hyperglycemia.[173] Furthermore, longer labor duration and decreased birth weight have been reported among pregnant women who had nighttime sleep duration <7 hours.[149,151] Likewise, increased risk for low birthweight, [149,151] small-for-gestational-age (SGA), [149,151] and LGA[150] infants due to shorter sleep duration, increased disordered breathing,[150] and more leg twitching[150] have also been reported. However, other studies report no effect of maternal sleep (sleep-disordered breathing, quality, or duration) on neonatal outcomes such as SGA,[150,177,178] preterm birth,[179177] or fetal distress.[150] The fetal, neonatal, and maternal adverse health outcomes associated with sleep loss are sizeable. To some extent, sleep is a modifiable factor with the potential to impact various health outcomes; therefore, the promotion of adequate sleep habits is necessary during pregnancy.

Physiological changes that accompany pregnancy tend to interfere with restful sleep. Pregnancy-related physical symptoms that have also been associated with disturbed, inadequate,

or insufficient sleep include frequent urination, discomfort, nausea, heartburn, pain (hip, pelvic, or back), vivid dreams, and worry/anxiety.[34,180] Hormonal changes (increased progesterone and oxytocin) also occur which cause nocturnal sleep fragmentation and increased daytime sleepiness.[170,180] Additionally, previous studies have found a relationship between excessive gestational weight gain and shorter sleep duration, increased sleep disruption, and more daytime sleepiness in overweight women.[33] Conversely, Abeysena et al. found that women with greater sleep deprivation were more likely to gain inadequate GWG.[181] These biochemical and physical alterations that occur during pregnancy modify sleep with time-specific changes. The complexity of the relationship between sleep and pregnancy is highlighted by the multiple factors that impact sleep and the adverse outcomes associated with inadequate sleep. It is important; therefore, that sleep health is also prioritized during pregnancy in order to improve outcomes for both mom and baby.

METHODS

Research Design

This study was a randomized controlled observational trial of pregnant women (n=28). Participants were randomized using a schedule developed in REDCap. The Breezing™ group (n=16) used the Breezing™ device whereas the control group (n=12) did not use the Breezing™ device. Use of the Breezing™ device occurred in the home of the participants. Study staff brought the device to each visit with the participant's assigned mouthpiece and sensors. The participant was instructed to sit comfortably and to breath normally until the data collection was complete. After completion, the Breezing™ output data were provided on the study iPad and reviewed with the participant. All participants had their height and weight recorded at the first study visit and their weight recorded at all subsequent visits. At each study visit, study staff completed a Dietary Screener Questionnaire and a 24-hour dietary recall. Sleep data via Pittsburgh Sleep Symptom Questionnaire Insomnia, Pittsburgh Sleep Quality Index, and Berlin questionnaires were collected at three different timepoints throughout the study. Additionally, the participants wore an actigraph watch and completed a sleep diary three times during the study. The women were followed for approximately 13 weeks, to capture weight gain during the second trimester (weeks 13 to 27) as

this trimester has previously been associated with a greater risk of adverse pregnancy outcomes including EGWG. Minimizing the study to a period of 13-weeks also allowed us to complete this study in the required one-year funding period. This study was submitted and approved by Arizona State University's Institutional Review Board (Appendix A).

Sample size and Study Participants

We aimed to recruit and enroll 50 pregnant women to ensure that at least 30 women, 15 in the intervention group and 15 in the control group, would complete this pilot study. We recruited 1-2 women per week during the first 12 weeks of the study to assure that recruitment numbers were met and that the study was completed within the required 12-month period. Appendix B provides the consort diagram of participants screened and enrolled in the study. Women were recruited in-person and using flyers from Adelante Healthcare clinics, social media advertising, and participant or friend referral throughout the greater Phoenix metro area (Appendix C). Potential participants were identified and screened, by research staff, in-person or over the phone. Study staff also screened pregnant women referred to the study by word-of-mouth or from social media advertisements. If initially eligible, contact information was exchanged, and thereafter, study staff communicated directly with the participants. Enrollment and written informed consent were obtained at the first in-home visit.

All English and Spanish-speaking, pregnant women with a gestational age <17 weeks and who were ≥18 years old were eligible to participate. High-risk pregnancies that included the following diseases or conditions were excluded from the study: fetal growth problems, medical history of hypertension, gastrointestinal disorders, malabsorptive diseases, hyper or hypo-parathyroid conditions, HIV, diabetes (Types 1 and 2 or gestational diabetes), asthma/lung disease, cardiac diseases and conditions, current smoker (i.e. women who have smoked 100 cigarettes in their lifetime and now smoke every day or some days), history of eating disorders, or other metabolic conditions known to affect maternal health and fetal development. Additionally, women pregnant with multiples were not eligible for the study. Appendix D provides the Screening Form that was used to assess eligibility of participants prior to obtaining informed consent.

Procedures

Home visits by study staff were completed up to seven times across the study to assess height and weight using a portable Seca scale and stadiometer. Additionally, participants from both study groups completed interviewer-administered 24-hour dietary recalls (Appendix E), Dietary Screener Questionnaires (Appendix F), and a health history questionnaire (Appendix G) with research staff at each of the study visits. At baseline, women provided demographic information (Appendix G). All data were shared (through data sharing options in the apps) with study staff and compiled in a secure REDCap database. Regular communication between research staff and study participants was established. During the duration of the study, study staff frequently contacted participants by phone or text message to check in on the participants, answer any questions or concerns, and to remind them of upcoming appointments.

Participants were compensated for their voluntary participation. At the completion of each home-visit, study staff provided participants with monetary compensation on an incrementally increasing scale to minimize the risk of drop-out/loss to follow-up over time. The compensation was as follows (Appendix I): $5 (study visit 1), $20 (study visit 2), $15 (study visit 3), $30 (study visit 4), $25 (study visit 5), $30 (study visit 6), and $55 (study visit 7). Participants were compensated a total of $180 for their time across the entire study period and monetary amounts corresponded both to the number of assessments and length of participation in the study.

Instruments

Resting energy expenditure (Breezing™ group only) was determined using the Breezing™ device. REE measurements were obtained approximately every two weeks during the 13-week study period to capture variation in the metabolic rate. Prior to obtainment of this measurement, participants remained seated for approximately 20 to 30 minutes to reduce the impact of physical activity on the REE measurement. The participant remained in a seated position when the measurement was being obtained using the Breezing™ device. They were instructed to breathe in and out of the device for two continuous minutes. The Breezing™ device measures oxygen uptake and carbon dioxide production in order to determine REE. Data were loaded onto an accompanying electronic tablet using a corresponding "app" and transmitted electronically to the

study investigators. If the device indicated irregular breathing, the study participant would perform the measurement for a second time and the average values were used as the final measurement. After the study participant successfully completed the measurement, study staff reviewed the results with them by showing them the data from the Breezing™ device mobile app (See Appendix J). Study staff told the participants that REE is the amount of calories needed to maintain basic organ function, respiration, circulation, digestion, and other bodily functions needed for survival. They also stated that REE comprises approximately 60% of their total daily energy expenditure with the remaining 40% comprised of the thermic effect of feeding and activity. The study staff did not provide any dietary or behavioral counseling as the study goal was to focus on the impact of awareness of REE on GWG. Therefore, in order to minimize other factors (e.g. dietary counseling) that could impact weight gain, the intervention did not include providing the participants with any additional information beyond their REE output and interpretation of this information.

Demographic data was collected at the first study visit. It consisted of seven items including, occupation, date of birth, age (calculated based off current date and date of birth), marital status, race, ethnicity, and education. See Appendix H. A health history questionnaire was completed at each of the seven study visits and contained questions about both personal health history and health habits (Appendix G). Personal health history items included current gestational age in weeks and days, past medical history, and current use of prescribed or over-the-counter medications. Health habit items included current exercise category, dieting status, average per day meal consumption, average salt intake, average fat intake, consumption of caffeinated beverages, average drinks per week for caffeinated beverages, consumption of alcohol, and amount and type of alcohol consumed.

Dietary assessments were completed by study staff administration of 24-hour dietary recalls[182] (Appendix E) and Dietary Screener Questionnaires (Appendix F) at each visit to assess habitual dietary intake. The 24-hour dietary recalls were obtained via interview where research staff asked the study participants what foods and beverages they had eaten during the previous 24-hour period. The 24-hour dietary recall aims to capture detailed information about all foods

and beverages consumed by the study participant.[182] It also allows the interviewer to ask for more detailed information including brands, cooking methods, etc.[182] Each of the 24-hour dietary recalls (seven per participant) were entered into Nutrition Data System for Research (NDSR) by one study staff member. NDSR is a dietary analysis program designed to collect and analyze data from 24-hour dietary recalls.[183] The nutrient information was exported to Microsoft Excel and imported into SPSS Version 25.0 for statistical analyses. The Dietary Screener Questionnaire is a 26-item checklist of foods and beverages.[184] The questionnaire captures intakes of fruits and vegetables, added sugars, dairy products, whole grains or fiber, and red and processed meats.[184] Research staff asked study participants how often they ate or drank these different items in the last month. The screener includes a scoring algorithm that allows the calculation of daily consumption estimates of the above-specified food groups.

Participants were asked to wear a wrist-worn actigraph on their non-dominant wrist along (See Appendix K for Actigraph instructions) with completing an accompanying sleep diary (Appendix L) for three weeks after the baseline visit and for two weeks after week 5 and 11 home visits. The Actiwatch Spectrum Plus (Philips Respironics, Inc) were provided to the women. Actiware data were imported into Philips Actiware Version 6.0.9 with 30-second epochs software to quantify the data. 24-hour total sleep time (TST), nocturnal TST, and sleep efficiency were the variables of primary of interest. 24-hour TST is the total amount of time spent asleep in a 24-hour period. Nocturnal TST is the total amount of time spent asleep at night. Sleep efficiency is the ratio of the total time spent asleep at night compared to the total amount of time spent in bed with normal sleep efficiency being around 85%. These sleep variables were of primary interest because previous literature has shown that sleep duration and sleep efficiency decrease during pregnancy.[34,147–150]

Sleep assessments were obtained at baseline (1st), 5-week (3rd), and 11-week (6th) home visits, during which participants completed brief questionnaires about sleep disorder symptoms and sleep quality. Detailed information about each of the questionnaires are provided below.

- Pittsburgh Sleep Quality Index (PSQI):[185] The PSQI is a 10-item questionnaire used for assessing sleep quality. Previous research has found good construct validity and

reliability for assessing sleep quality using the PSQI in pregnant women reporting a Cronbach's alpha of 0.74.[186] Individual responses to the various items are provided a numerical value between 0 to 3 in order to determine an overall PSQI score. The overall PSQI score ranges from 0 to 21 with lower scores indicating better sleep quality. See Appendix M.

- Berlin Questionnaire:[187] This questionnaire consists of three categories that asses the risk of having sleep apnea. Category 1 consists of items 1 through 5, Category 2 consists of items 6 through 8 and Category 3 contains item 9. The Berlin Questionnaire has been shown to have fair predictive values (AUC 0.72, p=0.003) of sleep apnea during the first trimester with the predictive values increasing as pregnancy progresses with a reported AUC of 0.84 and 0.81 during the second and third trimesters.[188] A recent meta-analysis reported a pooled sensitivity and specificity of 0.66 (95%CI: 0.45, 0.83; I^2 = 78.65%) and 0.62 (95%CI: 0.48, 0.75; I^2 = 81.55%).[189] Participants were classified into High Risk or Low Risk based on their responses to the individual items and their overall scores in each symptom category. High risk was defined as a positive score in two or more of the three categories. Low risk was defined as a positive score in no more than one of the three categories. See Appendix N.
- Pittsburgh Sleep Symptom Questionnaire – Insomnia (PSSQ-I):[190] This questionnaire consists of 13 self-rated items. The PSSQ-I has a high reliability with a Cronbach alpha of 0.89 and high specificity (>90%) but low sensitivity (32.4%).[190] Insomnia disorder is determined by the individual responses for questions 1, 2, or 5. Identification of the daytime consequences of insomnia are determined by the individual responses to questions 6 through 13. After completion of the questionnaire, study staff scored individual responses in order to determine the presence of an insomnia disorder. If questions 1, 2, and 5 had a sleep symptom criterion of frequently or always, a duration criterion of greater than 4 weeks, and daytime impairment criterion of quite a bit or extremely, then an assignment of insomnia disorder was made. See Appendix O.

Anthropometrics were collected at every study visit for both groups. Research staff collected height using a stadiometer at the first study visit and weight using a portable Seca scale at each study visit. These measurements were used to calculate body mass index (BMI) as kg/m^2 using a calculated field in REDCap (Appendix P). Total weight gain was determined by the difference between the participant's weight at Study Visit 7 and their weight at Study Visit 1. Rate of weight gain was calculated by the total weight gain in pounds divided by the number of weeks the participant was followed.

Adverse events were assessed by study staff at each study visit. These adverse events were reviewed by one of the PIs (Drs. Reifsnider or Whisner) to determine their relationship to the study. If the adverse event was deemed relevant to study procedures, the IRB was immediately notified and appropriate action taken including withdrawal of participants from the study, medical referral, etc. See Appendix Q. No adverse events occurred as a result of the intervention.

Data Storage and Management

All data were recorded in REDCap, a secure, web-based data manager. Participants were each assigned a unique study ID number. This study ID number was used for all REDCap data entries and on all forms. All of the attached forms/questionnaires were imported into a REDCap database. Deidentified data from the actigraph software were exported into an Excel spreadsheet and subsequently entered into the REDCap database. Data were entered directly into REDCap via the electronic or application. There was a separate REDCap form with the study participants' first name, last name, study ID number, and contact information that served as the linking document to other study information. Only research staff had access to the REDCap database via user assignment. Data were kept by the principle investigators (PIs) of the project for five years after completion of the study. All consent forms were maintained in a participant binder and kept in the secure office of the PI.

Statistical Analysis

All statistical procedures were performed using SPSS (SPSS 25, Chicago, IL, USA). Data were tested for normality and homogeneity and appropriate parametric or non-parametric analyses were used to assess data. Outcome variables were tested for normality by exploration

of Shapiro-Wilk test statistic, Skewness, and Kurtosis values. Additionally, visual inspection of histograms, Q-Q plots, and evaluation of boxplots for normal distribution and potential outliers occurred. In order to preserve the small sample size of the current study, no outliers were removed due to normality tests being highly sensitive to sample size. If the variables were not normally distributed, non-parametric tests were used (e.g. Kruskal-Wallis) and median and interquartile range (IQR) were reported. Homogeneity of variance was also checked, and if violated, unequal variances were assumed. Demographic characteristics and baseline factors were summarized using counts and percentages for categorical variables, and the mean and standard deviation or median and standard deviation and the interquartile range for continuous measures. All statistical tests were two-sided with significance evaluated at the 5% level.

Primary Outcome: Gestational weight gain was the primary outcome of interest. The rate of GWG was ultimately chosen as the primary outcome as it was highly correlated with total GWG ($r=.963$, $p<0.001$) and is clinically more meaning due to the limited study duration. The rate of GWG was evaluated by calculating differences in weight between each study visit and dividing it by the difference in study weeks between each study visit. Overall rate of GWG was calculated by the overall GWG divided by the total study duration in weeks. Early and late rate of GWG were calculated by the difference in GWG between study visit 4 and study visit 1 and study visit 7 and study visit 4, respectively, and dividing by the total study duration during the same time period. Group differences were initially evaluated using an Independent samples t-test for normally distributed variables and a Kruskal-Wallis for non-normally distributed variables. The overall, early, and late rates of GWG and were compared between Breezing™ and control groups using a one-way ANCOVA with gestational age at study start and maternal education level as covariates. The standardized residuals for all outcome variables were evaluated for normality and homogeneity of variance was evaluated by assessing Levene's test statistic. Adherence to IOM gestational weight gain recommendations were determined by calculating the number of women who gained the appropriate amount of weight based on their BMI at the first study visit. Adherence to the GWG guidelines across the 13-week study was compared between the two groups using a Chi-square test statistic.

Secondary Outcome: Resting energy expenditure among the Breezing™ group was evaluated and change in REE determined by calculating Delta between the study visits (Study Visits 1 and 4 for early changes; Study Visits 4 and 7 for late changes, and Study Visits 1 and 7 for overall changes.). Calculation of the rate of GWG at each timepoint were calculated the same way as described for the primary outcome analysis. Correlations between the early, late, and overall changes in REE and early, late, and overall changes in total and rate of GWG were estimated using the Pearson Correlation coefficient after controlling for maternal education and initial BMI. All correlations were reported as r with statistical significance evaluated at the 5% level.

Tertiary Outcome: The mediator effects of dietary composition [total energy consumption (kcals), fat (grams), carbohydrate (grams), and protein (grams)] on the relationship between group assignment and rate of GWG were explored. The residualized change scores were calculated for early, late, and overall changes in the dietary composition variables. These were calculated by regressing the baseline values onto the outcome values to obtain the unstandardized residuals. Utilizing residualized change scores instead of difference scores minimizes the error in the variable. ANCOVA tests were performed to determine which dietary composition variables significantly differed between groups. Due to the exploratory nature of this study, all dietary composition variables were entered into simple mediation models regardless of ANCOVA findings. Additionally, we developed multiple mediations models for each of the timeframes (i.e. overall, early, and late) entering all dietary variables (e.g. fat, protein, and carbohydrates) into each study timeframe model.

