Effects of Sleep-Extend on glucose metabolism in women with a history of gestational diabetes

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Principal Investigator:

Sirimon Reutrakul, MD., Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, University of Illinois at Chicago, Tel: 312-413-5357, Email: sreutrak@uic.edu

Co-Investigators:

Jennifer Duffecy, Ph.D., Department of Psychiatry, Laurie Quinn, Ph.D., Department of Biobehavioral Health Science, Pamela Martyn-Nemeth, Ph.D., Department of Biobehavioral Health Sciences,

Study Location(s): Clinical Research Center, University of Illinois at Chicago, 912 South Wood Street, 2nd floor, Room 200S

College of Nursing, 845 S. Damen Ave

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List of Abbreviations

COI	Conflict of Interest
DSMP	Data and Safety Monitoring Plan
GDM	Gestational Diabetes
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
OPRS	Office for the Protection of Research Subjects
PHI	Protected Health Information
PI	Principal Investigator
SMC	Safety monitoring committee

1.0 Project Summary/Abstract

Women with a history of gestational diabetes (GDM) are at high risk of developing diabetes in the future. Lifestyle intervention with diet and exercise have been shown to help reduce this risk. Sleep disturbances are emerging as risk factors for incident diabetes. Studies have shown that those sleeping <5-6 hours/day had 5-45% increase in the risk of diabetes. We have also shown that in women with a prior history of GDM, those reporting sleeping <6 hours/night had a significantly higher fasting glucose levels. In healthy volunteer who were short sleepers, sleep extension in a few studies have been shown to improve glucose metabolism. Therefore, in this study, we propose to test the effects of 6-week sleep extension, using technology-assisted sleep intervention, in women with a history of GDM and short sleep on glucose metabolism by randomized controlled study.

2.0 BACKGROUND/SCIENTIFIC RATIONALE

Gestational diabetes mellitus (GDM) affects 4-9% of pregnant women [1]. Women with a history of GDM are at a 7-fold higher risk of developing future type 2 diabetes compared to those with normoglycemia during pregnancy [2]. Public health impact of GDM is significant as it was estimated that 10-31% of parous women with type 2 diabetes had a prior history of GDM[3]. While risks of future diabetes include traditional factors such as obesity, physical inactivity and family history of diabetes, sleep is increasingly recognized as an independent risk factor [4]. Despite the findings that insufficient sleep in women with a prior history of GDM is common, and associated with impaired glucose metabolism, our present understanding of the effects of sleep extension on glucose metabolism and future diabetes risk in these women is very limited.

Insufficient sleep has been shown to increase diabetes risk by multiple pathways. Experimental sleep restriction resulted in increased insulin resistance without adequate compensatory increase in insulin secretion[5]. This is likely a result of changes in appetite regulating hormones promoting hunger and weight gain, alterations in inflammatory markers, changes in energy expenditure and abnormal adipocyte function [6].

The primary aim of this study is to evaluate the effects of a sleep extension intervention in women with a prior history of GDM and habitual short sleep duration on the outcomes of glucose metabolism. **This proposal is based on recent observations and newly developed sleep intervention from our group.** (1) Women with a prior history of GDM who reported sleeping ≤6h/night had significantly higher fasting glucose and glucose response following oral glucose tolerance test than those sleeping >6h/night [7]. (2) Half of the women with a prior history of GDM reported insufficient sleep ≤6h/night [7] (3) A pilot study of a 2-week behavioral sleep optimization in adults without

diabetes who had habitual short sleep duration led to improved fasting insulin resistance. (4) A pilot trial of our newly developed technology-assisted behavioral sleep optimization intervention in individuals with short sleep duration demonstrated a clinically significant sleep duration increase (median 35 minutes)**. Therefore, this proposal seeks to improve glucose metabolism in women with a prior history of GDM and habitual short sleep using sleep extension intervention under a randomized controlled design.**

Our novel technology-assisted sleep intervention was developed to leverage a rapidly increasing public interest in sleep tracking, especially wearable sleep tracker use by consumers (+500% in 3 years). Our technology employs four elements -- a wearable sleep tracker, didactic content, an interactive smartphone application and brief telephone counseling [8]. This study will randomize 60 non-diabetic women with a history GDM who report short sleep duration to an eight-week sleep extension intervention group or a healthy living information control group. We hypothesize that this sleep extension intervention will be feasible, acceptable and improve glucose metabolism.

