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Feasibility Trial of a Lifestyle Intervention for Pregnant People with Gestational Diabetes

Feasibility Trial Protocol Version 1.3

Funded by: Clinical Research and Innovation Seed Program (CRISP)

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Institution: UConn Health, Obstetrics & Gynecology

Title:

Feasibility Trial of a Lifestyle Intervention for Pregnant People with Gestational Diabetes

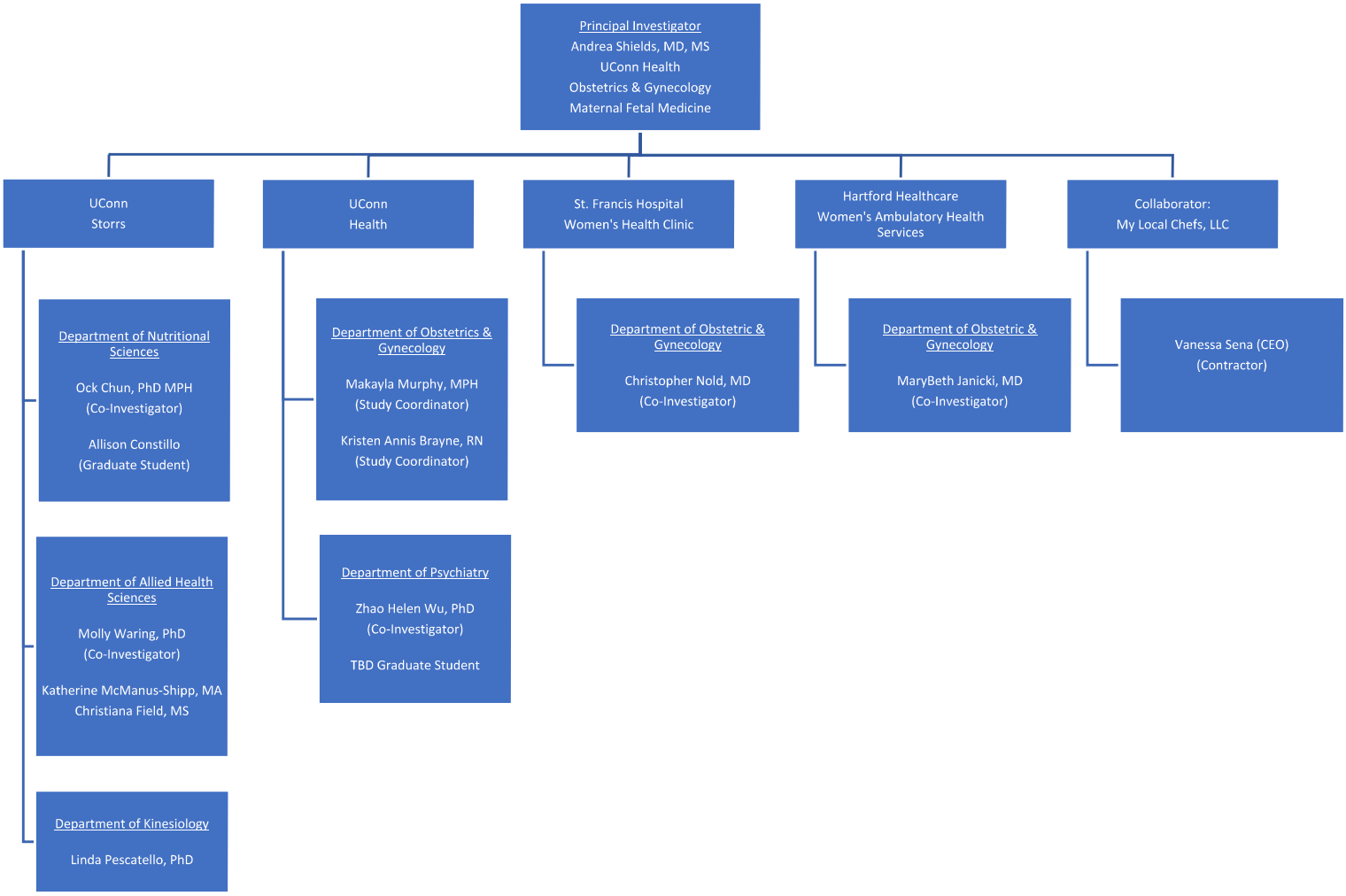
Summary/Background:

Gestational diabetes mellitus, or GDM, affects 2-10% of pregnancies in the United States (CDC)[1]. Approximately 50% of patients with GDM will progress to develop Type 2 diabetes in their lifetime[1]. Patients must have immediate access to nutrient-rich food and ongoing education and support regarding healthy meal preparation. GDM, therefore, is a perfect window of opportunity for prevention of diabetes. The opportunity provided by a diagnosis of GDM can be utilized only if optimal medical and obstetric care and sustainable educational interventions are provided to patients who are pregnant with GDM.

The socioeconomic impact of GDM is significant. Dietary non-compliance and poor reliability of glucose monitoring increase adverse pregnancy outcomes[2,3]. Compared with pregnancies without GDM, women with GDM are more likely to have pregnancy complications, including antepartum hospitalization, cesarean delivery (50.3% vs 35.3%), and a longer length of stay during antepartum or delivery admissions[3-6]. Infants of mothers with GDM are more likely to suffer several adverse neonatal outcomes, including metabolic and hematologic disorders, respiratory distress, cardiac disorders, and neurologic impairment due to perinatal asphyxia and birth traumas, and higher rates of admission to the neonatal intensive care unit[7].

Optimal outcomes in patients who are pregnant with GDM require education and adoption of an ADA-specific diet, daily glucose monitoring and physical activity, and compliance with prenatal visits[3-6]. To improve pregnancy outcomes, patients must understand and adopt these interventions on a significantly accelerated pathway compared with patients who are not pregnant as, on average, patients with GDM will have 8 to 10 weeks before they deliver. Thus, to achieve these goals quickly, patients must have immediate access to nutrient-rich food and on-going education and support regarding healthy meal preparation, including portion sizes, frequency, and composition of healthy snacking. There are ongoing studies on subsidized healthy food prescription programs to assess meaningful changes in average blood glucose levels and other clinically relevant outcomes in type 2 diabetes[8], however similar trials have yet to be performed in patients with GDM.

Most previous exercise interventions for blood glucose control in patients who are pregnant with GDM have included supervised exercise sessions and thus are difficult to translate to the health care system[9-12]. Lifestyle interventions that promote self-efficacy with unsupervised exercise and evidence-based behavioral strategies (e.g., goal setting, monitoring, and feedback) and incorporate the use of physical activity tracking devices to support these strategies are needed.[13]



Aims and Objectives:

This study will assess the feasibility of a community-based lifestyle intervention called Meals for Mom (M4M) for pregnant persons diagnosed with gestational diabetes (GDM). In previous work, we developed the intervention and received feedback from women living with gestational diabetes via focus groups (UCONN IRB # 23-190SSF-2.

The Specific Aim of this project is to conduct a pilot feasibility randomized clinical trial of Meals for Moms (M4M) program in patients diagnosed with gestational diabetes. Feasibility outcomes include recruitment, retention, intervention receipt, and program acceptability. We will also measure and describe clinical

Gender: Any gender identity

Ethnicity: Any

Inclusion Criteria:

- 18-49 years old
- Current singleton pregnancy
- GDM diagnosis between 24+0 and 31+6 weeks gestation, and no more than 4weeks from time of diagnosis at time of enrollment.
- Currently receiving gestational diabetes management at the UConn Health Maternal Fetal Clinic, St. Francis Hospital Women's Health clinic, Hartford Healthcare Women's Ambulatory Health Services (WAHS)
- Intends to deliver at either UConn Health, St. Francis Hospital or Hartford Healthcare
- Able to read and understand English well enough to participate in the study in English
- Daily access to the internet from smartphone, tablet computer, or laptop/desktop computer that they can use to participate in the study
- Medical clearance to participate from prenatal care provider including clearance to engage in physical activity
- Able to provide verbal or written consent for each component of the study procedures and data collection
- Currently lives within one of the following cities/towns in Connecticut to allow for meal delivery:

Avon	Barkhamsted	Berlin	Bloomfield
Bristol	Burlington	Canton	Cromwell
East Granby	East Hartford	East Windsor	Enfield
Farmington	Glastonbury	Granby	Hartland
Hartford	Manchester	Marlborough	New Britain
Newington	New Hartford	Plainville	Rocky Hill
Simsbury	South Windsor	Southington	Suffield
West Hartford	Wethersfield	Windsor	Windsor Locks

recruitment and prevent duplicated efforts, a screening log will be maintained to track which GDM patients are approached by MFM clinicians or staff.