Exploratory Outcomes: The mediator effect of objective sleep parameters [total 24-hour sleep time, total nocturnal sleep time, and sleep efficiency] on the relationship between dietary composition [total energy consumption (kcals), fat (grams), carbohydrate (grams), and protein (grams)] and the rate of weight gain were explored. This relationship was of interest because of previous research showing the impact that short sleep has on hormone levels,[165] caloric intake and dietary composition,[166] and obesity.[165] The residualized change scores were calculated for early, late, and overall changes in sleep parameter variables. These were calculated by

regressing the baseline sleep values onto the outcome values to obtain the unstandardized residuals. Utilizing residualized change scores instead of difference scores minimizes the error in the variables being evaluated. The residualized change scores for both the sleep parameters and dietary composition changes were used in the simple mediation models.

The PROCESS package for SPSS described by Hayes (2018)[191] was used (with baby sex, and gestational age at study start as covariates) to evaluate whether early, late, or overall changes in dietary composition mediated the intervention effect as well as if changes in sleep parameters mediated the relationship between dietary composition and GWG. Prior to entry into mediation models, mediator variables were converted to residualized change scores with the values centered at 0 to reflect changes from baseline. This provided the total, direct, and indirect effects through the proposed mediators of the predictor (i.e. intervention vs. control or sleep parameter) on health outcomes (rate of weight gain). This method also generated confidence intervals for inference about the indirect effects using bootstrapping. Due to the small sample size, the bootstrapping function built into PROCESS SPSS macro was used with 10,000 bootstrap samples with biased-corrected and accelerated intervals, to make inferences about the specific indirect effects. Sobel test statistics (Z) were calculated using the online calculator developed by Preacher (2010).[192] Separate simple mediation models for early, late, and overall changes in the dietary composition were developed in order to determine significant mediators (**Figures 3**) for the tertiary aim of this study. Similarly, separate simple mediation models were developed for each combination of early, late, and overall changes in sleep parameters and early, late, and overall changes in dietary composition variables in order to determine significant sleep mediators of the relationship between dietary changes and rate of GWG (**Figure 4**).

Risk/Benefits

There were no anticipated risks to the participants while taking part in this study. Participants may have felt different when initially breathing into the Breezing™ device. To account for potential effects on REE outcomes, a practice session was scheduled after consenting to assure that REE measurement collections felt commonplace. This device measures oxygen and carbon dioxide exchange in the lungs which occur naturally as we breathe. The sensors for these

measures are contained within the device and the participant was only exposed to a separate breathing tube with a reusable mouth piece. Mouthpieces were cleaned and sterilized between uses and the same materials were used by the same participant throughout the study to minimize risk of exposure to potentially harmful microbes or substances.

RESULTS

Demographic and Baseline Data

Of the 34 women who were eligible for the study, 28 were randomized resulting in 16 in the Breezing™ group and 12 in the Control group. Of the six participants who dropped out of the study, three withdrew prior to randomization. All six participants withdrew from the study prior to the initial study visit for reasons including miscarriage and loss-to-follow up. As a result, no baseline data were collected from these participants. The Control group had a mean study duration of 13.43 (12.93, 14.00) weeks compared to the Breezing™ group with a mean duration of 13.43 (13.29, 14.79) weeks. This difference was not statistically different (Kruskal-Walli H test, $\chi 2=1.20$, $p=0.273$). The mean gestational age was 14.806±2.25 weeks at study visit 1, 17.89±2.36 weeks at study visit 2, 20.16±2.46 weeks at study visit 3, 22.42±2.39 weeks at study visit 4, 24.32±2.65 weeks at study visit 5, 26.65±2.75 weeks at study visit 6, and 28.87±2.62 weeks at study visit 7.

Complete demographic data by group assignment and for the entire sample are provided in **Table 2**. The mean maternal age at the first study visit was 29.8±4.9 years which did not significantly differ between groups ($t(26)=-0.185$, $p=0.855$). The majority of women were Non-Hispanic White (78.6%), had at least a four-year college degree (67.8%), and were married (85.7%). No significant differences were noted for these demographic variables. Employment classification had an almost equal distribution of women in professional (39.3%) and homemaker/stay at home mom (35.7%) roles. Employment classification slightly differed between groups with more women in professional roles in the control group and more women as homemakers/stay-at-home moms in the Breezing™ group. However, this was not statistically significant ($\chi^2=2.164$, $p=0.706$).

Table 2. Participant Demographics of Women Participating in a Two-Arm Energy Expenditure Evaluation Study During Pregnancy

	Total (n=28)	Control (n=12)	Breezing™ (n=16)	P-value
Maternal age, mean±SD	29.8±4.9	29.6±5.9	29.9±4.3	0.855
Race/Ethnicity, % (n)				0.359
Non-Hispanic Caucasian	78.6 (22)	75.0 (9)	81.3 (13)	----
Hispanic Caucasian	14.3 (4)	25.0 (3)	6.25 (1)	----
Asian	3.6 (1)	0 (0)	6.25 (1)	----
More than one race	3.6 (1)	0 (0)	6.25 (1)	----
Employment classification, % (n)				0.706
Service and sales workers	14.3 (4)	16.7 (2)	12.5 (2)	----
Managerial jobs	3.6 (1)	0 (0)	6.3 (1)	----
Professional	39.3 (11)	50.0 (6)	31.3 (5)	----
Clerical support workers	7.1 (2)	8.3 (1)	6.3 (1)	----
Home maker or Stay at home mom	35.7 (10)	25.0 (3)	43.8 (7)	----
Marital Status, % (n)				0.623
Single	3.6 (1)	0 (0)	6.3 (1)	----
Married	85.7 (24)	91.7 (11)	81.3 (13)	----
Partnered/Significant Other	10.7 (3)	8.3 (1)	12.5 (2)	----
Education Level, % (n)				0.174
Less than 8th grade	3.6 (1)	0 (0)	6.3 (1)	----
High School/GED	10.7 (3)	25.0 (3)	0 (0)	----
Two-year college	17.9 (5)	8.3 (1)	25.0 (4)	----
Four-year college	32.1 (9)	25.0 (3)	37.5 (6)	----
Post-graduate	35.7 (10)	41.7 (5)	31.3 (5)	----

Employment categories were determined using the International Standard Classification of Occupations-08. The employment classifications include the following jobs: Service and sales workers (personal service or care workers, sales workers, protective services workers), managerial jobs (chief executives, administrative and commercial managers, production and specialized services mangers, hospitality, retail, and other services managers), professional (science and engineering, health and teaching, business and administration, legal, social, or cultural professionals), clerical support workers (general and keyboard, customer service, numerical and maternal recording, and other clerks). Independent t-tests were performed for all continuous variables to determine if there were statistically significant differences between groups. Chi-Square tests were evaluated for all baseline categorical variables to determine if there were statistically significant difference between groups. Abbreviations: SD= standard deviation;

Maternal baseline data at study visit one by group assignment and for the entire sample is provided in **Table 3**. The majority (71.4%) of women were taking one to three supplements and/or medications which remained relatively constant throughout the duration of the study. Similarly, 82.1% of women reported that they were taking prenatal vitamins which continued throughout the entire study. There were two participants that indicated that they were not taking prenatal vitamins for the entire duration of the study. Self-reported exercise for the majority (57.1%) of women was classified as mild, with others reporting no exercise (14.3%), occasional vigorous exercise (21.4%), and regular vigorous exercise (7.1%). Exercise level did not significantly differ between groups (χ^2=0.321, p=0.321) at the initial study visit. Throughout the

duration of the study, 57.1-71.4% of the women reported mild exercise. Similarly, the proportion of women participating in other exercise levels did not substantially fluctuate throughout the study.

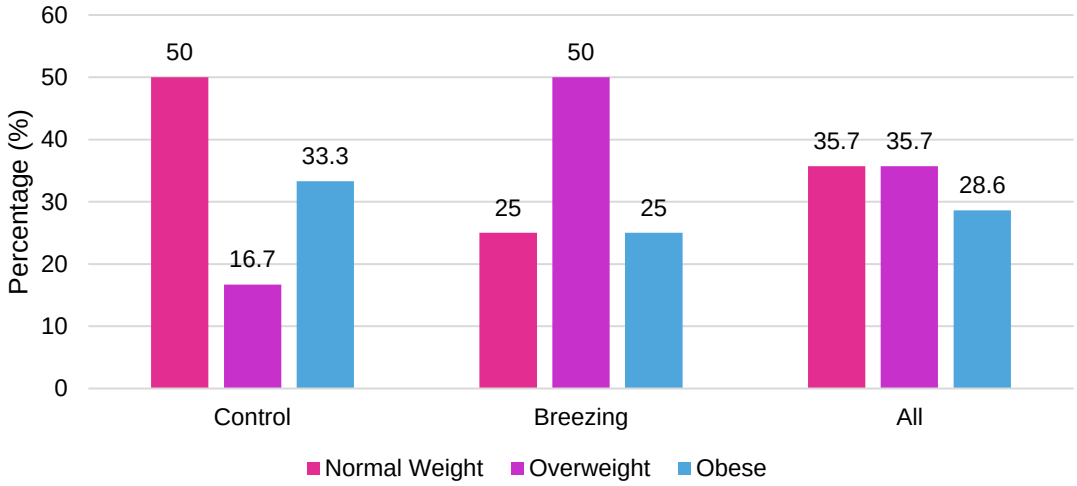
Table 3. Anthropometric, Behavioral, and Prenatal Baseline Data

	Total (n=28)	**Control (n=12)**	**Breezing™ (n=16)**	**P-Value**
Weight (kgs), mean±SD	73.7±16.0	70.3±15.8	76.2±16.2	0.349
Height (cms), mean±SD	164.06.5	163.5±6.6	164.4±6.6	0.723
Body Mass Index (kg/m^2), mean±SD	27.4±5.8	26.3±5.8	28.2±5.9	0.397
Gestational age (weeks), mean±SD	14.8±2.2	15.3±1.5	14.4±2.7	0.286
Exercise Level, % (n)				0.321
Sedentary	14.3 (4)	25.0 (3)	6.3 (1)	------
Mild	57.1 (16)	50.0 (6)	63.5 (10)	------
Occasional vigorous	21.4 (6)	25.0 (3)	18.8 (3)	------
Regular vigorous	7.1 (2)	0 (0)	12.5 (2)	------
Medication Use, % (n)				0.692
None	7.1 (2)	8.3 (1)	6.3 (1)	------
1 to 3	71.4 (20)	66.7 (8)	75.0 (12)	------
4 to 6	17.9 (5)	16.7 (2)	18.8 (3)	------
More than 6	3.6 (1)	8.3 (1)	0 (0)	------
Prenatal Vitamin Use, % (n)	82.1 (23)	83.3 (10)	81.3 (13)	0.887

Exercise level were defined as the following: sedentary (no exercise), mild (climbing stairs, waking a few blocks, golfing), occasional vigorous (less than 4 times per week for 30 mins), and regular vigorous (at least 4 times per week for 30 mins or more). Medication use included both prescribed and over-the-counter medicines. Prenatal vitamin use was based off self-report and did not include multivitamin use. Independent samples t-tests were performed for all normally distributed data and mean (SD) were reported. Chi-Square tests were evaluated for all baseline categorical variables to determine if there were statistically significant difference between groups. Abbreviations: SD= standard deviation;

Body mass index (BMI) categories of the women at the initial study visit were equally distributed with 35.7% (n=10) classified as normal weight, 35.7% (n=10) as overweight, and 28.6% (n=8) as obese. There were slight, non-significant study group differences in BMI at the initial study visit; the Control group had slightly more women at normal weight (50%, n=6) compared to the Breezing™ group (25%, n=4). Conversely, the Breezing™ group had more overweight women (50%, n=8) compared to the Control group (16.7%, n=2). These differences were not statistically significant, χ^2=3.50, p=0.174. **Figure 5** provides the distribution of initial study visit BMI category for the two study groups and the entire cohort.

Figure 5. Distribution of Women by Weight Status Categorized by Body Mass Index (Normal Weight BMI: 18.5-24.9 kg/m^2; Overweight BMI: 25-29.9 kg/m^2; Obese BMI: >30 kg/m^2) at the Initial Study Visit



Maternal and infant delivery information are presented in **Table 4**. Self-reported maternal weight at delivery did not significantly differ between the two groups, t(21)=-1.071, p=0.296. Additionally, there were no differences in gestational age at delivery, Group B Streptococcus status, or delivery mode. There was a difference for gravidity with the control group being pregnant significantly fewer times than the Breezing™ group (1.6±0.67 vs. 3.0±1.3 pregnancies, t(21)=-3.153, p=0.005). Infant sex, birthweight, and length did not significantly differ between the groups. The mean birthweight for the Control and Breezing™ group participants were 3617±552 and 3570±398 kgs, respectively. There were four infants with a birthweight greater than 4000 grams, three of which were born to women in the Control group.

Table 4. Maternal and Infant Information at Delivery Provided by Maternal Self-Report

	Total (n=23)	**Control (n=11)**	**Breezing™ (n=12)**	**P-Value**
Maternal Information				
Maternal Weight (kgs), mean±SD	85.2±18.7	80.8±15.6	89.1±21.0	0.296
Gravidity, mean (SD)	2.4±1.2	1.6±0.67	3.0±1.3	**0.005**
Parity, mean (SD)	2.0±1.0	1.6±0.67	2.3±1.1	0.079
Gestational Age (weeks), mean±SD	39.6±1.2	39.4±1.6	39.7±0.77	0.533
Group B Streptococcus, % (n)				0.128
Positive	34.8 (8)	18.2 (2)	50.0 (6)	-------
Negative	60.9 (14)	81.8 (9)	41.7 (5)	-------
Unknown	4.3 (1)	0 (0)	8.3 (1)	------
Delivery mode, % (n)				0.752
Vaginal	69.6 (16)	72.7 (8)	66.7 (8)	-------
Cesarean Section	30.4 (7)	27.3 (3)	33.3 (4)	-------
Infant Information				
Sex, % (n)				
Male	52.2 (12)	45.5 (5)	58.3 (7)	-------
Female	47.8 (11)	54.5 (6)	41.7 (5)	-------
Birthweight (grams), mean±SD	3640±509	3617±552	3570±398	0.502
Length (cms), mean±SD	51.9±2.1	52.3±2.1	51.6±2.2	0.430

Nutrition

Baseline nutrition information for macronutrients, fiber, cholesterol, sugar and caffeine consumption are provided in **Table 5**. There were no statistically significant differences for any of the baseline macronutrient, fiber, cholesterol, sugar or caffeine intakes. However, there were slight non-significant differences between groups for total energy, total fat, monosaturated fat, carbohydrates, total dietary fiber, insoluble fiber, caffeine, and total and added sugar intakes.

Table 5. Baseline Maternal Macronutrient, Fiber, Cholesterol, Caffeine, and Sugar Consumption at the Initial Study Visit

	Total (n=28)	Control (n=12)	Breezing™ (n=16)	P-Value
Total Energy (kcal)	1690.2±495.7	1751.1±493.8	1644.6±508.2	0.583
Total Fat (gm)	68.8±29.3	71.0±29.0	67.2±30.3	0.745
Saturated Fat (gm)	22.2 (13.1, 33.4)	18.8 (14.9, 26.3)	26.1 (11.4, 33.5)	1.000
Monounsaturated Fat (gm)	56.7±25.3	27.3±14.3	23.8±12.2	0.487
Polyunsaturated Fat (gm)	28.5±13.0	12.5±5.7	13.4±8.0	0.725
Cholesterol (mg)	178.9 (94.5, 283.3)	185.2 (89.4, 273.5)	166.1 (103.3, 292.0)	0.853
Total Carbohydrate (gm)	207.8±58.2	219.2±55.9	199.2±60.3	0.380
Total Dietary Fiber (gm)	19.6±9.6	22.1±11.2	17.7±8.1	0.234
Soluble Fiber (gm)	15.3±5.9	6.6±3.5	5.4±2.3	0.290
Insoluble Fiber (gm)	13.6±7.5	15.4±8.5	12.3±6.7	0.277
Total Protein (gm)	68.3±24.0	68.6±24.0	68.0±24.7	0.948
Caffeine (mg)[a]	3.1 (0.0, 47.4)	2.9 (0.0, 88.5)	3.5 (0.0, 44.5)	0.686
Total Sugars (gm)[a]	69.6 (51.7, 107.2)	78.7 (66.0, 104.5)	62.3 (42.9, 121.1)	0.330
Added Sugars (gm)	38.9±29.4	32.0±20.7	44.0±34.4	0.261

Independent samples t-tests were performed for all normally distributed data and mean (SD) were reported. [a] Kruskal-Wallis non-parametric test was performed for all non-normally distributed data and median (IQR) were reported. Abbreviations: SD= standard deviation; IQR= interquartile range, defined as the difference between the third and first quartile; kcal=kilocalories; mg=milligrams; gm=grams. All data are based on an interview conducted 24-hour dietary recall at the initial study visit.

The control group had higher total energy (1751.1±493.8 kcal), total fat (71.0±29.0 gm), monosaturated fat (27.3±14.3 gm), carbohydrates (219.2±55.9 gm), total dietary fiber (22.1±11.2 gm), insoluble fiber (15.4±8.5 gm), caffeine (median=2.9 mg; 0.0, 88.5), and total sugars (median=78.7 gm; 66.0, 104.5) whereas the Breezing™ group had higher consumption of added sugars (48.4±35.9 gm). The mean calories from fat, protein, and carbohydrate were similar between the Control and Breezing™ group; however, both groups exceeded the ADMR for fat while remaining within the recommendations for carbohydrates and protein (**Table 6**).