3.0 Objectives/Aims

The specific aims are to determine:

Aim 1: Feasibility and acceptability of sleep extension intervention. Rationale: Analysis of recruitment, retention and participant program evaluation will provide feasibility and acceptability data. Hypothesis: Sleep extension intervention will be feasible and acceptable to the target population. Approach: Feasibility will be determined through analysis of recruitment and retention. Acceptability will be determined through participant evaluation.

Aim 2: Efficacy of sleep extension intervention on primary outcomes of glucose metabolism. Rationale: Short sleep duration was associated with abnormal glucose metabolism in women with previous GDM. Sleep optimization in short sleeping individuals without diabetes resulted in improved insulin resistance. Hypothesis: Sleep extension intervention will result in improved glycemic control. Approach: A randomized controlled trial of an 8-week sleep extension intervention compared to a healthy living information control group on glucose metabolism as measured by an oral glucose tolerance test and A1C at baseline and at the end of intervention.

Aim 3: Efficacy of sleep extension intervention on secondary outcomes of weight, appetite regulating hormones, energy expenditure, inflammatory markers, depressive symptoms and subjective sleep quality.

4.0 Eligibility

We will recruit 60 subjects for this study

4.1 Inclusion Criteria

- Premenopausal women, age 18-45, with a history of GDM who currently do not have diabetes
- At least one year post-partum
- Reported habitual sleep duration <7h/night during work- or weekdays with a desire to sleep longer
- Reported time spent in bed ≤8 h
- Own a smartphone compatible with Fitbit.
- No need to provide care at night for her child(ren), defined as >3 times per week and > 30 minutes at a time
- No history of obstructive sleep apnea, insomnia, or restless leg syndrome
- No use of sleeping medications or sleep aids

4.2 Exclusion Criteria

- A1C ≥6.5%
- Currently pregnant or planning pregnancy or breast feeding
- Insomnia symptoms defined as severe as assessed by the Insomnia Severity Index (score ≥15)
- Rotating shift or night shift work
- High risk for obstructive sleep apnea screened by STOP BANG questionnaire.
- Significant medical morbidities, such as congestive heart failure, cirrhosis, chronic obstructive pulmonary disease requiring oxygen, active treatment for cancer or psychiatric problem, history of stroke with neurological deficits, cognitive impairment, kidney failure requiring dialysis, illicit drug use.

Eligibility determination and source of subjects

- Subjects will come from those receiving care at UIHealth and those responding to advertising materials (please see subject enrollment in the following section 5)
- Inclusion/exclusion criteria will be obtained by participant self-report on all criteria except A1C and urine pregnancy test which will be obtained by a blood and urine test. For those with medical records at UIC (please see subject enrollment in the following section 5), medical record review will be performed by study personnel.
- Study personnel will assess subjects for eligibility by study inclusion and exclusion criteria. Those ineligible will not be pursued. A password protected file will be maintained of subjects approached but not interested, and those who expressed interest but did not meet inclusion/exclusion criteria.

4.3 Excluded or Vulnerable Populations

- Non-English speaking subjects- unable to participate in questionnaires

5.0 Subject Enrollment

- *Describe screening and enrollment.*
- *Describe from where subjects will be recruited and any advertising or recruitment materials that will be used.*
- *Describe what happens with screen failures and any data obtained from screen failures.*
- *Describe the methods to minimize coercion and undue influence on the subjects.*
- *Describe the procedures to separate clinical responsibilities and influence from research responsibilities and influence.*

We will employ the following recruitment/enrollment methods:

1. Passive Advertising: We will distribute study advertisement materials throughout UI Health and local health centers, including clinical environments. Emails through UIC email system will beused. Individuals will call research assistants (RAs) or principal investigator (PI) or co-PIs for eligibility assessment by phone.
2. Active Recruitment in Clinical Sites within UIHealth: On-site RAs will receive additional referrals directly from staff or patients interested in the study. In these situations, PI, co-PIs or RAs will discuss the study and assess eligibility in a private exam room within the clinic before or after a clinical encounter. Additionally, we will work with Mile Square Health Centers to screen the appointment list of patients visiting the clinics. Potential eligible subjects will be identified by EMR and PI/RAs will discuss the study at the visit as described.
3. Active Recruitment from Registries: The research assistants will work from a CCTS-approved list of patients with previous GDM, identified from the electronic medical record. A list of UIC patients with a history of gestational diabetes or abnormal 3-hour oral glucose tolerant test in the past 10 years will be obtained from CCTS. In addition, CCTS will retrieve a list of patients with a diagnosis of gestational diabetes from July 2018 onwards throughout the duration of this protocol. This is essential to identify potential subjects and without this information, the research will be very difficult to conduct. The information from CCTS will include diagnoses, laboratory report (of glucose values and HbA1c), name, age, medical record numbers, address and phone numbers. Medical records will then be reviewed to ensure eligibility. We will send letters informing patients that they may be eligible for the study and may opt-out of further contact. After one week of mailing the letters, those who do not opt out will be contacted by the RAs to assess interest and eligibility. In addition, if the potentially eligible subjects have an appointment at UIC clinics, a research assistant will go and meet with the subjects either before or after the appointments and ask if they may be interested in hearing more about the study using the approved script. If the subjects express interest but do not have time, a flyer will be given to them if