Research staff will call interested patients to screen them for eligibility. During this call, staff will obtain verbal permission from the patient to perform a chart review to confirm eligibility (i.e., current patient of UConn Health or St. Francis Hospital Maternal Fetal Medicine Clinic or Hartford Healthcare Women's Ambulatory Health Services clinic, singleton gestation, gestational age at GDM diagnosis, time since GDM diagnosis). Maternal Fetal Medicine Fellows overseeing patient's care at St. Francis Hospital clinic or Hartford Healthcare WAHS clinic will confirm eligibility for study participation. A partial HIPAA Waiver will be submitted for approval to the IRB for phone screening/chart review to determine eligibility. If participants are interested and eligible to participate, research staff will explain the study in more detail, including benefits and potential risks of participation.

Each participant screened for inclusion will be assigned a study identification number sequentially. The link between the study identification number and the patient's contact information will be stored in a password protected file only accessible to relevant study staff. The study identification will not be derived from or include any direct personal identifiers (e.g., name, birthdate, medical record number). The screening log will be password protected and housed on the Obstetrics & Gynecology network drive.

For eligible individuals who decline participation, study staff will keep a list of reasons why.

Consent Process

We request a partial waiver of consent to confirm eligibility screening (via medical chart review or with the referring St. Francis or Hartford Healthcare clinician or clinical staff) for participation in the feasibility study.

Once eligibility has been confirmed and a patient has been confirmed eligible to participate, study staff will conduct an informed consent discussion via phone or virtually using either WebEx or Zoom. A member of the study team will review the consent form with the participant, discuss the research process including why we randomize participants and why follow-up is important, discuss challenges and facilitators of participating in the Meals 4 Moms intervention, and answer any questions the patient has. Following this conversation, staff will email the eligible individual a link to the baseline survey in REDCap. Before proceeding to the survey, participants will review the consent form and provide consent electronically.

Randomization:

We will randomize 40 participants 1:1 to the Meals 4 Moms (M4M) and Usual Care (UC) conditions in randomly permuted blocks of size 4 and 6. Randomization will be stratified by site (UCHC vs SFH vs HH) and whether there are children currently living in the participant's home (0 children vs 1+ children) to balance any differences in clinical care and experiences changing diet due to family configuration, respectively. Randomization will be conducted via the randomization module in REDCap based on randomization tables created by Dr. Waring. A participant will only be randomized once they have completed all baseline assessments. Study participants will be informed which treatment condition they have been assigned to by a member of the research team.

Usual Care:

Usual care will consist of the current treatment care that is provided by the participant's prenatal care provider. Usual care consists of a special diet, monitoring of blood glucose levels and encouragement/guidance of increasing a participant's exercise.

Meals 4 Moms:

The Meals 4 Moms Program has been developed based on providing continued education and support with a focus on physical activity/fitness and nutrition.

The program is centered around providing a subsidized food prescription program designed to promote the consumption of nutritious GDM-specific meals. My Local Chefs (MLC), a local Connecticut-based small business, that will package and deliver nutrient-rich American Diabetes Association (ADA)-compliant weekly customizable prepared meals that contain locally sourced, culturally acceptable, nutritionally adequate foods and nutritionist-approved GDM-specific recipes that guide participants to make healthy meals at home.

Participants randomized to the M4M condition will receive an individualized URL link to the My Local Chefs website, where they will have access to a meal budget of $266 food credits per week. Participants will have the ability to customize their selection of meals and produce using this weekly food budget. Prepared meals will be delivered to the participant's home from their first order post-randomization until 1 week after the

tracker and Wi-Fi scale will include instructions that detail how to download and use the activity tracker app, how to set up the activity tracker device, and how to wear and charge the device during the study. The instructions are included as an appendix. Study staff will offer additional support over the phone or via videoconference to set up the device and app if needed.