Table 6. Mean Percent of Calories from Fat, Protein, and Carbohydrates across All Study Visits

	AMDR	Total	Control	Breezing™	P-Value
Carbohydrate	45-65%	47.6±5.3	48.0±6.1	47.3±4.9	0.748
Fat	20-35%	35.8±4.4	35.7±5.5	35.9±3.7	0.896
Protein	10-35%	16.6±3.1	16.3±2.3	16.8±3.5	0.715

Percent of total calories from carbohydrates, fat, and protein were averaged across all study timepoints and compared between groups. Independent samples t-tests were performed for all normally distributed data and mean±SD were reported.

Complete micronutrient, mineral, and vitamin information are provided in **Table 7**. Vitamin C and thiamine were the only baseline vitamins that were trending statistical differences between

groups. For Vitamin C, the median intake for the Breezing™ group was 48.3 mg (25.92, 90.51) and for the control group was 98.5 mg (59.07, 187.66), X^2=3.45, p=0.063. Similarly, the control group (1.93±0.61 mg) had higher intakes of thiamine when compared to the Breezing™ group (1.50±0.54 mg; t(26)=1.992, p=0.057). There were slight non-significant differences between the groups for niacin, total folate, vitamin E, and calcium. The Breezing™ group had higher niacin (median=21.6, 18.49, 24.67 vs. median=17.5, 14.00, 25.21; X^2=2.071, p=0.150) and calcium (841.5±470.0 vs. 770.1±362.7; t(26)=-0.437, p=0.666) consumption but lower folate (393.2±157.4 vs. 454.0±214.6, t(26)=0.866, p=0.394) and vitamin E (11.2±7.4 vs. 7.6±4.3; t(26)=1.663, p=0.108) consumption when compared to the Control group.

Table 7. Baseline Maternal Micronutrient, Minerals, and Vitamins Intakes at the Initial Study Visit

	Total (n=28)	**Control (n=12)**	**Breezing™ (n=16)**	**P-Value**
Thiamine (mg)	1.69±0.60	1.93±0.61	1.50±0.54	**0.057**
Riboflavin (mg)	2.68±0.52	1.82±0.54	1.55±0.49	0.183
Niacin (mg)[a]	20.94 (17.05, 24.67)	17.51 (14.00, 25.21)	21.58 (18.49, 24.67)	0.150
Total Folate (mcg)	419.22±182.92	453.95±214.56	393.16±157.41	0.394
Vitamin B12 (mcg) [a]	3.10 (1.22, 4.52)	1.97 (1.18, 4.32)	3.23 (1.31,5.52)	0.816
Vitamin D (mcg) [a]	1.71 (0.36, 3.92)	1.85 (0.33, 3.53)	1.71 (0.49, 5.14)	0.745
Vitamin D2 (mcg) [a]	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)	0.864
Vitamin D3 (mcg) [a]	1.71 (0.34, 3.92)	1.85 (0.29, 3.52)	1.71 (0.48, 4.60)	0.710
Vitamin E (mcg)	9.15±5.91	11.23±7.24	7.59±4.29	0.108
Vitamin C (mg) [a]	68.82 (28.65, 127.87)	98.49 (59.07, 187.66)	48.34 (25.92, 90.51)	0.063
Omega-3 Fatty Acids (gm) [a]	1.17 (0.76, 1.63)	1.13 (073, 1.54)	1.17 (0.78, 2.19)	0.458
Calcium (mg)	810.88±421.40	770.10±362.67	841.46±469.96	0.666
Iron (mg)	15.23±5.31	13.61±3.97	16.45±5.96	0.164
Zinc (mg) [a]	8.75 (6.32, 13.02)	9.12 (6.34, 13.80)	8.74 (5.90, 12.81)	0.745
Sodium (mg)	2916.37±1178.04	2869.26±1109.49	2951.70±1261.82	0.859

Independent samples t-tests were performed for all normally distributed data and mean (SD) were reported. [a] Kruskal-Wallis non-parametric test was performed for all non-normally distributed data and median (IQR) were reported. Abbreviations: SD= standard deviation; IQR= interquartile range, defined as the difference between the third and first quartile; kcal=kilocalories; mg=milligrams; gm=grams. All data are based on an interview conducted 24-hour dietary recall at the initial study visit. Vitamin B12 is cobalamin form; Vitamin D is calciferol, Vitamin D2 is ergocalciferol, Vitamin D3 is cholecalciferol; Vitamin E is total alpha-tocopherol; Vitamin C is ascorbic acid.

Table 8 summarizes the predicted intakes of fiber, calcium, whole grains, added sugars, and fruits and vegetables across early, middle, and late timepoints across the study. There were no significant time, group, or group*time effects for any of the predicted values of each nutrient. The control group had an increase in fiber intake between the first and fourth study visits whereas the Breezing™ group fiber intake did not change; however, this was not statistically significant. Similarly, the Control group had an increase in calcium intake between the first and fourth study visits. Fruit and vegetable consumption did not change with both groups' intakes ranging from 2.6 to 2.8 cups per day at the different time points.

Table 8. Predicted Maternal Intakes from the Dietary Screener Questionnaire During Early, Middle, and Late Study Visits.

	Control			Breezing™			P-Value Time	P-Value Group	P-Value Group* Time
	SV1	SV4	SV7	SV1	SV4	SV7			
Whole Grains (oz)	0.75±0.37	0.94±0.35	0.94±0.42	0.88±0.34	0.67±0.24	0.82±0.38	0.225	0.358	0.083
Added sugars (tsp)	13.4±1.3	15.0±1.4	14.4±0.9	14.6±2.2	13.9±3.0	14.6±2.7	0.719	0.827	0.242
Dairy (cups)	1.5±0.4	1.6±0.6	1.5±0.2	1.5±0.4	1.5±0.4	1.6±0.3	0.502	0.782	0.914
Fruits & Vegetables* (cups)	2.7±0.6	2.8±0.8	2.9±1.0	2.7±0.6	2.6±0.7	2.7±0.7	0.151	0.647	0.325
Vegetables (cups)	1.4±0.3	1.4±0.2	1.5±0.4	1.4±0.2	1.3±0.3	1.3±0.3	0.116	0.880	0.239
Fruits (cups)	1.3±0.4	1.4±0.5	1.4±0.6	1.3±0.5	1.2±0.4	1.3±0.5	0.225	0.534	0.219

Comparisons between timepoints were assessed using repeated measures analysis of variance with covariates of maternal education level, group assignment, and gestational age at study start. All data were collected using the Food Frequency Questionnaire which predicts the intake of nutrients based on a 26-item survey. Fruits and vegetables included legumes but excluded French fries. Abbreviations: SV=study visit.

The primary nutrient variables of interest were total energy, fat, protein, and carbohydrate. We evaluated the early, late, and overall residualized change scores of these nutrients among the two study groups. ANCOVA tests were performed to identify which of the proposed mediators significantly differed between groups throughout the study (**Table 9**). Overall changes in energy significantly differed between the Breezing™ and Control groups (mean diff=-349.08±150.77, 95% CI: -660.26 to -37.90, p=0.029). Similarly, late changes in energy significantly decreased in the Breezing™ group relative to the Control group (mean diff=-379.90±143.89, 95% CI:-676.87 to -82.93, p=0.014).

Table 9. Mean±SD of Proposed Mediators for Overall, Late, and Early Changes by Study Arm (N=28)

Variable	Control (n=12)	Breezing™ (n=16)	Cohen's d	P-Value
Energy (kcal)				
Overall Changes	191.75±422.23	-143.81±339.21	0.183	**0.029**
Late Changes	207.06±416.47	-155.30±309.22	0.225	**0.014**
Early Changes	-42.97±766.15	32.22±642.55	0.003	0.793
Protein (gm)				
Overall Changes	13.26±31.03	-9.94±24.00	0.147	**0.053**
Late Changes	13.38±32.97	-10.04±22.86	0.151	**0.050**
Early Changes	-9.94±19.85	7.44±30.77	0.142	**0.058**
Carbohydrates (gm)				
Overall Changes	19.30±57.76	-14.47±58.71	0.100	0.116
Late Changes	19.25±58.03	-14.44±55.83	0.105	0.107
Early Changes	-2.44±73.62	1.83±87.85	0.001	0.864
Fat (gm)				
Overall Changes	7.38±25.47	-5.53±14.93	0.101	0.114
Late Changes	7.78±25.19	-5.84±14.51	0.114	0.091
Early Changes	0.52±60.75	-0.39±28.03	0.001	0.870

ANCOVA was performed with maternal education and gestational age at study start as covariates to test for group differences. Abbreviations: SD= standard deviation; kcal=kilocalories; gm=grams.

There were also trending statistical differences between groups for the overall, late, and early changes in protein. Overall changes in protein were mildly different between Breezing™ and Control group participants (mean diff=-22.45±11.03, 95% CI: -45.20 to 0.31, p=0.053). Likewise, late changes in protein decreased slightly more for the Breezing™ group when compared to the Control group (mean diff=-23.16±11.23, 95% CI: -46.33 to 0.01, p=0.05). Early changes in protein were marginally increased in the Breezing™ group relative to the Control group (mean diff=20.3±10.19, 95% CI: -0.74 to 41.34, p=0.058). There were no other statistically or marginally

significant differences for overall, late, and early changes in carbohydrates and fat. Overall and late changes in energy consumption and overall, late, and early changes in protein were therefore included in the mediator models for both the relationship between the intervention and rate of GWG and the relationship between sleep parameters and rate of GWG.

Resting Energy Expenditure

Data obtained from the Breezing™ device are presented in **Table 10** which included REE and total daily energy expenditure (TDEE)**.** Despite changes in REE throughout the study, a repeated measures ANCOVA revealed that these differences were non-significant ($F(6,60)=0.140$, $p=0.990$). There were variations in the changes in REE between

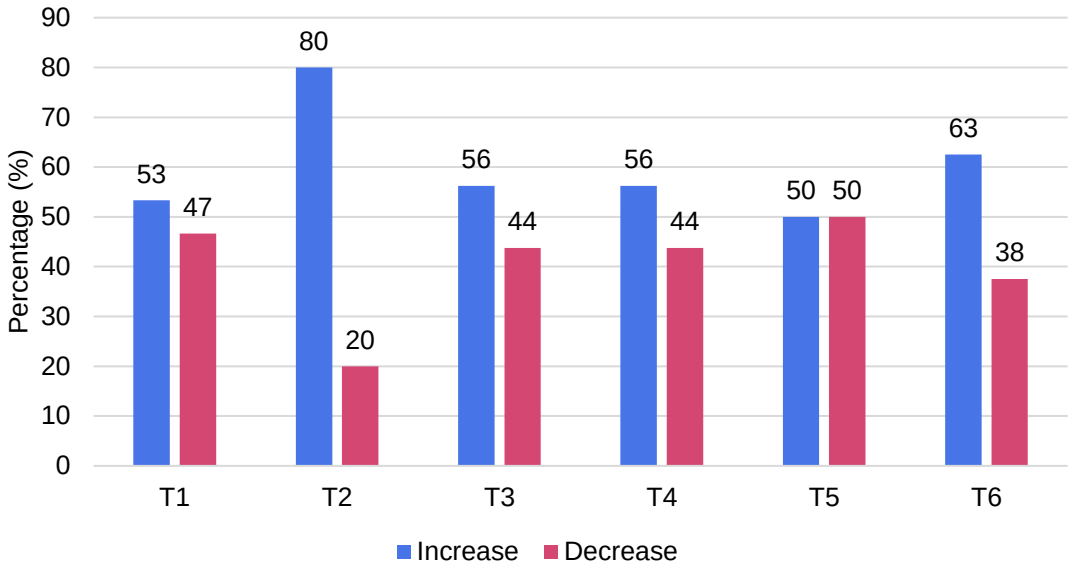
Table 10. Mean±SD of Resting and Total Daily Energy Expenditure from Breezing™ Device

	Resting Energy Expenditure	**Total Daily Energy Expenditure**
Study Visit 1	1544±237	2004±269
Study Visit 2	1511±220	1974±332
Study Visit 3	1628±242	2105±300
Study Visit 4	1616±253	2103±341
Study Visit 5	1708±338	2210±425
Study Visit 6	1706±367	2206±444
Study Visit 7	1744±384	2257±468

Comparisons between timepoints were assessed using repeated measures analysis of variance with covariates of maternal education level and gestational age at study start. All data are presented as mean±SD and were obtained from the Breezing™ device.
Abbreviations: SD=standard deviation.

the study visits with the majority of women experiencing an increase in REE at each study visit (**Figure 6**). Approximately 80% (n=12) of women had an increase in their REE between the second and third study visit with increases in REE ranging from 10 to 350 kcal/day. The

Figure 6. Percentage of REEs that Increased versus Decreased between the Study Visits for Women in the Breezing Group



differences between the remaining study visits were almost evenly split among women who had an increase (range: 53-63%) compared to those who had a decrease (range:38-50%) in REE. The TDEE also had non-significant ($F(6,60)= 0.175$, $p=0.983$) changes throughout the study duration with a 11.2% increase between the first and last measurement.

Early, late, and overall changes in REE demonstrated that early changes in REE (72±211 kcals) were relatively small but late changes (128±294 kcals) were more substantial, almost twice that of early changes. The mean overall changes in REE was 200±316 kcals with a range from -340 to 950 kcals. There was a 11.5% increase in total REE from the first study visit to the last study visit among the Breezing™ group participants. **Figures 7 and 8** show the mean change in REE for all of the six timepoints through the study. The longitudinal timepoints indicate the difference in REE between the study visits for the women who experienced an increase or decrease in REE.

Figure 7. Mean Change in REE Among Pregnant Women Who Experienced an Increase in REE

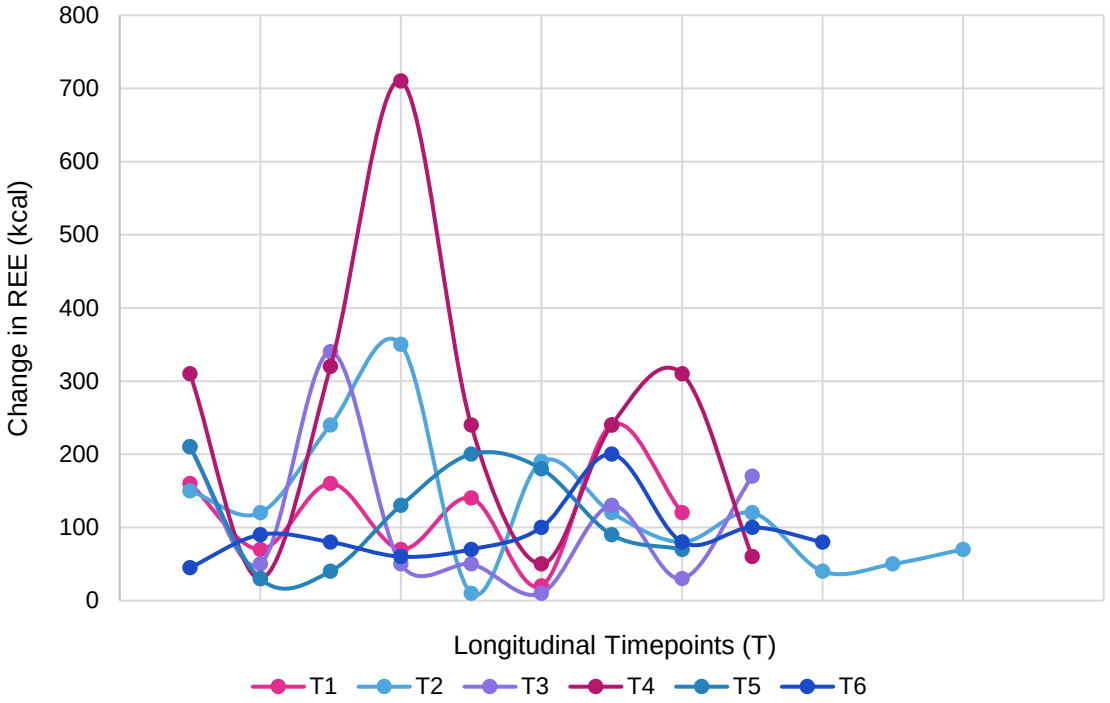
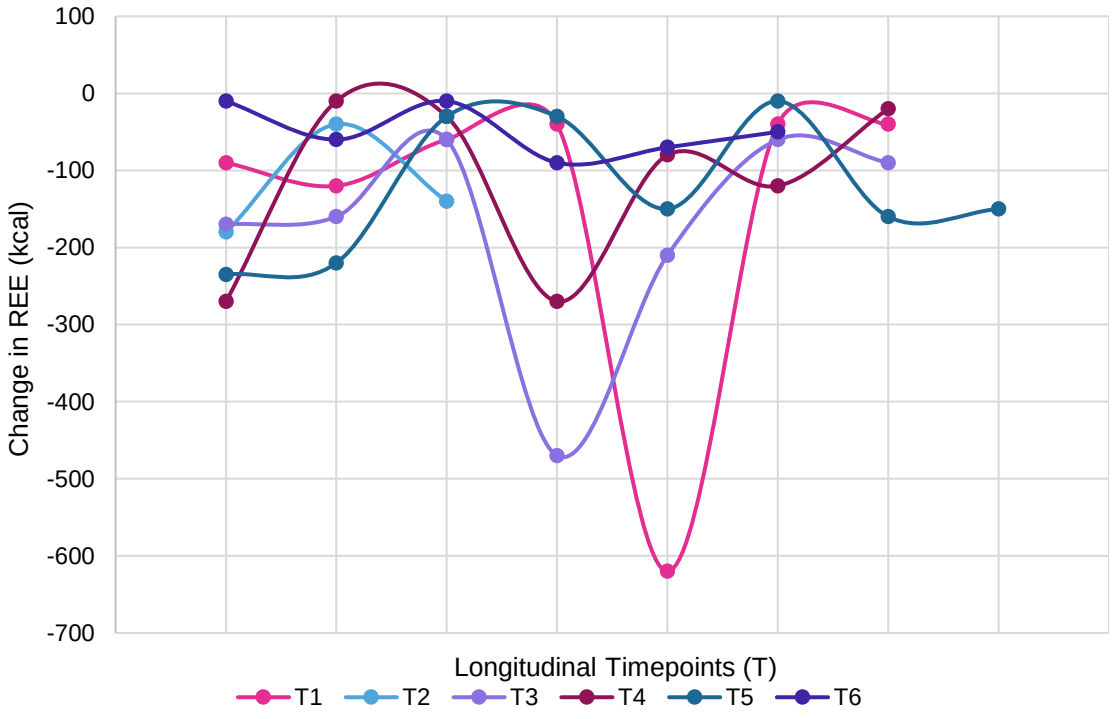


Figure 8. Mean Change in REE Among Pregnant Women Who Experienced a Decrease in REE



Sleep

Sleep disturbances were evaluated using the Berlin Questionnaire and the PSQI at three different timepoints throughout the study. Snoring was reported by 25.0% (n=7) of women in both the control and Breezing™ group (p=0.666, Fisher's exact test) at timepoint 1. Self-reported snoring among the entire sample did not significantly change between the three timepoints (T1:25.0% vs. T2: 28.6% vs. T3:35.7%, χ^2=0.797, p=0.671). However, snoring increased among the Breezing™ group participants as pregnancy progressed with 37.5% (n=6) and 43.8% (n=7) of women reporting snoring at time points 2 and 3, respectively. Conversely, the percentage of women that reported snoring in the Control remained relatively the same throughout the entire study (T2: 25% vs T3: 16.7%). Approximately 11% (n=3) of women received a positive Berlin score indicating high risk for sleep apnea at timepoint 1. The proportion of women receiving a positive (or high-risk level) Berlin score increased as pregnancy progressed with 17.9% (n=5) and 21.4% (n=6) being high-risk for sleep apnea at timepoints 2 and 3, respectively. These increases were not statistically significant (χ^2=1.2, p=0.549). Similarly, there were no group differences for being high-risk of sleep apnea at any of the three timepoints (T1: 16.7% vs. 6.25%, p=0.560; T2: 25% vs. 12.5%, p=0.624; T3: 8.3% vs. 31.3%, p=0.196).