they would like. If they would like to be contacted at a later time, an arrangement will be done with the RA.

4. Online Recruitment: will be done through *https://www.researchmatch.org/*. Potential subjects will contact investigators via email or telephone, after which eligibility will be determined as above.

Screening

- Upon a contact with subjects believed to be eligible, PI, co-PI or RA will inquire about potential interest in study participation following the IRB approved recruitment script. They will be screened verbally for inclusion/exclusion criteria utilizing an IRB approved script (see Eligibility check list and Recruitment script). If the subject is eligible and interested, study personnel will review the study in detail, using an IRB approved consent form as guidance, plan for informed consent form (ICF) signing and study participation dates if appropriate.
- It will be made clear on initial contact that participation is entirely voluntary and that acceptance or decline will not impact the care they receive at UIHHSS.
- A password protected file will be maintained of subjects approached but not interested, and those who expressed interest but did not meet inclusion/exclusion criteria.

6.0 Study Design and Procedures

Additional screening for eligibility

- After informed consent is obtained, the participants will undergo additional screening including A1C and urine pregnancy test. These will be done with spot urine samples and finger stick or blood tests. If the A1C test from the finger stick is abnormal (≥ 6.5%), blood test (5 ml) will be done to confirm eligibility.

Study protocol

1. Baseline assessment:

- One week of actigraphy will be recorded using an actiwatch spectrum. If during this assessment it is found that their sleep duration is ≥ 7 hours during the weekdays or work days, they will not be able to participate further.
- Subjects will answer sleep, physical activity,depression questionnaires, quality of life, anxiety symptoms and perceived stress symptoms.
- Weight, height, waist and hip circumference, and neck circumference will be obtained
- Eating behaviors, appetite and 24 hour food recall will be obtained through questionnaires.
- .
- At the end of one week, they will return to have a 75-gram oral glucose tolerance test (OGTT) done at the clinical research center (see below procedure).

- Blood will be assayed for A1C, serum creatinine, lipid panel and CBC.
- Blood will be saved for assay for genetic analysis, appetite regulating hormones (leptin, ghrelin, PYY, 2-arachidonoylglycerol (2-AG)), and inflammatory markers (CRP, IL-1, IL-6), and metabolomics profiles.
- Stool sample will be collected for stool microbiome assay
- Resting metabolic rate will be performed
- Additional serum samples will be stored for future analysis

2. The subjects will then be randomized to healthy living control group or sleep extension group for 6 weeks (see blow detail).

3. At week 6, they will be given an actiwatch to wear for one week. At week 7, the following procedures will take place
- They will return to the CRC to have a repeated 75-gram OGTT done.
- Weight will be obtained
- Subjects will answer sleep, depression questionnaires, quality of life, anxiety symptoms and perceived stress symptoms.
- Eating behaviors, appetite and 24 hour food recall will be obtained through questionnaires.
- Blood will be assayed for A1C, lipid panel.
- Blood will be saved for later assay for appetite regulating hormones (leptin, ghrelin, PYY, 2-arachidonoylglycerol (2-AG)), and inflammatory markers (CRP, IL-1, IL-6) and metabolomics profiles.
- Stool sample will be collected for stool microbiome assay
- Resting metabolic rate will be performed
- Additional serum samples will be stored for future analysis
- Participant evaluation of the program will be obtained through questionnaires and interview.

4. At week 10, subject will be given an actiwatch for one week. And,
- - They will return to the CRC to have fasting glucose and insulin level done.
- Weight will be obtained
- Subjects will answer sleep, depression questionnaires, quality of life, anxiety symptoms and perceived stress symptoms.
- Blood will be saved for later assay for appetite regulating hormones (leptin, ghrelin, PYY, 2-arachidonoylglycerol (2-AG)), and inflammatory markers (CRP, IL-1, IL-6) and metabolomics profiles.