Participants will be asked to weigh themselves daily using the Wi-Fi scale. Activity trackers and scales will be either provided to the participant at a prenatal care visit or shipped to the participant's home address.

The activity tracker app will allow the activity tracker to automatically sync and download data into a secure database (Fitabase). Fitabase is a fully hosted, cloud-based software solution that implements robust industry standards to maintain secure databases and keep data private. M4M participants will be informed that their activity data will be downloaded to the Fitabase. No GPS or other location information is collected.

We expect that M4M participants will spend up to 5 minutes each day unplugging/plugging in their device from the charger and/or keeping track of dates and times when the activity tracker is not worn utilizing a provided tracking log. Participants are expected to wear the activity tracker device as often as possible (20-24 hours per day).

Every two weeks, the exercise trainer will access the Fitabase database to review the downloaded data for each participant.

- The exercise trainer will assess whether M4M participants are meeting the ACOG (American College of Obstetrics & Gynecology) guidelines for exercise in pregnancy. Current recommendations include at least 150 minutes a week/30 minutes exercise 5 times a week. The exercise trainer will suggest to the participant to utilize the additional, PI-approved exercise resources within the curated exercise video library to help increase the level of activity.
- The exercise trainer will also monitor the participant's weights obtained from the Wi-Fi scale. If a participant were to experience a 1.0 kg (2.2lbs) weight gain or any decrease in weight within a week, the exercise trainer will inform the study coordinator and/or PI who will contact the participant's prenatal care provider for appropriate follow-up and management.

Follow up data collection:

Post-intervention survey:

- Maternal characteristics (body mass index, age, gravidity, parity) and preexisting medical conditions (e.g., hypertension, thyroid disease) and medications taken to treat preexisting medical conditions.
- GDM management outcomes (weekly capillary blood sugar readings, use of insulin or other medications for glycemic control)
- Pregnancy outcomes (preterm delivery < 37 weeks, preeclampsia or other hypertensive disorders, fetal growth restriction, hemorrhage, transfusion, chorioamnionitis, cesarean delivery, wound infection, low Apgar score (<7 at 5 minutes), small for gestational age, meconium aspiration, large for gestational age, macrosomia, and total gestational weight gain
- Neonatal/infant outcomes include intrauterine fetal demise/stillbirth, fetal growth restriction, and macrosomia. Adverse newborn outcomes include high c-peptide values, birth trauma, hyperbilirubinemia, hypoglycemia, neonatal demise, low Apgar score (<7 at 5 minutes), small for gestational age, meconium aspiration, large for gestational age, NICU admission, IV glucose treatment, respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, neonatal infection, and neonatal micronutrient deficiencies. Identification of large for gestational age (via birth weight and ponderal indices) will be collected and will use growth standards that account for race and Hispanic ethnicity[21].

Feasibility Outcomes

Below we detail our feasibility outcomes, how they will be measured, benchmarks for assessing feasibility, and how we will use resulting information to inform the design of the efficacy trial.

Feasibility outcome	How measured	Benchmark	How information will inform design of efficacy trial
Recruitment	Recruitment rates will be calculated from the number of patients approached and reasons for ineligibility and	At least 75% of the patients screened as eligible should be recruited but the trial will not be feasible if recruitment uptake is 50% or less; we anticipate	We will compare yield from different recruitment approaches and finalize our approach for the efficacy trial based on the most effective and efficient approaches. We will examine whether any eligibility criteria are excluding an inordinate proportion of otherwise eligible women, and if so, reassess

	had GDM in the future and if they would recommend the program to a friend with GDM (5-item Likert scales of likelihood)[16-18]	both measures of acceptability	procedures or intervention materials before moving to a full-scale efficacy trial. We will also examine responses to addition questions assessing frequency of use of and ratings of helpfulness and relevance of other aspects of the M4M intervention.

Subject Compensation

Participants randomized to the UC condition will be compensated for their time to complete the baseline and follow-up assessments and the completion of ASA-24 dietary recall.