Sleep disturbances and quality reported by the participating women on the PSQI are summarized in **Table 11**. The majority (53.6%, n=15) of women reported trouble sleeping because they needed to get up to use the bathroom at least three times per week at timepoint 1; this did not change as pregnancy progressed (X^2=0.386, p=0.824). Additionally, there was not a difference between groups with 50% vs. 56.3% (X^2=0.108, p=0.743), 58.3% vs. 62.5% (X^2=0.050, p=0.823), and 50% vs. 56.3% (X^2=0.108, p=0.743) of the Control and Breezing™ group

Table 11. Percentage of Participants with Sleep Disturbances as reported on the Pittsburgh Sleep Quality Index (PSQI)

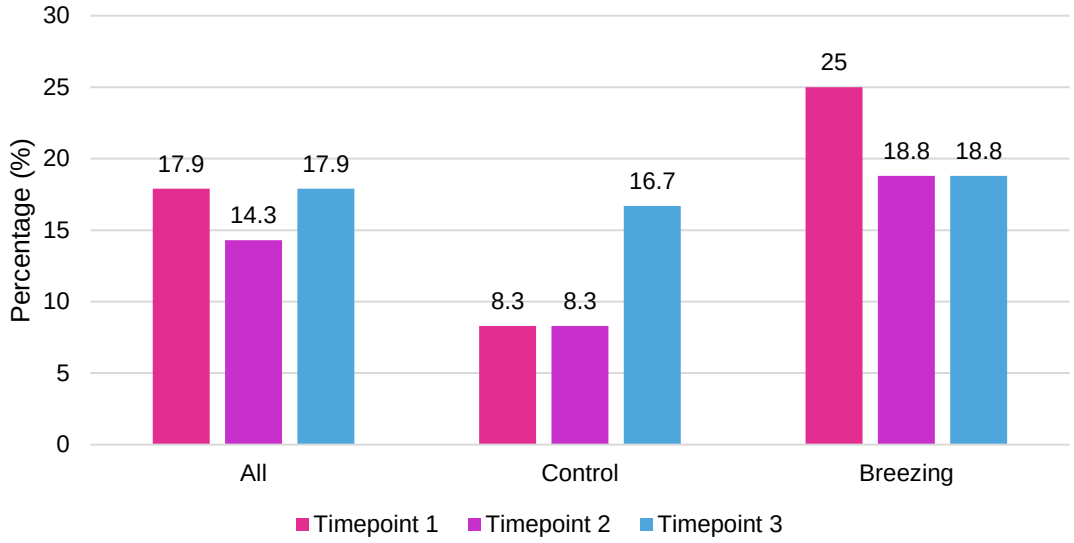
	Timepoint 1			Timepoint 2			Timepoint 3		
	All (n=28)	**Control (n=12)**	**Breezing™ (n=16)**	**All (n=28)**	**Control (n=12)**	**Breezing™ (n=16)**	**All (n=28)**	**Control (n=12)**	**Breezing™ (n=16)**
Cannot fall asleep within 30 mins[a]	7.1 (2)	0 (0)	12.5 (2)	21.4 (6)	0 (0)	0 (0)	3.6 (1)	0 (0)	6.3 (1)
Wake up awhile sleeping[a]	25.0 (7)	8.3 (1)	37.5 (6)	25.0 (7)	16.7 (2)	31.3 (5)	35.7 (10)	41.7 (5)	31.3 (5)
Get up to use the bathroom[a]	53.6 (15)	50.0 (6)	56.3 (9)	60.7 (17)	58.3 (7)	62.5 (10)	53.6 (15)	50.0 (6)	56.3 (9)
Cannot breathe comfortably[a]	10.7 (3)	16.7 (2)	6.3 (1)	3.6 (1)	0 (0)	6.3 (1)	10.7 (3)	0 (0)	18.8 (3)
Cough or snore loudly[a]	14.3 (4)	0 (0)	0 (0)	7.1 (2)	0 (0)	0 (0)	17.9 (5)	0 (0)	31.3 (5)
Feel too cold[a]	3.6 (1)	0 (0)	6.3 (1)	3.6 (1)	0 (0)	0 (0)	7.1 (3)	0 (0)	0 (0)
Feel too hot[a]	10.7 (3)	8.3 (1)	12.5 (2)	7.1 (2)	8.3 (1)	6.3 (1)	14.3 (4)	8.3 (1)	18.8 (3)
Have had bad dreams[a]	3.6 (1)	0 (0)	6.3 (1)	28.6 (8)	0 (0)	0 (0)	25.0 (7)	0 (0)	0 (0)
Have pain[a]	7.1 (2)	8.3 (1)	6.3 (1)	21.4 (6)	25.0 (3)	18.8 (3)	17.9 (5)	25.0 (3)	12.5 (2)
Sleep Quality Rating									
Very good	17.9 (5)	16.7 (2)	18.8 (3)	10.7 (3)	0 (0)	18.8 (3)	17.9 (5)	8.3 (1)	25.0 (4)
Fairly good	57.1 (16)	66.7 (8)	50.0 (8)	78.6 (22)	83.3 (10)	75.0 (12)	60.7 (17)	66.7 (8)	56.3 (9)
Fairly bad	25.0 (7)	16.7 (2)	31.3 (5)	10.7 (3)	16.7 (2)	6.3 (1)	21.4 (6)	25.0 (3)	18.8 (3)
Very bad	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Taken sleep medication[b]	14.3 (4)	25.0 (3)	6.3 (1)	21.4 (6)	41.7 (5)	6.3 (1)	14.3 (4)	25.0 (3)	6.3 (1)
Trouble staying awake[b]	3.6 (1)	0 (0)	0 (0)	3.6 (1)	0 (0)	0 (0)	3.6 (1)	0 (0)	0 (0)
Lack of enthusiasm a big problem[b]	10.7 (3)	8.3 (1)	12.5 (2)	3.6 (1)	0 (0)	6.3 (1)	0 (0)	0 (0)	0 (0)
Sleep Duration, mean±SD	7.3±1.0	7.3±1.1	7.2±1.0	7.3±1.1	7.1±0.9	7.5±1.2	7.4±1.3	7.2±1.2	7.5±1.3
PSQI Global Score, mean±SD	6.2±3.3	5.8±3.2	6.2±3.5	5.7±3.2	6.0±3.1	5.3±3.5	5.5±3.0	5.7±2.3	5.2±3.5
PSQI Domain Scores, mean±SD									
Duration of Sleep	0.3±0.6	0.2±0.4	0.3±0.7	0.3±0.5	0.3±0.5	0.3±0.6	0.4±0.6	0.4±0.5	0.4±0.7
Sleep Disturbance	1.3±0.5	1.2±0.4	1.4±0.6	1.4±0.6	1.3±0.5	1.4±0.6	1.4±0.6	1.3±0.5	1.4±0.6
Sleep Latency	0.9±0.9	0.8±0.7	1.0±1.1	0.7±0.8	0.5±0.7	0.8±0.8	0.8±0.8	0.7±0.7	0.8±0.9
Days Dysfunction	1.1±0.8	0.9±0.8	1.2±0.8	0.5±0.7	0.6±0.7	0.5±0.7	0.6±0.6	0.7±0,7	0.6±0.6
Sleep Efficiency	0.9±1.0	0.8±0.9	1.0±1.1	1.0±1.1	1.0±1.1	1.0±1.2	0.8±1.0	0.8±1.0	0.8±1.0
Sleep Quality	1.1±0.7	1.1±0.7	1.1±0.7	1.0±0.5	1.1±0.5	0.9±0.5	0.9±0.7	0.9±0.7	0.9±0.7
Need Meds to Sleep	0.5±1.1	0.9±1.4	0.2±0.8	0.8±1.3	1.3±1.5	0.4±0.9	0.5±1.10	0.8±1.3	0.3±0.8
PSQI Score Sleep Quality Rating									
Poor sleep quality	50.0 (14)	66.7 (8)	37.5 (6)	46.4 (13)	50.0 (6)	43.8 (7)	35.7 (10)	41.7 (5)	31.3 (5)
Good sleep quality	50.0 (14)	33.3 (4)	62.5 (10)	53.6 (15)	50.0 (6)	56.3 (9)	64.3 (18)	58.3 (7)	68.8 (11)

All data was obtained from the PSQI and summarized using percentages and counts, % (n) unless otherwise noted. Poor sleep quality is defined as a total PSQI score > 5. Good sleep quality is defined as a total PSQI < 5. PSQI-Global score range from 0 to 21. [a]indicates that the following variables are based on the proportion of women that reported having trouble sleeping 3 times or more per week. [b] indicates that the following variables are based on the proportion of women that reported this behavior occurring during the past 30 days.

participants, respectively, reporting trouble sleeping due to frequent bathroom use at timepoints 1, 2, and 3. There was a trending significant difference (X^2=3.11, p=0.078) among women in the Breezing™ group (37.5%, n=6) who reported that they woke up in the middle of the night or early morning at least three times per week when compared to the Control group participants (8.3%, n=1) at the timepoint 1. However, this changed at timepoint 3 with 41.7% (n=5) of the Control group participants indicated trouble sleep because of waking up in the middle of the night or early morning, surpassing the Breezing™ group (31.3%, n=5). However, this increase throughout the study among Control group participants was not statistically significant (X^2=4.179, p=0.124). Surprisingly, the majority (57.1%, n=16) reported 'fairly good' sleep quality at the first timepoint which increased to 78.6% (n=22) and 60.7% (n=17) at later timepoints. Furthermore, none of the participants reporting 'very bad' sleep quality at any of the timepoints. There were slight differences in reported sleep quality between the groups but these were not statistically significant (T1: X^2=2.333, p=0.127; T2: X^2=0.108, p=0.743; T3: X^2=0.698 Fisher's exact test, p=0.430). The average PSQI score ranged from 5.2 to 6.2 at the three different timepoints which did not significantly differ between groups (T1: t(26)=-0.275, p=0.786; T2: t(26)=0.434, p=0.564; T3: t(26)=0.409, p=0.686).

Insomnia disorders were evaluated using the Pittsburgh Sleep Symptom Questionnaire. Insomnia disorders were found among 17.9% (n=5), 14.3% (n=4), and 17.9% (n=5) of the participating women at the three different timepoints. This did not significantly differ between groups at timepoint 1 (X^2=0.355 Fisher's exact test, p=0.267), timepoint 2 (X^2=0.613 Fisher's exact test, p=0.417), or timepoint 3 (X^2=1.00, p=0.643). **Figure 9** provides the proportion of women found to have insomnia disorders during the study period by group and for the entire cohort.

Figure 9. Proportion of Women with Self-Reported Insomnia Disorders Throughout the Study by Group Assignment



The subjective self-reported sleep data for all three timepoints are provided in **Table 12.** Total sleep duration, total time spent in bed, and sleep efficiency were not significantly different between study groups for any of the three timepoints. There were significant differences in several of the subjective sleep variables. Morning wake time at timepoint one significantly differed between the Control (median=0:26; IQR: 0:16, 0:37) and Breezing™ (median=0:15; IQR: 0:12, 0:18) groups (χ^2=4.212, p=0.040). Additionally, the sum of wake time (i.e. the time to fall asleep

Table 12. Subjective Sleep Data from Self-Reported Sleep Diaries Across Three Timepoints for Pregnant Women Participating in a Two-Arm Observational Study of Resting Energy Expenditure

	Total (n=28)	**Control (n=12)**	**Breezing™ (n-16)**	**P-Value**
Total Sleep Time (hour)				
Timepoint 1	8:05±1:11	7:55±1:10	8:07±1:10	0.525
Timepoint 2	8:11±1:29	8:08±1:24	8:17±1:24	0.900
Timepoint 3	8:01±1:09	8:05±1:11	8:05±1:11	0.845
Total Sleep Time (mins)				
Timepoint 1	486.4±71.4	476.5±70.0	487.8±70.0	0.531
Timepoint 2	490.6±86.8	488.9±81.6	497.1±81.6	0.927
Timepoint 3	483.2±70.1	485.4±72.6	487.0±72.6	0.888
Time in bed (hours)				
Timepoint 1	9:13±1:01	9:16±1:04	9:11±1:04	0.828
Timepoint 2	9:16±1:21	9:22±1:22	9:20±1:22	0.771
Timepoint 3	9:04±1:07	9:20±1:09	9:09±1:09	0.290
Time in bed (mins)				
Timepoint 1	553.6±61.1	556.4±64.5	551.7±64.5	0.839
Timepoint 2	557.4±82.0	562.4±83.1	561.6±83.1	0.782
Timepoint 3	544.5±67.2	561.1±69.2	549.0±69.2	0.264
Morning Wake Time				
Timepoint 1[a]	0:16 (0:12, 0:30)	0:26 (0:16, 0:37)	0:15 (0:12, 0:18)	**0.040**
Timepoint 2[a]	0:16 (0:08, 0:26)	0:20 (0:09, 0:26)	0:15 (0:05, 0:24)	0.478
Timepoint 3[a]	0:12 (0:07, 0:23)	0:13 (0:10, 0:23)	0:10 (0:05, 0:22)	0.254
Sum Wake Time				
Timepoint 1[a]	0:54 (0:35, 1:20)	1:17 (0:53, 1:42)	0:36 (0:28, 1:04)	**0.008**
Timepoint 2[a]	1:01 (0:31, 1:30)	1:08 (0:44, 1:29)	0:42 (0:21, 1:32)	0.251
Timepoint 3[a]	0:58 (0:42, 1:21	1:15 (0:57, 1:40)	0:46 (0:27, 1:12)	**0.037**
Sleep Efficiency				
Timepoint 1	87.8±7.98	85.5±6.82	88.2±6.82	0.190
Timepoint 2	88.0±7.84	87.1±6.58	88.7±6.58	0.604
Timepoint 3	88.5±6.01	86.1±6.33	88.3±6.33	0.062

All data were obtained using the Core Consensus Sleep Diary.[193] Variables were defined as following: (1) Total sleep time defined as the total time spent asleep during 24 hours in minutes and hours; (2) Time in bed defined as the total time spent in bed in minutes and hours; (3) Morning wake time defined as the total time until full arousal; (4) Sum wake time defined as summation of total wake time during 24 hours. Independent samples t-tests were performed for all normally distributed data and mean (SD) were reported. [a] Kruskal-Wallis non-parametric test was performed for all non-normally distributed data and median (IQR) were reported. Asterisk indicates variables that were non-normally distributed. Homogeneity of variance was evaluated for all variables when violated unequal variances significance was reported.

plus total wake time at night and morning wake time) at timepoint one was significantly different between groups (χ^2=6.953, p=0.008) with the Control group (median=1:17; 0:53, 1:42) having a higher sum of wake time when compared to the Breezing™ group (median=0:36; 0:28, 1:04). These differences were not observed at timepoint 2 for either variable; however, the sum of wake time was significantly different between groups at timepoint 3. The Control group had significantly longer wake time (median=1:15; 0:57,1:40) than the Breezing™ group (median=0:46; 0:27, 1:12;

χ^2=4.365, p=0.037). These differences demonstrate the variability in sleep among a small cohort of pregnant women.