Study procedures: are detailed as follow

1. Questionnaires: Participants will complete standardized questionnaires. The Pittsburgh Sleep Quality Index (PSQI) assesses sleep quality in the past month,[9] Epworth Sleepiness Scale (ESS) assesses daytime sleepiness,[10], PROMIS Sleep questionnaire, Insomnia Severity Index (ISI) assesses insomnia symptoms,[11] the STOP BANG questionnaire assesses risk of obstructive sleep apnea,[12,13] the Center for Epidemiological Studies Depression (CESD) assess depressive symptoms [14], quality of life[15], anxiety symptoms (GAD-7)[16], perceived stress scale[17], PROMIS fatigue scale.

Three factor eating questionnaires and Internal Physical Activity Questionnaires (IPAQ) will also be collected. ISI and STOP BANG will be used to screen for eligible participants. PROMIS, PSQI, ESS, Eating questionnaire, IPAQ and CESD will be given at baseline and at the end of the protocol.

2. Wrist actigraphy to measure behavioral sleep Participants will wear an Actiwatch Spectrum Plus (Respironics, USA) on their non-dominant wrist for one week during baseline assessment, and at week 6 and week 10. Data will be collected in 30-sec epochs. Subjects will be asked to keep a daily sleep log and press an event marker on the Actiwatch at bedtime and wake-up time. Data will be downloaded and reviewed with each participant to clarify inconsistencies when the Actiwatch is returned. Rest intervals will be set using reported try-to-fall-asleep times and wake-up times on daily sleep logs or event markers if these times are missing. Using the Immobile Minutes algorithm in the Actiware 6 software, we will derive the following outcome variables: sleep onset, sleep offset, sleep duration, sleep efficiency (a measure of sleep quality), mid-sleep time (time point between sleep onset and wake time), and standard deviation (SD) of sleep duration, an indicator of sleep regularity which we previously showed to be related to glucose metabolism.[18]

3. Oral Glucose Tolerance Test (OGTT). After an overnight fast, the subject will arrive at the CRC between 8-9 am. Blood samples will be obtained at 0 minutes for glucose and insulin. Then 75 grams glucose solution will be given orally. Blood samples will be obtained at 30, 60, 90, 120 minutes for glucose and insulin. Extra blood samples will also be obtained at 0 minutes and stored for further analysis. **Total blood volume 60 ml per one OGTT visit.**

4. Blood samples will be obtained for lipid panel, creatinine and A1C at baseline and at week 6. CBC will be obtained at baseline. Fasting glucose and insulin will be obtained at week 10. Blood will be saved for later assay for genetic analysis, appetite regulating hormones (leptin, ghrelin, PYY, 2-arachidonoylglycerol (2-AG)), and inflammatory markers (CRP, IL-1, IL-6) and metabolomics profiles. **Total blood sample 20 ml at each visit.**

5. Microbiome Stool samples to measure the gut microbiome will be collected at week 0 and week 6. Changes in sleep may alter the gut microbiome and potentially influence glycemia. Participants will be provided a collection device (Easysampler®, ALPCO, Inc.) and return the specimen at a subsequent visit. Remaining stool samples will be stored in a freezer at the College of Medicine for later analysis by UIC researchers.

6. Resting energy expenditure: Oxygen consumption will be measured through indirect calorimetry using the Vyntus CPX system metabolic cart (Vyaire Medical, Mettawa, IL). In this test, a canopy hood is placed over the subject's head as he/she reclines in bed. One end of the canopy has tubing connected to the metabolic cart, while the other end of the canopy is open to room air. During the 30-40 minute procedure, expired gases are measured and resting energy expenditure is calculated using the Harris-Benedict equations. This will be performed during fasting.

7. Feasibility and acceptability of Sleep extension: Feasibility will be determined through analysis of recruitment (number recruited, screened, eligible, and consented) and retention (% session participation, program completion rates). Acceptability will be determined through participant evaluation (written evaluation and interview at program completion). See Appendix B.

8. Intervention Description: Sleep Extension The goal of sleep extension is to increase sleep time by ≥ 30 minutes. Participants randomized to the intervention will receive: (1) a wearable sleep tracker; (2) a smartphone application with interactive feedback and tools; (3) didactic content including weekly email lessons, reminders, and notifications; and (4) brief telephone coaching. The components are described below.

8.1 Wearable sleep tracker: A Fitbit Alta HR wearable sleep tracker allows participants to track their sleep and share results with the coach, not for the main study outcome (measured with actigraphy). Consumer sleep trackers provide an estimation of sleep but are less precise than actigraphy devices.[19,20] Therefore, our main outcome will be measured with actigraphy, which is validated but does not provide real-time feedback to the wearer.[21] Fitbit data will be used in coaching sessions and for providing weekly reports. The coach will have access to participants' sleep tracker data through a dashboard using the Fitabase platform.

8.2 Smartphone application: Participants will download the Fitbit smartphone application on their smartphone and participate in brief training in the intervention orientation session. Participants will be trained to review and edit their Fitbit sleep log each day, increasing the data validity. Though the application has the ability to enter sleep goals, these features will not be set on participants' applications.

8.3 Intervention content: Participants will receive automated content, including didactic lessons (weekly), individualized progress reports (weekly), and bedtime reminder text messages (30 min before scheduled bedtime; can be disabled for Weeks 4-6). The intervention content was developed by psychologists with advanced training in sleep and behavior change (Dr. Duffecy and Dr. Baron) and has been piloted in initial user testing. The 6 weekly didactic lessons (estimated duration 8-10 min), of written and video didactic content will be delivered via email and can be viewed on a smartphone, desktop, or tablet. Content from the lessons will be reinforced in the telephone coaching sessions (see Appendix A). Participants will receive an automatically generated report each week detailing their days of device usage, average bedtime, wake time, sleep duration, and an encouraging statement linked to weekly didactic content. They will be asked to fill the visual analog scale for hunger one day per week (once in the morning before breakfast and once before bedtime).

8.4 Coaching: All participants will be assigned to a sleep coach to monitor their progress during the study and provide weekly telephone coaching sessions related to their sleep-related goals*. Drs. Duffecy and Dr. Baron will act as coaches for this pilot.* The coaching protocol, developed by Dr. Duffecy, is based on the principles of Supportive Accountability.[22] The coach will establish **legitimacy** by their knowledge of

sleep and basic counseling principles. They will establish **goals** with the participants based on the participants' values and beliefs, including sleep-related goals and usage goals (e.g., number of days wearing the sleep tracker). **Performance monitoring** will be completed through an online dashboard visible to the coach (Fitabase Inc.). The dashboard will contain data from sleep diaries and the wearable sleep tracker. The first coaching session will be a 20-min engagement session, which includes introductions, rationale for the program, roles of the coach, and the participants' goals for the program. Coach will provide feedback to the participant based on wearable sleep tracker data. For coaching sessions 2-8, the coach and participant will also have weekly brief (5-10 min) follow-up support calls to review progress, problem solve barriers to progress, and set goals for the following week. Between sessions, coach will be available to troubleshoot any problems. The use of coaching has been demonstrated to improve adherence to technology-based interventions.[23,24] Drs. Duffecy and Dr. Baron have extensive experience in the use of coaching to improve adherence to technology-based interventions.[23,25-27]

8.5 Hunger rating based on visual analog scale (0-100) will be given to the subjects to fill one day per week, in the morning before breakfast and before bedtime.

9. Attention control: Health Education. Use of a control group is to control for the coach contact in the intervention group. Participants assigned to the control group will be provided weekly health education emails (e.g., nutrition, stretching exercises; Appendix A). They will be instructed to maintain their sleep schedule but not monitored with diaries or coaching, a technique that produces little change in sleep timing.[28] Participants will receive weekly brief telephone contact from the coach (≤ 5 min) to answer questions. They will be asked to fill the visual analog scale for hunger one day per week (once in the morning before breakfast and once before bedtime).After the final follow-up, control participants will receive a Fitbit fitness tracker and PDF files of the 6 didactic lessons by mail.

All procedures in the protocol are research related. The research will take place at the College of Nursing, 845 S. Damen or at the Clinical Research Center.

<u>Specimen collection</u>

The following describes specimen collection, processing, storage and assays.

- Blood collected will be labeled with coded ID only (containing no identifying information). Blood will be immediately processed to obtain plasma and will be stored. EDTA-preserved blood will be stored for future genetic analysis. (see below)

- Urine sample will be obtained for pregnancy testing during screening.

- CBC, serum creatinine, glucose and lipids will be assayed by Quest Diagnostics, with only coded ID. HbA1c will be assayed either by Quest Diagnostics or point-of-care testing.