The objective sleep data from actigraphy across all three timepoints are provided in **Table 13.** It is noteworthy, that two of the Control and four of the Breezing™ group participants' data were excluded at timepoint 2 due to inaccurate data collection due to not wearing the watch consecutively. One of the Control and two of the Breezing™ group participants' were excluded at timepoint 3 for the same reasons stated above.

Table 13. Objective Sleep Data from Actigraphy Across Three Timepoints for Pregnant Women Participating in a Two-Arm Observational Study of Resting Energy Expenditure

	Total (n=28)	**Control (n=12)**	**Breezing™ (n-16)**	**P-Value**
TST 24hr (mins)				
Timepoint 1	450.36±48.41	442.82±54.47	456.82±43.59	0.474
Timepoint 2	454.14±38.14	456.42±34.73	452.23±42.21	0.805
Timepoint 3	442.14±44.89	449.92±39.83	436.02±49.07	0.454
TST Nocturnal (mins)				
Timepoint 1	440.78±51.54	433.92±62.73	446.67±41.22	0.540
Timepoint 2	438.95±46.13	439.50±50.98	438.50±44.00	0.961
Timepoint 3	431.31±41.56	439.74±38.87	424.69±43.81	0.380
Sleep Efficiency				
Timepoint 1	84.91±4.56	83.73±4.35	85.93±4.64	0.229
Timepoint 2	85.15±4.60	83.49±4.77	86.53±4.14	0.126
Timepoint 3[a]	83.18 (77.11, 87.38)	80.26 (77.06, 86.08)	84.36 (80.50, 88.14)	0.584
Total number of nights				
Timepoint 1	18.93±3.41	19.22±3.96	19.20±1.69	0.829
Timepoint 2[a]	13.00 (10.00, 14.00)	14.00 (11.00, 14.00)	13.00 (10.00, 14.25)	0.310
Timepoint 3[a]	14.00 (11.00, 14.00)	13.00 (9.50, 14.00)	14.00 (10.75, 14.00)	0.952
Total number of naps				
Timepoint 1[a]	2.00 (0.00, 7.00)	2.00 (0.00. 7.00)	2.00 (0.75, 7.25)	0.833
Timepoint 2[a]	2.00 (0.00, 5.00)	2.00 (0.00, 6.00)	2.00 (0.00, 5.50)	0.758
Timepoint 3[a]	0.00 (0.00, 4.00)	0.00 (0.00, 4.00)	0.50 (0.00, 4.50)	0.949

All data were obtained using the Phillips Actiware watch. Data were averaged over each timepoint. Variables were defined as following: (1) Total sleep time (TST) 24hr defined as the total time spent asleep during 24 hours in minutes and hours; (2) TST Nocturnal defined as the total time spent asleep during the night; (3) Sleep Efficiency defined as the proportion of time the patient is asleep out of the total time in bed. Independent samples t-tests were performed for all normally distributed data and mean (SD) were reported. [a] Kruskal-Wallis non-parametric test was performed for all non-normally distributed data and median (IQR). Homogeneity of variance was evaluated for all variables when violated unequal variances significance was reported.

The women wore the actigraphy watches for an average of 18.92±3.41, 13.5 (4.00), 13.5 (3.00) days for timepoints 1, 2, and 3, respectively. This was not statistically different between groups at any timepoint. Total 24-hour sleep duration, total nocturnal sleep duration, and sleep efficiency were not significantly different between groups at any timepoint. Evaluation of both subjective and objective sleep revealed somewhat different results demonstrating the need to assess both types of sleep measurements.

The primary sleep variables of interest were early, late, and overall changes in objectively measured total 24-hour sleep time, total nocturnal sleep time, and sleep efficiency (**Table 14**). We evaluated the early, late, and overall residualized change scores of these sleep parameters among the different groups. ANCOVA tests were performed to identify which of the proposed mediators significantly differed between groups throughout the study. There were no statistically significant differences in early, late, or overall changes for TST 24-hour or sleep efficiency. However, late changes in total nocturnal sleep time were trending toward significance. The Breezing™ group had a marginally significant decrease in total nocturnal sleep time relative to the Control group (mean diff=-32.75, 95% CI: -68.34 to 2.84, p=0.069). There were no other differences between groups for overall or early changes in total nocturnal sleep time.

Table 14. Mean±SD or Median (IQR) of Early, Late, and Overall Changes in TST 24-Hr, TST Nocturnal, and Sleep Efficiency By Group

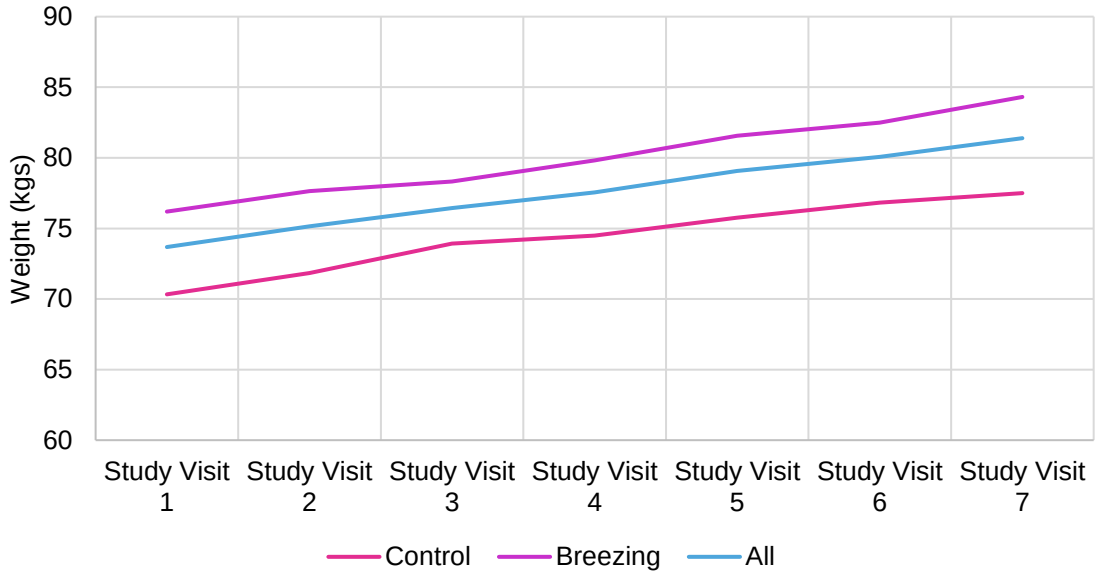
Variable	Control (n=12)	Breezing™ (n=16)	Cohen's d	P-Value
TST 24-hour				
Overall Changes	12.10±30.18	-10.24±29.51	0.147	0.078
Late Changes	9.20±27.53	-7.53±46.59	0.133	0.137
Early Changes	6.37±18.54	-5.30±25.30	0.035	0.428
TST-Nocturnal				
Overall Changes	11.62±24.54	-9.83±31.66	0.055	0.295
Late Changes	10.92±24.11	-8.93±44.85	0.192	*0.069*
Early Changes	5.28±18.65	-4.40±24.98	0.022	0.533
Sleep Efficiency				
Overall Changes[a]	-1.70 (-2.95, 2.13)	1.86 (-1.28, 3.93)	0.004	0.779
Late Changes [a]	-1.58 (-4.58, 3.44)	1.80 (-0.39, 5.49)	0.017	0.602
Early Changes	-0.09±2.87	0.07±1.94	0.002	0.864

ANCOVA was performed with maternal education and gestational age at study start as covariates to test for group differences. Non-normally distributed data are indicated with a superscript a. These variables were rank-transformed to meet normality before performing the ANCOVA. Abbreviations: SD= standard deviation; IQR= interquartile range, defined as the difference between the third and first quartile; TST=total sleep time.

Primary Outcome - Gestational Weight Gain

The Breezing™ group had a higher mean (76.2 kgs) weight at the initial study visit when compared to the Control group (70.3 kgs) but this was not statistically significant (t(26)=-0.955, p=0.349). **Figure 10** provides a graphical depiction of the change in weight throughout the entire study for both groups and the entire cohort. Despite having a greater initial weight, both the

Figure 10. Gestational Weight Gain Over the Study by Group Assignment



Control and Breezing™ group had a similar overall rate of weight gain (Control=0.49±0.25 kgs/wk; Breezing™= 0.58±0.19 kgs/wk, F(1,24)=-01.968, p=0.173). A one-way ANCOVA controlling for gestational age at study start and maternal education level demonstrated group differences in GWG. The Breezing™ group (0.67±0.26 kgs/wk) had a significantly higher rate of weight gain during the second half of the study when compared to the control group (0.39±0.27 kgs/wk; F(1,24)=8.148, p=0.009); however, there were no differences in overall [F(1,24)=1.968, p=0.173] or early [F(1,24)=0.563, p=0.460] rate of weight gain between groups. Interestingly, the Control group (4.17 kgs) gained more total GWG than the Breezing™ group (3.63 kgs) during the first half of the study; however, this was not statistically significant [F(1,24)=0.384, p=0.541]. This difference changed for the second part of the study with the Breezing™ group (4.38 kgs) gaining significantly more total GWG than the Control group (3.0 kgs; F(1,24)=5.06, p=0.034). These differences in timing of GWG resulted in no significant differences between groups for overall total

GWG [F(1,24)=1.56, p=0.224]. **Table 15** provides the overall, early, and late rate of GWG for each group and the entire cohort.

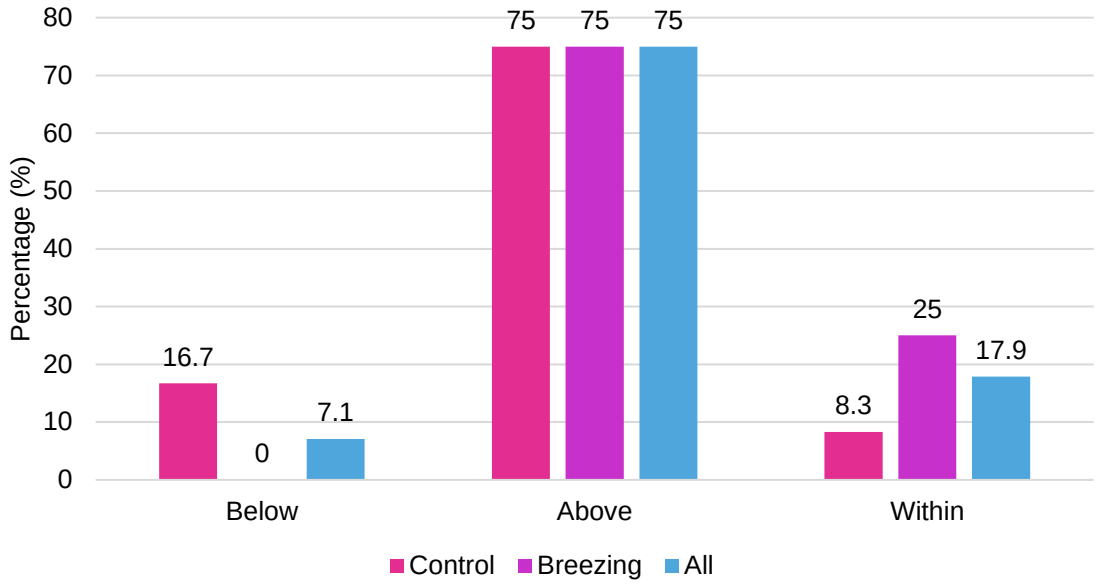
Table 15. Mean±SD of Rate of and Total Gestational Weight Gain (GWG) Among Study Participants

	Control (n=12)	Breezing™ (n=16)	Total (n=28)	Cohen's d	P-Value
Rate of GWG					
Overall Changes	0.49±0.25	0.58±0.19	0.54±0.22	0.40	0.173
Early Changes	0.59±0.28	0.49±0.31	0.53±0.30	0.35	0.460
Late Changes	0.39±0.27	0.67±0.26	0.55±0.29	1.08	**0.009**
Total GWG					
Overall Changes	7.12±2.62	8.13±2.92	7.71±2.79	0.36	0.224
Early Changes	4.17±1.70	3.63±2.03	3.86±1.88	0.29	0.541
Late Changes	3.00±1.35	4.38±1.67	3.79±1.66	0.91	**0.034**

ANCOVA with maternal education and gestational at study start were performed to compare group differences in rate and total GWG and mean (SD) were reported. Cohen's d was calculated using means and SDs. Cohen's d= .2 is a small effect, =.5 is a moderate effect, =.8 is a large effect. Abbreviations: SD= standard deviation; GWG= gestational weight gain; IQR= interquartile range, defined as the difference between the third and first quartile.

Regardless of these differences in overall and rate of GWG, 83.3% (n=10) and 87.5% (n=14) of the Control and Breezing™ group participants gained above the IOM recommendations for GWG (**Figure 11**). There were five women that gained within the recommended amount of weight with one being in the Control group and four being in the Breezing™ group. A Pearson Chi-square test revealed that the distribution of women that gained below, within, or above the IOM recommendations did not differ between groups (X^2=3.733, p=0.155).

Figure 11. Percentage of Women that were Below, Above, or Within IOM Recommendations for Rate of Gestational Weight Gain



Secondary Outcome – Resting Energy Expenditure

Partial Pearson correlations between change in REE and change in weight between the various study visits resulted in no significant correlations for timepoint 1 (r=0.358, p=0.230), timepoint 2 (r=0.291, p=0.335), timepoint 4 (r=-0.245, p=0.398), timepoint 5 (r=0.013, p=0.964), or timepoint 6 (r=0.282, p=0.328). However, there was a trending significant negative moderate correlation between the change in REE and change in weight at timepoint 3 (r=-0.469, p=0.091). Furthermore, there were no significant correlations between early (r=-0.422, p=0.132), late (r=-0.157, p=0.592), or overall (r=0.124, p=0.674) changes in REE and weight. Evaluation of correlations between early changes in REE with early changes in rate of GWG resulted in no significant association (r=-0.376, p=0.185). Similarly, there was no association between late changes in REE and late changes in GWG (r=-0.176, p=0.547). Likewise, there was no relationship between overall changes in REE and overall changes in GWG (r=0.014, p=0.961). However, there was a positive correlation between early changes in REE and late rate of GWG (r=0.528, p=0.052).

Tertiary Outcome – Mediation Effect of Dietary Composition on the Relationship between the Intervention and Rate of GWG

Results from simple mediation analyses indicated that group assignment was not indirectly related to rate of GWG through its relationship with overall, late, and early changes in fat consumption. For overall changes in dietary fat, a 95% biased-corrected confidence interval (bootstrapped BCa 95% CI) showed that the indirect effect was not entirely above zero (-0.05 to 0.13). Similarly, there was no indirect effect for early changes (BCa 95% CI: -0.08 to 0.11) or for late changes (BCa 95% CI: -0.07 to 0.14) in dietary fat composition. The simple mediation analyses evaluating the relationship between group assignment and rate of GWG through the dietary consumption of carbohydrates resulted in no significant indirect effects. Results from simple mediation analyses indicated that group assignment was not indirectly related to rate of GWG through its relationship with overall, late, and early changes in protein (OC: -0.04 to 0.12; LC: -0.04 to 0.21; EC: -0.05 to 0.12). Final simple mediation analyses investigating the relationship between group assignment and rate of GWG through overall, late, and early changes in energy consumption resulted in no significant indirect effects. **Table 16** provides the indirect effects, Sobel Z-test statistic, and the 95% biased-corrected confidence intervals based on 10,000 bootstrap samples of the simple mediation models for the effect of early, late, and overall changes in dietary composition on the relationship between the intervention and rate of GWG.

Table 16. Simple Mediation Models for the Effect of Early, Late, and Overall Changes in Dietary Composition on the Relationship between the Intervention and Rate of GWG

Mediator Variable	Point Estimate	Product-of-Coefficients method		Bootstrapped BCa 95% CI	
		SE	Z	Lower	Upper
OC Fat	0.009	0.044	0.33	-0.052	0.121
EC Fat	0.022	0.043	0.69	-0.076	0.105
LC Fat	0.037	0.052	0.79	-0.066	0.137
OC Carbohydrates	0.032	0.069	0.70	-0.035	0.240
EC Carbohydrates	0.003	0.034	0.10	-0.068	0.082
LC Carbohydrates	0.041	0.066	0.91	-0.031	0.227
OC Protein	0.007	0.042	0.22	-0.044	0.121
EC Protein	0.083	0.063	1.34	-0.040	0.207
LC Protein	0.004	0.042	0.11	-0.052	0.117
OC Energy	0.038	0.059	0.89	-0.045	0.187
EC Energy	0.031	0.043	0.68	-0.060	0.114
LC Energy	0.070	0.064	1.52	-0.021	0.227

Outcome for all of these models is overall rate of GWG throughout the study duration. Covariates included in all of the models are study GA and baby sex. Abbreviations: OC=overall changes; EC=early changes; LC=late changes; M=Mediator; Z= Sobel Z test statistic. Indirect effect was considered significant if the confidence interval did not include 0. Z > 1.96 in absolute value is significant.

A multiple mediation model was also performed with overall, early, and late changes for fat, carbohydrates, and protein entered as mediators in a single model. Results from these multiple mediation analyses indicated that group assignment was not related to rate of GWG via its relationship with overall, late, and early changes in dietary composition. **Table 17** provides the indirect effects, Sobel Z-test statistic, and the 95% biased-corrected confidence intervals based on 10,000 bootstrap samples of the multiple mediation models of the intervention on rate of GWG through the various dietary composition variables.