- Stool specimen will be labeled with coded ID only (containing no identifying information) and stored for microbiota assay (see below).

- Blood, and stool samples will be stored at at -80ºC in the lab of Dr. Brian Layden (835 South Wolcott Avenue, MC 640 Chicago, IL 60612). Serum insulin, appetite regulating hormones and inflammatory markers will be assayed using commercially available kits. Stool microbiota and serum metabolomics will be assayed at a later time using standard protocol and procedures of the collaborators. EDT containing blood will be saved for genetic analysis. Samples will be stored for future research or until 15 years has passed. Samples will then be destroyed according to institutional policy.

Protocol Overview

	Urine preg test Screening questionnaire	A1C	OGTT, and blood samples	Questionnaires, actigraphy (1 week)	Stool sample	Energy expenditure	Acceptability assessment
Screening	X	X					
Week 0-1		X	X	X	x	x	
RANDOMIZATION							
Week 6-7		X	X	X	x	x	X
Week 10			Fasting glucose and insulin	X			

7.0 Expected Risks/Benefits

Potential Risks

The potential risks to subjects include:

1. Bleeding, irritation, discomfort, or infection at the finger prick site (for A1C) and blood draw. The risk for these problems is very minor and is minimized by following standardized procedures using trained study personnel.
2. Loss of confidentiality. Standard procedures will be used to avoid breaches in confidentiality. We expect this risk to be low.
3. Completing self-report measures on sleep and mood may cause subjects some emotional distress.
4. Actiwatch may cause minor irritation but this is a rare event.
5. Risks associated with the intervention may include irritation due to wearing the Fitbit devices. No other risks are currently identified.
6. The intervention intends to increase sleep duration but it may or may not be able to do so. Since sleep is linked to glucose, it is possible that the glucose levels could worsen if the intervention could not increase sleep. However, this is expected to be minimal, if at all. The precaution is taken as subjects with diabetes are not eligible to participate.

7. Privacy and confidentiality: Despite best efforts, medical record collection could be compromised leading to a loss of privacy regarding confidential health information. To minimize this risk, no patient identifying information will be recorded in any research documents that are created. Indirect identifiers will be used to link data obtained from different methods. The key will be stored separately from the data and will be destroyed after data collection has been completed.

Protections Against Risk

Methods to minimize risk include:

1. Minimization of bleeding, irritation, discomfort, or infection at the blood draw site. The risk for these problems is very minor and is minimized by following standardized procedures. Blood draws will be done using sterile technique and standardized procedures. These will be performed by trained personnel.
2. Completing self-report measures on sleep and depressive mood may cause subjects some emotional distress. The risk is minimal. In our previous studies with the same population, no subjects reported emotional distress with these measures. However, study staff will be aware of the possibility and address any concerns that are voiced.
3. Actiwatch could cause minor irritation, however, this is rare. Should this happen, the subjects can choose to discontinue the study at anytime.
4. Drinking glucose solution may be unpleasant for some subjects. However, this solution is used in standard medical care to screen for diabetes. The subjects can discontinue their participation if deemed intolerable.
5. Should a subject require medical or other professional intervention due to an adverse event or illness, treatment may be obtained through the UIC Medical Center, the subject's regular doctor, or the treatment center or clinic of their choice. Subjects will be provided contact information for the PI should they want to talk to her about their illness or injury.
6. To prevent coercive contact from the application and coach, all email outreach is pre-scripted and user contact information is never revealed. Outreach emails will state that the coach has noticed they have not completed sleep diaries or worn the Fitbit in a few days and ask if they would like troubleshooting help or to return to the program. It will not include any coercive language or pressure. Email communication will be limited to pre-scripted content reminders and participant outreach.
7. Participants will be informed that they may discontinue the intervention at any time. In the event that an adverse event is experienced participants will be instructed to contact Dr. Reutrakul or Dr. Duffecy. Phone numbers will be provided through which one of the investigators can be reached 7 days/week, 24 hours/day.
8. If during the protocol, the A1C is found to be >6.5% but less than 7%, the participants will be kept in the study but informed of the test results at the end of the protocol. If A1C is >7%, the will be discontinued from the study as this will require medical treatment from their primary care physician.

Potential Benefits of the Proposed Research to Human Subjects and Others

There may be no direct benefits to participating in the study. However, subjects in the intervention group may increase sleep duration and experience increased glucose control. The potential to future participants is that this study may advance the knowledge of sleep interventions to extend sleep duration and improve glucose control. The possible risks are no greater than those experienced in normal day-to-day life.