Table 17. Multiple Mediation Models for the Effect of Early, Late, and Overall Changes in Dietary Composition on the Relationship Between the Intervention and Rate of GWG

Mediator Variable	Point Estimate	Product-of-Coefficients method		Bootstrapped BCa 95% CI	
		SE	Z	Lower	Upper
Overall Changes					
Total	0.0403	0.0911	0.52	-0.0601	0.2952
Fat	-0.0054	0.0648	0.12	-0.1180	0.1477
Carbohydrates	0.0339	0.0764	0.71	-0.0564	0.2502
Protein	0.0118	0.0637	0.27	-0.0714	0.1777
Early Changes					
Total	0.0768	0.0992	0.28	-0.1027	0.2857
Fat	-0.0145	0.0640	0.40	-0.1731	0.1002
Carbohydrates	0.0018	0.0321	0.10	-0.0598	0.0748
Protein	0.0895	0.1138	1.08	-0.0886	0.3522
Late Changes					
Total	0.0571	0.0908	0.42	-0.0660	0.2956
Fat	0.0333	0.0719	0.57	-0.1473	0.1574
Carbohydrates	0.0315	0.0782	0.68	-0.0471	0.2624
Protein	-0.0077	0.0579	0.19	-0.0859	0.1432

Outcome for all of these models is overall rate of GWG throughout the study duration. Covariates included in all of the models are study GA and baby sex. Abbreviations: OC=overall changes; EC=early changes; LC=late changes; M=Mediator; Z= Sobel Z test statistic. Indirect effect was considered significant if the confidence interval did not include 0. Z > 1.96 in absolute value is significant.

Exploratory Outcome – Mediation Effect of Sleep Parameters on the Relationship between Dietary Composition and Rate of GWG

Previously performed ANCOVA tests revealed that late changes in total nocturnal sleep time were the only sleep parameter that was marginally significant. However, since this was an exploratory aim and because we had a small sample size, we developed simple mediation models to evaluate the potential mediation effect of overall dietary composition variables on rate of GWG through overall, late, and early changes in TST-nocturnal, TST-24 hour, and sleep

efficiency. Results from simple mediation models indicated that overall changes in the dietary composition variables were not indirectly related to overall rate of GWG through their relationships with overall, late, and early changes in the sleep parameters. **Table 18** provides the indirect effects, Sobel Z-test statistic, and the 95% biased-corrected confidence intervals based on 10,000 bootstrap samples of the simple mediation models for the dietary composition variables and rate of GWG across various sleep parameters.

Table 18. Simple Mediation Models for the Effect of Early, Late, and Overall Changes in TST-Nocturnal, TST-24 hour, and Sleep Efficiency on the Relationship Between Changes in Dietary Composition and Rate of GWG

Mediator Variable	Point Estimate	Product-of-Coefficients method		Bootstrapped BCa 95% CI	
		SE	Z	Lower	Upper
Overall Changes Energy					
OC TST-Nocturnal	0.0000	0.0000	0.53	-0.0001	0.0001
LC TST-Nocturnal	0.0000	0.0001	0.52	-0.0001	0.0002
EC TST-Nocturnal	0.0000	0.0001	0.13	-0.0002	0.0001
OC TST-24 hour	0.0000	0.0001	0.75	-0.0001	0.0002
LC TST-24 hour	0.0000	0.0001	0.52	-0.0002	0.0002
EC TST-24 hour	0.0000	0.0001	0.49	-0.0004	0.0001
OC Sleep Efficiency	0.0000	0.0000	0.41	-0.0001	0.0001
LC Sleep Efficiency	0.0000	0.0001	0.12	-0.0002	0.0001
EC Sleep Efficiency	0.0000	0.0001	0.03	-0.0001	0.0001
Overall Changes Fat					
OC TST-Nocturnal	0.0004	0.0012	0.59	-0.0010	0.0039
LC TST-Nocturnal	0.0007	0.0022	0.56	-0.0020	0.0064
EC TST-Nocturnal	0.0001	0.0014	0.13	-0.0040	0.0016
OC TST-24 hour	0.0004	0.0014	0.49	-0.0015	0.0040
LC TST-24 hour	0.0003	0.0022	0.25	-0.0029	0.0064
EC TST-24 hour	0.0001	0.0022	0.27	-0.0073	0.0010
OC Sleep Efficiency	0.0000	0.0031	0.08	-0.0075	0.0050
LC Sleep Efficiency	0.0001	0.0015	0.15	-0.0031	0.0030
EC Sleep Efficiency	-0.0004	0.0015	0.38	-0.0026	0.0032
Overall Changes Carbohydrates					
OC TST-Nocturnal	0.0000	0.0003	0.18	-0.0005	0.0008
LC TST-Nocturnal	0.0000	0.0004	0.07	-0.0008	0.0008
EC TST-Nocturnal	0.0001	0.0006	0.39	-0.0014	0.0014
OC TST-24 hour	0.0003	0.0004	0.85	-0.0004	0.0011
LC TST-24 hour	0.0002	0.0005	0.57	-0.0011	0.0008
EC TST-24 hour	0.0001	0.0029	0.46	-0.0013	0.0009
OC Sleep Efficiency	0.0005	0.0006	1.05	-0.0007	0.0016
LC Sleep Efficiency	0.0003	0.0006	0.70	-0.0011	0.0016
EC Sleep Efficiency	0.0001	0.0004	0.17	-0.0010	0.0007
Overall Changes Protein					
OC TST-Nocturnal	0.0001	0.0006	0.26	-0.0007	0.0016
LC TST-Nocturnal	0.0001	0.0011	0.29	-0.0013	0.0027
EC TST-Nocturnal	0.0000	0.0012	0.08	-0.0037	0.0011
OC TST-24 hour	0.0000	0.0005	0.05	-0.0006	0.0013
LC TST-24 hour	0.0000	0.0009	0.03	-0.0012	0.0023
EC TST-24 hour	0.0001	0.0013	0.29	-0.0041	0.0008
OC Sleep Efficiency	0.0000	0.0005	0.10	-0.0012	0.0005
LC Sleep Efficiency	0.0000	0.0007	0.02	-0.0019	0.0010
EC Sleep Efficiency	0.0001	0.0007	0.09	-0.0013	0.0017

Outcome for all of these models is overall rate of GWG throughout the study duration. Covariates included in all of the models are study GA and baby sex. Abbreviations: TST-Nocturnal= total nocturnal sleep time; TST-24 hour=total 24-hour sleep time; OC=overall changes; EC= early changes; LC= late changes; SE=standard error; Z= Sobel Z test statistic. Indirect effect was considered significant if the confidence interval did not include 0. Z > 1.96 in absolute value is significant.

DISCUSSION

Maternal overweight and obesity is a growing public health problem and when coupled with excessive gestational weight gain may lead to poor health outcomes for mother and baby. The current study implemented an intervention that required pregnant women to use the Breezing™ device in order to obtain their resting energy expenditure across approximately 13 weeks of gestation. The simplicity of the current intervention was designed to provide the women awareness of actual caloric needs throughout pregnancy and evaluate whether exposure to this information impacted appropriate GWG. This intervention is in contrast to previous intervention studies that have implemented dietary or physical activity programs to improve GWG which required more time and resources for both participants and research staff. These interventions have had inconsistent outcomes.[25,69,70]

The women who used the Breezing™ device gained approximately 0.95 kgs more throughout the 13-week study period when compared to the Control group; however, this difference was not significant. This is similar to other intervention studies among pregnant women that have had little to no effect on GWG.[22,70,78–80] Surprisingly, there were significant differences in the rate of weight gain between study groups depending on timing of the study. In the first half of the study, the Breezing™ group gained less total weight and had a lower rate of GWG when compared to the Control group. This changed in the latter half of the study resulting in the Breezing™ group having a higher total and rate of weight gain. This may indicate that timing of GWG primarily during the second trimester might have been impacted by the study intervention but that awareness of REE did not have a lasting impact. Regardless of negligible findings regarding GWG, to our knowledge, this is the first study that has implemented the use of a real-time metabolism tracker among pregnant women to monitor resting energy expenditure and investigate the impact of REE monitoring (with no educational component) on GWG.

Evaluation of the variation in REE revealed interesting findings. Overall, REE increased throughout the study. This is similar to other studies that have assessed resting energy expenditure finding gradual increases of 10.7 kcal per week.[20] However, there was a significant proportion of women who experienced decreases in REE throughout the study. Approximately

40% of the women had a decrease in REE at various timepoints in the study. These decreases ranged from 10 to 620 kcal. Similarly, the women who had an increase in REE had substantial variations ranging from 10 to 350 kcal. These differences among the current cohort of women demonstrate that REE is prone to fluctuations throughout pregnancy. Eto et al. found that the REE was significantly lower during the first trimester as compared to the third trimester.[139] Similarly, Berggren and colleagues reported a 27% increase in resting energy expenditure among healthy pregnant women.[10] This is a substantially greater increase than what we observed in the current study of approximately 11.5%.

Previous research has found a moderate positive correlation between REE and GWG,[8,10] however, we only found a positive correlation between early changes in REE and late changes in GWG. These insignificant findings may be due to the small sample size of our study but may also relate to the number of women with huge variations in their REE throughout the study. The current body of work demonstrates the need for a more in-depth evaluation of energy needs during pregnancy and the potential relationship with GWG as some women might have drastic fluctuations in REE increasing their risk for excessive GWG or other pregnancy-related health conditions. Future studies may benefit from more regular sampling across gestation to fully understand these fluctuations and how they relate to GWG.

In this cohort of pregnant women, approximately 35.7% were overweight and 28.6% were obese. This equates to approximately 64.3% of the study population being overweight or obese, which is slightly higher than the national estimates[38,42] of overweight and obesity during pregnancy but similar to overweight and obesity rates among pregnant women in other studies.[39,51] Previous reports have indicated substantial differences in the proportion of pregnant women with obesity with some indicating lower rates[40,53,55,194] while others had higher rates of obesity among their study cohorts when compared to our study.

Surprisingly, the majority of women in this study gained above the IOM recommendations for GWG. This rate was higher than the national average[62] demonstrating that excessive GWG is problematic for a primarily Caucasian, highly educated cohort of women in the Phoenix, AZ metro area. Previous studies have demonstrated that overweight and obese women are at higher risk of

gaining more than the recommended amount of weight during pregnancy.[64–67] In contrast to other studies, excessive GWG among the present cohort was relatively evenly distributed among the different BMI categories.

Despite an increase in the rate of GWG throughout the study, none of the women in the study reported gestational diabetes, preeclampsia, or other pregnancy-related complications related to maternal overweight and obesity. This is in contrast to other studies that have found high rates of maternal comorbidities during pregnancy associated with excessive gestational weight gain and maternal overweight and obesity.[44,47,50] Furthermore, only one woman reported an infant-related delivery complication (i.e. fetal macrosomia subsequently resulting in shoulder dystocia) despite four women delivering an infant > 4000 grams. The rate of fetal macrosomia of 14.3% was lower than national averages of 20%.[47] Conversely, the fetal macrosomia infants in this study were not among the women with obesity pre-pregnancy but instead delivered to normal and overweight women. Whether lower rates of maternal and neonatal complications observed in this study were related to knowledge of REE would require a larger sample but merit investigation.

The current study also assessed the composition of maternal diets during pregnancy. We found no differences in any nutrient by study group except that the control group had significantly higher thiamine intakes at baseline. Baseline intakes of total fat for the entire study population were comparable to other studies.[101,103,195,196] It has been previously reported that maternal dietary patterns consist of approximately 25-32% of calories from fat.[100,103,196,197] In the current study, 35.7% of calories came from dietary fat. However, the total energy consumption among the current study cohort averaged 1690 per day which is much lower than other studies have reported (1970-2480 kcal/day).[101,103,196,197] However, Chen et al did report a mean energy consumption of 1861 kcal/day[100] which is closer to the caloric intake of the current study population.

Likewise, percent of calories from carbohydrates (48%) was slightly lower than other studies.[100,101,103,196,197] Previous studies have reported a range of 238-269 grams of carbohydrates consumed per day among pregnant women[100,101,103] which is about 31-62 grams less than

carbohydrate intake in our current population. The percent of calories from protein (17%) was slightly higher than other studies[100,101] which have reported a range from 14-16%. Total grams of protein (68.3 grams per day) consumed per day among the current study participants were lower than the national average of 78.1 grams per day.[101] Despite these minor differences, the overall macronutrient composition of the current cohort of pregnant women resembles that of other studies, indicating a potentially representative sample.

When assessing early, late and overall changes in macronutrients, the Breezing™ group had significant reductions in overall and late changes in total energy and protein consumption. However, early changes in protein intake seemed to differ with increases among the Breezing™ group participants and decreases among the Control group. Previous studies have found inconsistent finding pertaining to changes in macronutrient intake throughout pregnancy.[102,195] Blumfield et al. reported an increase of 184±86 kcal of energy, 5.9 grams of protein, 10.1 grams of fat, and 17.8 grams of carbohydrates per day from the first to the third trimester.[195] We observed increases of 191±422 kcal of energy, 13.3 grams of protein, 7.4 grams of fat, and 19.3 grams of carbohydrates among the Control group over the 13-week study period. These changes are interesting as previous studies have found that diets low in carbohydrates but high in protein and fat[198] or lower adherence to a Mediterranean diet[115] to be associated with GDM risk. Despite macronutrient changes among the Control group, no women reported developing GDM; however, the study durations of these two studies drastically differed. The Breezing™ group had overall reductions in all of the macronutrients but increases early in the second trimester for several of the macronutrients. Maternal diet is important to the growth and development of the fetus and has been associated with increased adiposity[103,120] and higher childhood BMI.[100,109] The current study did not find differences in birthweight between the two groups; however, we did not assess other measures of neonatal adiposity.

We assessed both subjective and objective sleep parameters. Although, pregnant women are at risk for a multitude of sleep problems ranging from increased daytime sleepiness to insomnia, our current cohort reported minimal sleep problems. Approximately 57% of the women in our study reported fairly good sleep at the first timepoint. Surprisingly this increased to 78%

and 60% as pregnancy progressed. This is in contrast to studies reporting that sleep quality worsens as pregnancy progresses.[161] Our study population had similar average PSQI-Global scores of 6.2 at baseline when compared to other studies.[33,161] Despite self-report of fairly good sleep, women in our study had a PSQI-Global score that decreased by 0.7 throughout the study. Previous studies have reported a decrease of 1.68 in the PSQI-Global score from the first to the third trimester.[161] Our study indicates that almost half of this decrease might be occurring during the second trimester. Likewise, previous studies have reported an average sleep duration of 6.44 to 8.39 hours per night[33,34,147,151–154,172] and sleep efficiency of >80% among pregnant women.[156,157,199] The women in our study had similar sleep duration (~7 hours) and good sleep efficiency (80%).

Surprisingly, the sleep duration for the Control group increased but their sleep efficiency decreased as pregnancy progressed. The opposite was true for the Breezing™ group. Previous research has found a incidence of insomnia among pregnant women, with approximately 57% reporting symptoms of insomnia.[34] Less than 25% of the current cohort of women were positive for insomnia disorders at any of the three timepoints. This might be because we primarily assessed women during the second trimester which may be too early for symptoms of insomnia to emerge. Our findings resemble that of Okun and colleagues, who found that insomnia diagnoses was less frequent in early gestation.[168] Overall, the current cohort of pregnant women had good sleep duration and sleep efficiency, and reported minimal sleep disturbances throughout pregnancy.

The current study also evaluated how dietary composition mediates the relationship between the intervention and rate of GWG. We were unable to demonstrate mediation for any of the dietary composition variables. This is primarily due to the study being underpowered to detect mediation effects. Despite these negligible results, there were emergent differences in the changes of macronutrient composition with the Breezing™ having overall decreases in all macronutrients and the Control group having overall increases. Previous research has argued that GWG is related to increased energy consumption.[8,10,141] In the current study, the opposite was true as the Breezing™ gained more weight but had an overall decrease in their energy

consumption. However, other studies have reported considerably differences in energy requirements among women with higher pregnancy BMI[20] or who gained excessive weight[6,80] during pregnancy. This could potentially indicate an effect of using the Breezing™ device but the dietary changes might not have reached a magnitude that translates into reduced GWG. Regardless, to our knowledge, this is the first study that has assessed the impact of using a real-time metabolism tracker on GWG and potential dietary composition mediators of that relationship.

Lastly, we investigated the relationship between dietary composition and rate of GWG through sleep parameter variables. Unfortunately, we were unable to show any mediation effect of sleep on the relationship between dietary composition and GWG. Once again, this is primarily due to the study being underpowered to detect mediation; however, it might also be due to the overall good sleep duration and efficiency seen in the current cohort of pregnant women. Previous research has found that 76% of pregnant women reported poor sleep quality[34] which has been reported to worsen as pregnancy progresses.[158,161] In the current study, 57% of women reported 'fairly good' sleep at timepoint 1 which only improved at later timepoints. Additionally, the current study followed women primarily during the second trimester which might have been too early for many of the previously reported sleep problems to emerge, making it difficult to assess mediation without an overall main effect of sleep on GWG. Nonetheless, sleep restriction has demonstrated detrimental effects on metabolism resulting in a 2.6% reduction in resting metabolic rate.[36] Therefore, combining the impact of two highly variable but influential behavioral factors (diet and sleep) on GWG adds to the current body of knowledge on how behaviors interact to influence obesity risk.

There are several strengths of the current study including the randomized controlled design, high study completion, and overall adherence to longitudinal data collection over a 13-week period. To our knowledge, there have been no other randomized controlled trials that have implemented use of a real-time metabolism tracker among pregnant women. The current study randomized and followed 28 pregnant women with all of the women completing all seven study visits. There were six women that dropped out or were lost-to-follow-up; however, this was prior to the first study visit. One reason for this high adherence was due to the design of the study. All

study visits occurred at the participants' homes instead of in a clinical setting or research laboratory. This made the completion of study visits extremely convenient for participants, significantly reducing the burden to them. Furthermore, the study followed the women for 13 weeks collecting anthropometric, diet, sleep, and metabolic information at multiple timepoints. This longitudinal collection of data allowed for evaluation of changes in dietary composition and sleep parameters over time, providing a more complete picture of the fluctuations among these factors during pregnancy.

The current study is not without limitations. A major limitation of this study was the small sample size which might have impacted our ability to find significant results, specifically for the mediation analyses performed. Historically, it was a requirement that there was a direct effect among the independent and dependent variables before mediation analysis could occur. This is an outdated point-of-view; however, without a direct effect to mediate the likelihood of obtaining a significant indirect effect is minimized. Furthermore, our sample consisted of primarily Caucasian, highly educated women which might not be generalizable to the general population in the United States. Regardless, considering this was a pilot study, the feasibility of implementing a similar study in a larger, more diverse population is promising. Another limitation of this study was the potential inaccuracy of the resting energy expenditure measurements collected from the Breezing™ device. The most accurate resting energy expenditure measurement would be obtained immediately upon waking prior to consumption of any food or before any exercise. However, this was not possible in the current study as the study visits were scheduled at the most convenient times for the study participants, ranging from early morning to evening visits. Additionally, two women reported inconsistent shift work. These two women remained in the analyses for the exploratory aim despite the impact that this may have on the sleep variables of primary interest. This is due to the small sample size and exploratory nature of the sleep mediation models. Lastly, data collection was performed primarily by one individual; however, there were three other research assistants that helped with study visits. This may have introduced bias as data collection might have varied across these individuals. All research assistants were

trained on proper measurements for height, weight, and resting energy expenditure in order to reduce variability in collection methods.

Next steps to continue to explore the relationship between REE and GWG would be to make modifications to the study design, methodology, setting, and analytical approach. First, instead of performing a randomized controlled trial, it would be interesting to conduct a prospective observational or case-control study. An observational study would allow for a larger sample size allowing us to explore variations in REE among a more diverse cohort. A case-control study would allow for evaluation of differences in REE and GWG among different race and ethnicities as well as control for various factors such as age, education, and socioeconomic status. Second, future studies could make changes to the methodology of the current study. It would be ideal to follow the women from preconception through the postpartum period; however, such a study would be difficult due to the long timeframe. Therefore, it would be beneficial to conduct a study during the same pregnancy time period but collect REE daily. By collecting daily REE measurements, we would be able to better assess fluctuations throughout the entire second trimester. Additionally, we would be able to collect REE at the most ideal time – immediately upon waking prior to consumption of any food or performance of any physical activity. Furthermore, it would also be vital to collect weight on a more frequent basis, specifically every week, which would allow for better evaluation of weight changes during this critical period of growth and development. Another methodology modification would be to provide dietary counseling (e.g. caloric intake, increased fiber, and fruit and vegetable consumption) in conjunction with REE data output to determine if counseling coupled with REE awareness effects GWG. Finally, future studies could conduct a similar study in a different setting, particularly a clinical study. Integration of the Breezing™ device into physicians' offices, particularly during well-women or prenatal visits, would be convenient and may stimulate discussion around nutrition and weight gain during pregnant. Lastly, changes in the analytical approach to standardized the variables to gestational age instead of study duration would increase the clinical relevance of the study results and make the results easily interpretable by the general population. These slight modifications in study

design, methodology, and setting would allow future studies to expand on the current study findings and to continue to add to the body of knowledge.

CONCLUSION

In conclusion, the use of a real-time metabolism tracker to monitor variations in REE among a cohort of healthy pregnant women did not impact the rate of GWG. However, this study did demonstrate substantial fluctuatations in REE, with an approximate 13% increase, indicating the need for further research evaluating REE as an alternative physiological variable associated with differences in weight gain during pregnancy. Additionally, we found that early changes in REE were correlated with late changes in rate of GWG demonstrating that early changes might impact GWG. Furthermore, we found no mediation effect of macronutrient composition on the relationship between the intervention and rate of GWG but did reveal considerable differences in changes in macronutrients between groups. This may indicate that awareness of REE might impact dietary intake. Furthermore, there was no observed mediation effect of sleep on relationships between dietary composition and GWG. Despite null findings, the high variability in REE found in this study indicates that this very individualized physiological variable might still play a role in gestational weight gain. Future research investigating the effect of both biological and behavioral factors in combination are needed in order to better understand the large differences in weight gain during pregnancy. Next steps include exploring these relationships with a larger population during the entire course of a pregnancy.

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APPENDIX A

IRB APPROVAL LETTER & CONTINURING REVIEW APPROVAL

ASU Knowledge Enterprise Development

APPROVAL FULL BOARD

Corrie Whisner
SNHP: Nutrition
602/827-2261
Corrie.Whisner@asu.edu

Dear Corrie Whisner:

On 8/25/2017 the ASU IRB reviewed the following protocol:

Type of Review:	Initial Study
Title:	Metabolic Tracking During Pregnancy to Promote Adequate Gestational Weight Gain
Investigator:	Corrie Whisner
IRB ID:	STUDY00006557
Funding:	Name: Biodesign Institute (BDI)
Grant Title:	
Grant ID:	
Documents Reviewed:	• Randomization List, Category: Other (to reflect anything not captured above); • IRB Application, Category: IRB Protocol; • External Site Letter of Support, Category: Off-site authorizations (school permission, other IRB approvals, Tribal permission etc); • Health History Questionnaire, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Dietary Screener English, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Portion Size Handout 24hr Dietary Recall, Category: Participant materials (specific directions for them); • Adverse Event Form, Category: Other (to reflect anything not captured above); • Study Completion, Category: Screening forms; • Screening Form, Category: Screening forms; • Breezing Report Form, Category: Technical materials/diagrams; • Randomization Form, Category: Screening forms; • Dietary Recall Form, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Flow Chart Study Activities, Category: Technical materials/diagrams; • Flyer, Category: Recruitment Materials; • Consent, Category: Consent Form;

The IRB approved the protocol from 8/16/2017 to 8/15/2018 inclusive. Before 8/15/2018, you are to submit a completed Continuing Review application and required attachments to request continuing approval or closure.

If continuing review approval is not granted before the expiration date of 8/15/2018 approval of this protocol expires on that date. When consent is appropriate, you must use final, watermarked versions available under the “Documents” tab in ERA-IRB.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

Sincerely,

IRB Administrator

cc: Kiley Vander Wyst
Elizabeth Reifsnider
Corrie Whisner
Kiley Vander Wyst

ASU Knowledge Enterprise Development

APPROVAL:CONTINUATION

Corrie Whisner
Nutrition
602/827-2261
Corrie.Whisner@asu.edu

Dear Corrie Whisner:

On 6/20/2018 the ASU IRB reviewed the following protocol:

Type of Review:	Continuing Review
Title:	Metabolic Tracking During Pregnancy to Promote Adequate Gestational Weight Gain
Investigator:	Corrie Whisner
IRB ID:	STUDY00006557
Category of review:	
Funding:	Name: Biodesign Institute (BI)
Grant Title:	None
Grant ID:	None
Documents Reviewed:	• Consent_Tracked, Category: Consent Form; • Spanish Flyer, Category: Recruitment Materials; • English Flyer Tracked, Category: Recruitment Materials; • Consent_Clean, Category: Consent Form; • Spanish Consent, Category: Consent Form; • English Flyer Clean, Category: Recruitment Materials;

The IRB approved the protocol from 6/20/2018 to 6/19/2019 inclusive. Three weeks before 6/19/2019 you are to submit a completed Continuing Review application and required attachments to request continuing approval or closure.

If continuing review approval is not granted before the expiration date of 6/19/2019 approval of this protocol expires on that date. When consent is appropriate, you must use final, watermarked versions available under the "Documents" tab in ERA-IRB.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

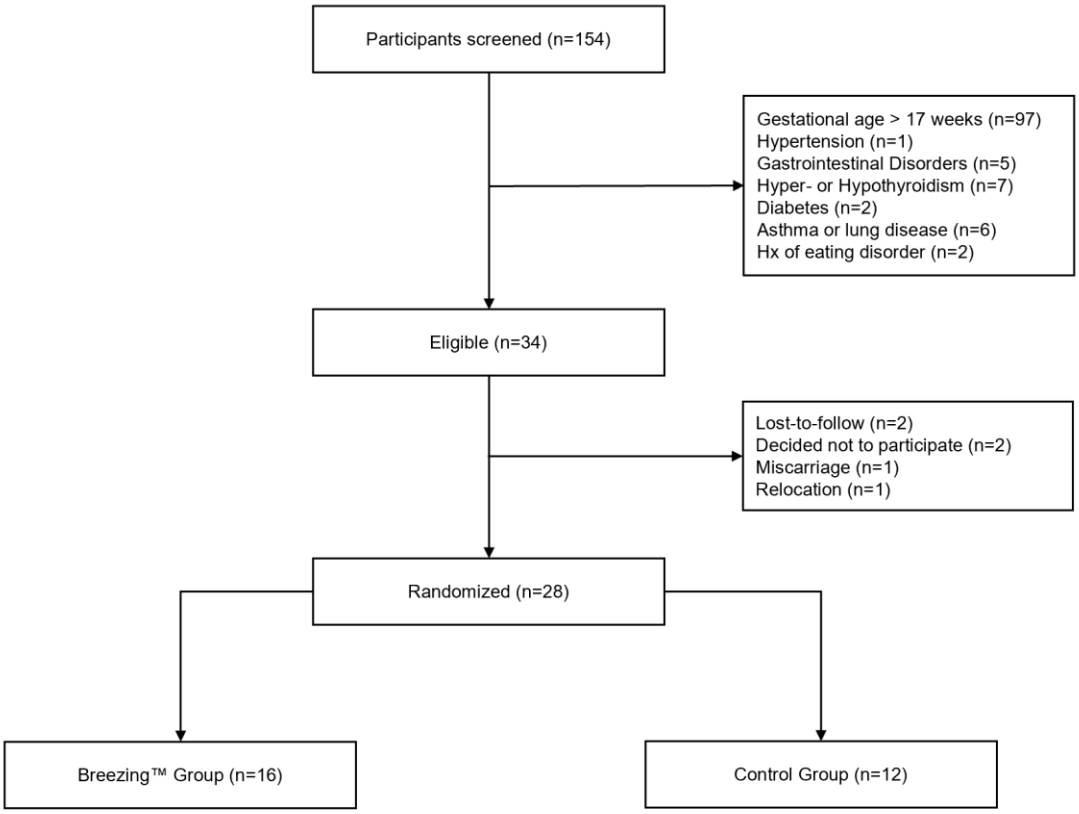
Sincerely,

IRB Administrator

cc: Kiley Vander Wyst
Meredith Delp
Rachel Geiser
Ritika Gupta
Megan Petrov
Kaitlyn Felix
Jamielee Richardson
Nicole Hoffmann
Anjali Agrawal
Elizabeth Reifsnider
Lindsay Wong
Corrie Whisner
Jacqueline Godinez Lopez
Kiley Vander Wyst
Bettie Coplan

APPENDIX B

STUDY CONSORT DIAGRAM


Participants screened (n=154)
Gestational age > 17 weeks (n=97)
Hypertension (n=1)
Gastrointestinal Disorders (n=5)
Hyper- or Hypothyroidism (n=7)
Diabetes (n=2)
Asthma or lung disease (n=6)
Hx of eating disorder (n=2)
Eligible (n=34)
Lost-to-follow (n=2)
Decided not to participate (n=2)
Miscarriage (n=1)
Relocation (n=1)
Randomized (n=28)
Breezing™ Group (n=16)
Control Group (n=12)

APPENDIX C

STUDY RECRUIMENT FLYER

VOLUNTEERS NEEDED FOR RESEARCH STUDY

We are researching how your energy needs during pregnancy change using a mobile tracking device called the Breezing™ device.

We need healthy, pregnant women currently 17 weeks gestation or less to use the Breezing device for 13 weeks and complete seven at-home study visits.

We will ask you what you eat and obtain your height and weight at each study visit. Each visit will last approximately 2 hours.

Participation is voluntary. You may withdraw from the study at any time.

If you are interested, please contact study staff or answer the following questions: https://asuhealthpromotion.co1.qualtrics.com/jfe/form/SV_e51PH4FT0Sgmmln

WHAT'S INVOLVED?

SEVEN AT-HOME STUDY VISITS

Tracking of:
DIET
WEIGHT
ENERGY
SLEEP

COMPENSATION UP TO $180

CONTACT:

KILEY VANDER WYST, MPH
khvanderwyst@asu.edu
262-989-7062

APPENDIX D

SCREENING FORM

Screening Form

Study ID _____

Inclusion Criteria

Pregnant with a gestational age < 17 weeks	○ Yes ○ No

Exclusion Criteria

History of Hypertension	○ Yes ○ No
Gastrointestional disorders	○ Yes ○ No
Malabsorptive disorders	○ Yes ○ No
Hyper or Hypothyroid conditions	○ Yes ○ No
HIV/AIDS	○ Yes ○ No
Type 1, Type 2, or gestational diabetes	○ Yes ○ No
Asthma or lung disease	○ Yes ○ No
Do you currently smoke (cigarettes, chew, or any other form of tobacco)?	○ Yes ○ No
A current smoker is a women who has smoked 100 cigarettes in their lifetime and now smoke every day or some days.	
History of eating disorder	○ Yes ○ No
Cardiac disease or conditions	○ Yes ○ No
Multiple gestation pregnancy	○ Yes ○ No
Fetal growth problems	○ Yes ○ No
Other metabolic conditions	○ Yes ○ No
Did the participant meet the eligibility requirements for this study	○ Eligible ○ Ineligible

Research staff signature:

_____

APPENDIX E

INTERVIEW-ADMINISTERED 24-HOUR DIETARY RECALLS

Dietary Recall

Study ID _____

24-Hour Dietary Recall
Arizona State University

We would like to know everything that you ate and drink in the past 24 hours.

- Eat and drink as you USUALLY do.
- Bring your food diary with you EVERYWHERE you go. Fill in the food diary at SCHOOL and at HOME.
- Use a NEW LINE for every food and drink that you eat.
- Write down EVERYTHING you eat and drink, HOW MUCH of it you had and the TIME you ate or drank it at.
- List foods such as sandwiches as SEPARATE food items. For example, a ham sandwich is written as: 2 slices of white bread, mustard and 1 slice of ham.
- Include brand names of food items that you ate during the day. For example:
  - Cereal: Honey Nut Cheerios, Cinnamon Toast Crunch, Twix, etc.
  - Chips: Lay's Wavy Potato Chips, etc.
  - Soda: Mountain Dew, Coke, Pepsi, and Regular vs. Diet.
- Don't forget all those LITTLE EXTRAS that you eat with your meals. Some examples are salt, sugar, butter, ketchup, and mayo.
- Don't forget to include all SNACKS AND DRINKS that you have in between meals. Some examples are candy, chips, fruit and drinks such as tea, water, soda.
- For any FAST FOOD, write down the NAME of the restaurant such as McDonald's or Burger King. You can write this in the "where" box.
- For all cooked foods, tell us HOW it was COOKED. Some ways of cooking foods are frying, boiling, roasting, baking, and grilling.
- Include all SUPPLEMENTS you take at the bottom of log for each day.

Breakfast ○ Yes ○ No

Time of Breakfast: _____

Location of Breakfast: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

Lunch ○ Yes ○ No

Time of Lunch: _____

Location of Lunch: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

Dinner ○ Yes ○ No

Time of Dinner: _____

Location of Dinner: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

Snack

Did you have a snack anytime during the day?

- ☐ Morning
- ☐ Afternoon
- ☐ Evening
- ☐ None

Time of Morning Snack: _____

Location of Morning Snack: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

Time of Afternoon Snack: _____

Location of Afternoon Snack: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

Time of Evening Snack: _____

Location of Evening Snack: _____

What type of food and drink did you have? _____

How much did you EAT or DRINK? _____

How much was LEFTOVER? _____

How was you food cooked? _____

APPENDIX F

INTERVIEW ADMINISTERED DIETARY SCREENER QUESTIONNAIRE

The pdf of the total questionnaire can be found at the following URL: https://epi.grants.cancer.gov/nhanes/dietscreen/questionnaires.html For study related data collection, all participant responses were inputted into the electronic questionnaire.

APPENDIX G

HEALTH HISTORY QUESTIONNAIRE

Health History Questionnaire

Study ID _____

Today's Date: _____

Personal Health History

Current Gestational Age (weeks) _____

Current Gestational Age (days) _____

Past Medical History

- ☐ Arthritis ☐ Heart disease
- ☐ Gallstones ☐ Liver disease
- ☐ Epilepsy ☐ Blood transfusions
- ☐ Thyroid disease ☐ Bronchitis
- ☐ Other

How many prescribed or over-the-counter drugs (such as vitamins or inhalers) do you currently take on?

- ○ None
- ○ 1-3
- ○ 4-6
- ○ More than 6

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Name of Drug _____

Strength of Drug _____

Frequency of Drug _____

Health Habits

Exercise

- ○ Sedentary (no exercise)
- ○ Mild exercise (i.e. climb stairs, walk 3 blocks, golf)
- ○ Occasional vigorous exercise (i.e. less than 4x/week for 30 min)
- ○ Regular vigorous exercise (i.e. at least 4x/week of 30 minutes or more)

Are you dieting?

- ○ Yes
- ○ No

If yes, are you on a physician prescribed medical diet?

- ○ Yes
- ○ No

How many meals do you eat in an average day?