Importance of Knowledge to be Gained.

The risks to the study participants are minimal and no more than those encountered in daily life. Knowledge gained from this study may provide an important intervention for improving sleep and glycemic control in the future in women with previous GDM. If effective, this intervention has important clinical implications for improving glycemic control and improving quality of life in this population. This intervention is scalable and could have public health impact.

8.0 Data Collection and Management Procedures

Loss of confidentiality. Strict procedures will be put into place to minimize the risk of breach of confidentiality. All study staff will be trained on methods of maintaining subject confidentiality. Subjects will be assigned a unique code number. A master list that links the subject identity to the data will be kept by the principal investigator (PI) and stored in a locked office separately from the data. **Data storage**: All data will be stored and analyzed by code number. This consists of coded questionnaires, blood draw results, actigraphy. The coded data will be entered into a password-protected computer with a secure server for analysis, REDCap. Hard copy (paper copy) data (blood draw results) will be stored in a locked office. No identifiers (except subject ID) will be included. Only members of the research team will be able to access these data. **Procedures during data collection:** Privacy will be provided during recruitment by screening potential subjects in a private setting. The screening data that contain personal identifiers will be kept separate from the coded study data and stored in a locked office. All data collection and study procedures will take place in a private location. All data collected via the intervention (e.g. internet intervention materials, data entry, etc.) will be transmitted using Transport Layer Security (TLS) encryption to prevent eavesdropping and tampering information while it is in the transmission pipeline. To prevent unauthorized access to internet sites, they will be password protected.

Signed original informed consent documents and paper questionnaires will be stored in a locked cabinet in a locked room in the Division of Endocrinology and accessible only to the study PI. Access to the data will be determined by the PI and include study personnel at the level appropriate to complete their role in the study.

Samples will be stored as above described in Dr. Layden's lab at -80degC. This lab is accessible only to approved endocrinology personnel with locked door access only.

Records (including the ICFs) will be maintained for at least 15 years following study completion.

9.0 Data Analysis

- The data will be analyzed by the PI and team. Statistical assistance will be obtained from CCTS if needed.

10.0 Quality Control and Quality Assurance

Actiwatch data will be analyzed by a software provided by the manufacturer. Fitbit data will be automatically analyzed by the software of the manufacturer.

Data collected through the EMR will be obtained by study personnel and should a question of result validity be raised, the study PI will adjudicate entry or omission.

Dr. Reutrakul and Dr. Duffecy will monitor the research and evaluate the data quality.

11.0 Data and Safety Monitoring

- *Addresses how problems/side effects will be identified and handled.*
- *For studies that are minimal risk, describe how potential problems will be monitored and handled (e.g., breaches of confidentiality, emotional upset).*
- *For research involving more than minimal risk to subjects, describe:*
  - *Who will monitor adverse events (AEs) and unanticipated problems (UPs) involving risks to subjects or others and when events will be assessed.*
  - *How AEs or UPs will be recorded and communicated amongst research team members and who is responsible for making the reports.*
  - *The composition of the Data and Safety Monitoring Board (DSMB) and how frequently the DSMB meets, if one has been formed for the study.*
  - *Identify how often AEs and UPs will be monitored and what events will be reported to the sponsor and/or the IRB.*
  - *Describe stopping rules for the study.*
  - *Describe what occurs if a subject withdraws prematurely.*

Data Safety Monitoring Plan
CO PIs: Sirimon Reutrakul, Jennifer Duffecy, Pamela Martyn-Nemeth

The risk associated with this study is minimal for the interventions and data collection methods employed by the study. The potential for a serious adverse event is very low. Dr. Reutrakul will be the primary monitor, and a Safety Monitoring Committee will share the responsibility of monitoring the data.