- ○ Less than 3
- ○ Approximately 3
- ○ More than 3

Please rank your salt intake on an average day

High — Medium — Low

(Place a mark on the scale above)

Please rank your fat intake on an average day

High — Medium — Low

(Place a mark on the scale above)

Do you drink beverages that contain caffeine? ○ Yes ○ No

If yes, what type of beverages do you drink?

☐ Coffee ☐ Tea ☐ Soda ☐ Other

If you selected other, what drinks do you consume that have caffeine in them? _____

How many drinks with caffeine do you consume per week?

○ One to three ○ Four to six
○ Six to eight ○ Eight to ten
○ Ten or more

Do you drink alcohol?

○ Yes ○ No

If so, what kind of alcohol?

_____

How many drinks per week do you typically have?

_____

Comments

_____

APPENDIX H

DEMOGRAPHIC FORM

Demographic Information

Study ID _____

Today's Date: _____

Demographic Information

Occupation _____

Date of birth _____

Age (years) _____

Marital Status

- ◯ Single
- ◯ Partnered
- ◯ Married
- ◯ Separated
- ◯ Divorced
- ◯ Widowed

Race

- ◯ American Indian/Alaska Native
- ◯ Asian
- ◯ Native Hawaiian or Other Pacific Islander
- ◯ Black or African American
- ◯ White
- ◯ More Than One Race
- ◯ Unknown / Not Reported

Ethnicity

◯ Hispanic or Latino ◯ NOT Hispanic or Latino ◯ Unknown / Not Reported

Education

- ◯ < 8th Grade
- ◯ High School/GED
- ◯ 2 Yr. College
- ◯ 4 Yr. College
- ◯ Post Graduate

Comments

_____

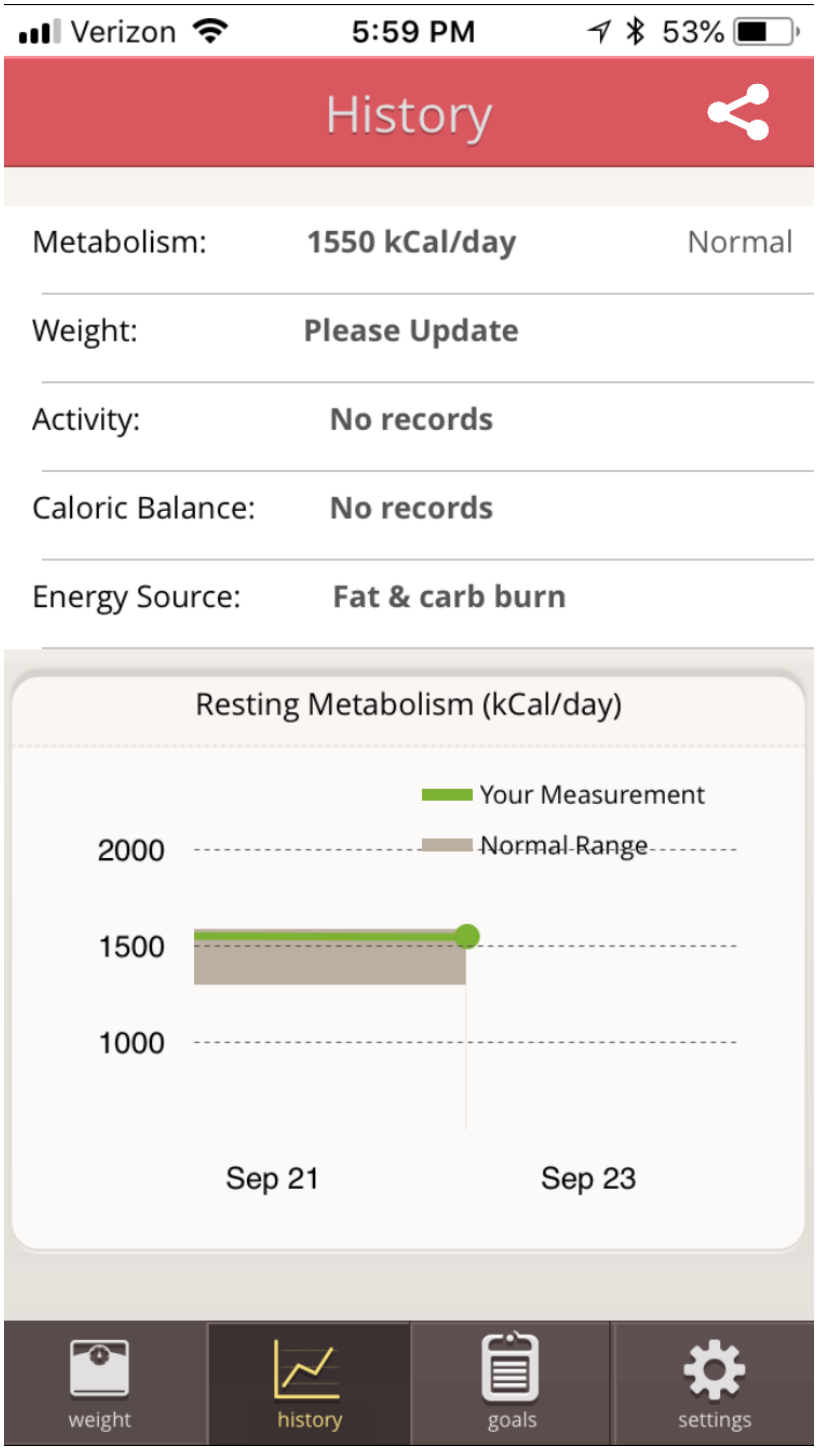
APPENDIX I

STUDY PARTICIPANT COMPENSATION TABLE

Table 1. Payment Schedule	
Time	Amount
Study Visit 1	$5
Study Visit 2	$20
Study Visit 3	$15
Study Visit 4	$30
Study Visit 5	$25
Study Visit 6	$30
Study Visit 7	$55

APPENDIX J

SCREENSHOT OF RESTING ENERGY EXPENDITURE DATA FROM THE BREEZING™ DEVICE MOBILE APP.


Verizon
5:59 PM
53%
History
Metabolism:
1550 kCal/day
Normal
Weight:
Please Update
Activity:
No records
Caloric Balance:
No records
Energy Source:
Fat & carb burn
Resting Metabolism (kCal/day)
Your Measurement
Normal Range
2000
1500
1000
Sep 21
Sep 23
weight
history
goals
settings

APPENDIX K

ACTIGRAPH WATCH INSTRUCTIONS

SLEEP WATCH INSTRUCTIONS AND CARE

As part of your sleep evaluation, you are being asked to wear a special watch. This watch can tell us about when you are asleep and when you are awake. Please wear the watch on the wrist that you *don't* write with (for example, if you are right-handed, wear the watch on your left wrist).

Here are some other important things for you to know:

The sleep watch is not a toy. Please be VERY CAREFUL with it!

- If you are going someplace where the watch might get lost or damaged, please leave the watch at home.
- Do not try and take the sleep watch apart, this will ruin it and we won't be able to use it again.
- These watches cost a lot of money to replace (more than if you bought two Apple iPads), so again, please be careful!

The sleep watch is water resistant, but *not* water proof

- This means that it is okay if the watch gets wet, but if you are showering, bathing, or swimming, you should take off the watch (but don't forget to put it back on afterwards!).

There are two buttons on the sleep watch (the *left* button and the *right* button)

- Pressing the *left* button turns on the watch light.
- The *right* button is the **EVENT MARKER**. You should press the event marker (*right* button) once at the following times:
    1. When you first try to fall asleep at bedtime (after you turn the light out)
    2. When you wake up during the night (if you wake up during the night)
    3. When you wake up in the morning to start your day
    4. When you try to nap (if you take a nap)

APPENDIX L

SLEEP DIARY WITH INSTRUCTIONS

Sleep Diary Instructions

General Instructions

What is a Sleep Diary? A sleep diary is designed to gather information about your daily sleep pattern.

How often and when do I fill out the sleep diary? It is necessary for you to complete your sleep diary every day. If possible, the sleep diary should be completed within one hour of getting out of bed in the morning.

What should I do if I miss a day? If you forget to fill in the diary or are unable to finish it, leave the diary blank for that day.

What if something unusual affects my sleep or how I feel in the daytime? If your sleep or daytime functioning is affected by some unusual event (such as an illness, or an emergency) you may make brief notes on your diary.

What do the words "bed" and "day" mean on the diary? This diary can be used for people who are awake or asleep at unusual times. In the sleep diary, the word "day" is the time when you choose or are required to be awake. The term "bed" means the place where you usually sleep.

Will answering these questions about my sleep keep me awake? This is not usually a problem. You should not worry about giving exact times, and you should not watch the clock. Just give your best estimate.

Item Instructions

Use the guide below to clarify what is being asked for each item of the Sleep Diary.

Date: Write the date of the morning you are filling out the diary.

1. What time did you get into bed? Write the time that you got into bed. This may not be the time that you began "trying" to fall asleep.

2. What time did you try to go to sleep? Record the time that you began "trying" to fall asleep.

3. How long did it take you to fall asleep? Beginning at the time you wrote in question 2, how long did it take you to fall asleep.

4. How many times did you wake up, not counting your final awakening? How many times did you wake up between the time you first fell asleep and your final awakening?

5. In total, how long did these awakenings last? What was the total time you were awake between the time you first fell asleep and your final awakening. For example, if you woke 3 times for 20 minutes, 35 minutes, and 15 minutes, add them all up (20+35+15= 70 min or 1 hr and 10 min).

6. What time was your final awakening? Record the last time you woke up in the morning.

7. What time did you get out of bed for the day? What time did you get out of bed with no further attempt at sleeping? This may be different from your final awakening time (e.g. you may have woken up at 6:35 a.m. but did not get out of bed to start your day until 7:20 a.m.)

8. How would you rate the quality of your sleep? "Sleep Quality" is your sense of whether your sleep was good or poor.

9. In total, how long did you nap or doze? Estimate the total amount of time you spent napping or dozing, in hours and minutes. For instance, if you napped twice, once for 30 minutes and once for 60 minutes, and dozed for 10 minutes, you would answer "1 hour 40 minutes." If you did not nap or doze, write "N/A" (not applicable).

10. Comments If you have anything that you would like to say that is relevant to your sleep feel free to write it here.

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing prospective sleep self-monitoring. *Sleep, 35*, 287-302.

Consensus Sleep Diary-Core   ID/Name:___________________

Today's date	Sample 4/5/11							
1. What time did you get into bed?	10:15 p.m							
2. What time did you try to go to sleep?	11:30 p.m							
3. How long did it take you to fall asleep?	55 min.							
4. How many times did you wake up, not counting your final awakening?	3 times							
5. In total, how long did these awakenings last?	1 hour 10 min.							
6. What time was your final awakening?	6:35 a.m.							
7. What time did you get out of bed for the day?	7:20 a.m							
8. How would you rate the quality of your sleep?	☐ Very poor ☒ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good
9. In total, how long did you nap or doze?	1 hour 30 min.							
10. Comments (if applicable)	I have a cold							

APPENDIX M

PITTSBURGH SLEEP QUALITY INDEX (PSQI)

Subject's Initials_____ID#_____Date_____Time_____AM PM

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?

   BED TIME _____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

   NUMBER OF MINUTES _____

3. During the past month, what time have you usually gotten up in the morning?

   GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

   HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

f) Feel too cold

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

g) Feel too hot

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

h) Had bad dreams

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

i) Have pain

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

j) Other reason(s), please describe_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good _____

Fairly good _____

Fairly bad _____

Very bad _____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____

_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: Psychiatry Research, 28:193-213, 1989.

APPENDIX N

BERLIN QUESTIONNAIRE

BERLIN QUESTIONNAIRE

Height (m) _____ Weight (kg)_____ Age_____ Male / Female

Please choose the correct response to each question.

CATEGORY 1

1. **Do you snore?**
   - ☐ a. Yes
   - ☐ b. No
   - ☐ c. Don't know

If you snore:

2. **Your snoring is:**
   - ☐ a. Slightly louder than breathing
   - ☐ b. As loud as talking
   - ☐ c. Louder than talking
   - ☐ d. Very loud – can be heard in adjacent rooms

3. **How often do you snore**
   - ☐ a. Nearly every day
   - ☐ b. 3-4 times a week
   - ☐ c. 1-2 times a week
   - ☐ d. 1-2 times a month
   - ☐ e. Never or nearly never

4. **Has your snoring ever bothered other people?**
   - ☐ a. Yes
   - ☐ b. No
   - ☐ c. Don't Know

5. **Has anyone noticed that you quit breathing during your sleep?**
   - ☐ a. Nearly every day
   - ☐ b. 3-4 times a week
   - ☐ c. 1-2 times a week
   - ☐ d. 1-2 times a month
   - ☐ e. Never or nearly never

CATEGORY 2

6. **How often do you feel tired or fatigued after your sleep?**
   - ☐ a. Nearly every day
   - ☐ b. 3-4 times a week
   - ☐ c. 1-2 times a week
   - ☐ d. 1-2 times a month
   - ☐ e. Never or nearly never

7. **During your waking time, do you feel tired, fatigued or not up to par?**
   - ☐ a. Nearly every day
   - ☐ b. 3-4 times a week
   - ☐ c. 1-2 times a week
   - ☐ d. 1-2 times a month
   - ☐ e. Never or nearly never

8. **Have you ever nodded off or fallen asleep while driving a vehicle?**
   - ☐ a. Yes
   - ☐ b. No

If yes:

9. **How often does this occur?**
   - ☐ a. Nearly every day
   - ☐ b. 3-4 times a week
   - ☐ c. 1-2 times a week
   - ☐ d. 1-2 times a month
   - ☐ e. Never or nearly never

CATEGORY 3

10. **Do you have high blood pressure?**
    - ☐ Yes
    - ☐ No
    - ☐ Don't know

APPENDIX O

PITTSBURGH SLEEP SYMPTOM QUESTIONNAIRE – INSOMNIA (PSSQ-I)

PSSQ_I

ID ___ ___ ___ ___ ___ ___ Date ___ ___ / ___ ___ / ___ ___
m m d d y y

Instructions: Below is a list of common sleep complaints. **During the past month**, how many nights or days per week have you had, or been told you had, the following symptoms? If you have experienced any of these symptoms please indicate how long it has lasted in weeks, months or years.

During the past month . . .	**Never**	**Do not know**	**Rarely** less than once per week	**Sometimes** 1-2 times per week	**Frequently** 3-4 times per week	**Always** 5-7 times per week	**How long has the symptom lasted?** (# of weeks, months or years)
1. Difficulty falling asleep.	0	1	2	3	4	5	____ ☐ **wks** ☐ **mos** ☐ **yrs**
2. Difficulty staying asleep.	0	1	2	3	4	5	____ ☐ **wks** ☐ **mos** ☐ **yrs**
3. Frequent awakenings from sleep.	0	1	2	3	4	5	____ ☐ **wks** ☐ **mos** ☐ **yrs**
4. Feeling that your sleep is not sound.	0	1	2	3	4	5	____ ☐ **wks** ☐ **mos** ☐ **yrs**
5. Feeling that your sleep is unrefreshing.	0	1	2	3	4	5	____ ☐ **wks** ☐ **mos** ☐ **yrs**

If you checked "never" or "do not know" for **all of these symptoms** YOU MAY STOP.

If you checked "rarely" to "always" for **any of these symptoms** please continue with questions 6-13.

PSSQ_I

ID ___ ___ ___ ___ ___ ___

Date ___ ___ / ___ ___ / ___ ___
m m d d y y

Instructions: If you have experienced **any** sleep symptoms **during the past month** please circle the appropriate number to let us know how your sleep is affecting your daily life.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
6. How much do your sleep problems bother you?	0	1	2	3	4
7. Have your sleep difficulties affected your work?	0	1	2	3	4
8. Have your sleep difficulties affected your social life?	0	1	2	3	4
9. Have your sleep difficulties affected other important parts of your life?	0	1	2	3	4
10. Have your sleep difficulties made you feel irritable?	0	1	2	3	4
11. Have your sleep problems caused you to have trouble concentrating?	0	1	2	3	4
12. Have your sleep difficulties made you feel fatigued?	0	1	2	3	4
13. How sleepy do you feel during the day?	0	1	2	3	4

 Developed by Okun,M.L., Kravitz,H.M., Sowers,M.F., Moul,D.E., Buysse,D.J., and Hall,M. of the University of Pittsburgh using National Institute of Mental Health Funding.

APPENDIX P

ANTHROPOMETRICS REDCAP FORM

Height and Weight Data

Study ID	_____
Height (cm)	_____
Weight (kilograms)	_____
BMI	_____

APPENDIX Q

ADVERSE EVENT ASSESSMENT FORM

Adverse Event Assessment

Study ID _____

Did the study participant indicate that they had an adverse event since the last study visit?
- ○ Yes
- ○ No

Date Reported: _____

Adverse Event Description: _____

Start Date: _____

End Date: _____

Outcome
- ○ Fatal
- ○ Not recovered/not resolved
- ○ Recovered w/sequelae
- ○ Recovered w/o sequelae
- ○ Recovering/Recovered

Severity Grade
- ○ Mild
- ○ Moderate
- ○ Severe

AE Treatment
- ○ None
- ○ Medication treatment
- ○ Non-medication treatment
- ○ Hospitalization

Action taken with study participation
- ○ None
- ○ Interrupted
- ○ Discontinued
- ○ Not Applicable

Relatedness to study:
- ○ Definite
- ○ Probable
- ○ Possible
- ○ Unlikely
- ○ Unrelated

Reported to the IRB
- ○ Yes
- ○ No

Date reported to IRB: _____

PI Signature:

_____