The individuals responsible for data safety and monitoring will be Dr. Sirimon Reutrakul, Dr. Laurie Quinn, Dr. Pamela Martyn-Nemeth and Dr. Jennifer Duffecy, and a Study Monitoring Committee (SMC). A SMC will be appointed to provide oversight and monitoring of our data on an annual basis by individuals not directly associated with the study. The SMC will consist of: (1) Cynthia Fritschi , PhD, RN, Assistant Professor, Department of Biobehavioral Health Science, College of Nursing; (2) Elena Barengolts, MD, Professor of Medicine, Department of Medicine, Endocrinology, Diabetes and Metabolism; and (3) Mary Kapella, PhD, RN, Assistant Professor, Department of Biobehavioral Health Science, College of Nursing; —all at UIC. Drs. Fritschi, Dr. Barengolts and Dr. Kapella have expertise in reviewing the scientific design, conduct of study, intervention fidelity, evaluation of safety and risks to subjects, interpretation of data, and making recommendations concerning continuation, modification, suspension, or termination of the study.
Dr. Sirimon Reutrakul, Dr. Laurie Quinn, Dr. Pamela Martyn-Nemeth and Dr. Jennifer Duffecy, will meet with the SMC annually and provide a written and verbal progress report. The report will include a summary of cumulative recruitment, randomization, cumulative retention and attrition rate, study group demographics, adverse events, and data completeness and quality. The SMC will provide oversight of the study, as well as consider factors external to the study that may impact the safety of the participants or the ethics of the study. A written report of the meeting will be compiled that summarizes the review of data and outcomes, as well as any recommendations with respect to modification of the protocol.

Subjects feeling uncomfortable with the procedures can choose to terminate their participation at anytime. Should this occur, the PI will record the events and share the information with the investigators.

The subjects will be compensated $200 for completing the protocol, and they will be given a fit bit that is used during the protocol. If the baseline actigraphy revealed that their sleep duration is ≥7 hours during the work days or weekdays, they will receive $30 but not be able to participate further. The control subjects will receive fitbit as well.

Potential breaches of confidentiality are guarded against by the above measures (section 8.0). However should personal information be mistakenly disseminated, action will be taken to secure study data, and study procedures for data safety and security will be re-evaluated. If necessary, subjects and the IRB will be notified according to Institutional policy.

12.0 Statistical Considerations

- *If a study incorporates qualitative rather than quantitative methods, indicate this and describe qualitative analysis and disregard the rest of this section.*

- Mean differences in glucose parameters between control and intervention groups will be analyzed using independent t-tests.

- Using a mean difference in fasting glucose values between women with a history of GDM who slept <6 hr vs ≥6 hr of 8 mg/dL, a total of 40 patients will have to be randomized to achieve power of 80% to detect a treatment difference at a two-sided 0.05 significance.

- For this pilot study, we will randomize at 2:1 sleep extension: control ratio.

13.0 Regulatory Requirements

13.1 Informed Consent

Potentially eligible interested subjects will be screened by study personnel for inclusion and exclusion criteria. Informed consent will be obtained by study personnel who have been appropriately trained. Study personnel will thoroughly review the ICF with subjects. Patients will be given adequate time to review ICF themselves and ask questions about protocol prior to signing. All involved study personnel will complete necessary ethics and IRB training to participate in research study administration. Signed original informed consent documents will be stored in a locked cabinet in a locked room in the Division of Endocrinology and will be accessible only to the study PI.

The waiver for recruitment purposes will be applied to facilitate identification of potential subjects. There will be only minimal risk in allowing access to patient's diagnosis only. Complete informed consent will take place once eligibility is confirmed

13.2 Subject Confidentiality

Confidentiality will be maintained by limiting access to only study personnel. Additionally, collected data will be stored by subject number rather than by name or medical record number, with the exception of one password protected file which will be able to link a given subject number to an individual patient. This file will be maintained in a password protected location on REDCap system. After study completion, the file linking de-identified subject number with identifiable patient name and medical record number will be maintained but access will be provided only to study PI.

13.3 Unanticipated Problems

Procedures for identifying, reviewing, and reporting adverse events and unanticipated problems to the IRB.

Throughout the study, Dr. Reutrakul will monitor the participants for adverse events (AEs). Dr. Reutrakul and study staff will review AEs individually in real time and in aggregate on a monthly basis and consult with co-investigators as needed. Dr. Reutrakul will review serious adverse events (SAEs) in real time. Dr. Reutrakul will ensure that all protocol deviations, AEs, and SAEs are reported to the UIC IRB according to applicable IRB requirements, and corrective actions will be taken as deemed necessary by the IRB. Events determined by the PI to be unanticipated problems that are SAEs involving risks to subjects or others will be reported by the PI to the UIC IRB per IRB policy or within 1 week. Unanticipated problems that are determined by the PI to be not serious will be reported per IRB policy or within 2 weeks.

All study staff will be informed by Dr. Reutrakul about AEs. If any protocol changes are needed, a modification request will be submitted to the UIC IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation, according to IRB policy.

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