- UC participants will receive a $10 gift card (i.e., Amazon) for completion of the baseline assessments.
- UC participants will receive a $20 gift card (i.e., Amazon) for completion of follow-up assessments.
- UC participants will receive a $10 gift card (i.e., Amazon) for each completed ASA 24 diet recall at baseline and follow-up assessment timepoints. UC participants can receive up to $60 for completing all the ASA-24 diet recalls.
- UC participants will receive up to $90 in gift cards for their participation in the study.

Participants randomized to the M4M condition will be compensated for their time to complete the baseline and follow-up assessments and the completion of the ASA-24 dietary recall.

- M4M participants will receive a $10 gift card (i.e., Amazon) for completion of the baseline assessments and a $20 gift card for follow-up assessments. To receive the gift card at follow-up participants in the M4M condition must complete both the online survey and interview.
- M4M participants will receive a $10 gift card (i.e., Amazon) for each completed ASA 24 diet recall at baseline and follow up assessment timepoints. M4M participants will receive up to $90 in gift card reimbursement for their participation in the study.

pregnancy. Participants who experience discomfort will be asked to meet with their PCP /OBGYN prior to returning to physical activity.

Participants will be educated by study staff to measure their capillary blood sugar levels prior to exercise. If capillary glucose levels are below 70 mg/dl, participants will be instructed to consume an appropriate snack prior to exercising[22]). To take advantage of the hyperglycemic effect of food, it may be advantageous to exercise an hour after a meal[22]. It also may be important to consider taking insulin medication well before exercise to further reduce the risk of hypoglycemia.

Psychological Risks:

Participants will be reminded that they do not have to answer any questions they do not wish to in any of the baseline or follow-up assessments. All participant surveys will be completed via a secure web form via REDCap. Participants will be asked to answer some questions about their mood (i.e., depressive symptoms). If the study team finds that answers on the survey are concerning, we will ask the participant to consult with their primary care provider or obstetrician/gynecologist to discuss their symptoms. We also will encourage participants to talk to their prenatal care provider if they feel depressed or experience any unexpected mood changes at any point during the study. If study personnel finds that a participant reports they are a safety concern to themselves or someone else, study staff will need to release the participant's confidential information for emergency care purposes.

Additional efforts to protect participant confidentiality are described below.

Confidentiality Risks:

The informed consent discussion will occur virtually, either by phone or by using a secure virtual platform such as WebEx or Zoom. A member of the study team conducting the consent process will suggest that the participant utilize a room that provides privacy prior to conducting the virtual consent.

Research records will be labeled with a Participant ID, an assigned unique identifier. All contents of the research record will be labeled with the assigned ID. A complete record of

the prenatal care provide that the participant's EPDS score was suggestive for depression.

- Women who score positive on the EPDS suicide question (#10) will be considered at acute risk of injury or harm. In the unlikely event, the study PI or project manager will be contacted immediately, and the participant will be assessed for the need for immediate referral for psychiatric evaluation. Urgent evaluation will be arranged for the participant as indicated, and the participant's provider will be made aware of the situation. Staff will confirm participant's contact information prior to each study follow-up assessment including contact information for their prenatal care provider.

Participants will be made aware of this protocol in the original consent for the study. All referrals will be documented and reported to the study PI.

Protections Against Risks to Human Subjects: All adverse events (AE) that are serious, unexpected, and considered related to the study judged by the PI will require expedited reporting. All available information relevant to the evaluation of the serious adverse event (SAE) will be reported.

A SAE is any untoward medical occurrence or effect that at any dose:

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect

Fatal or life-threatening serious, unexpected, related cases occurring in clinical investigations qualify for very rapid reporting. The Institutional Review Board will be notified (e.g., by telephone, fax, or in writing) as soon as possible, but no later than 7 calendar days after first knowledge by the principal investigator that a case qualifies for expedited reporting, followed by a report that must be as complete as possible within 8 additional calendar days.

Serious cases that are unexpected and related and are not fatal or life-threatening, must be submitted as soon as possible but no later than 7 calendar days after first knowledge by the principal investigator that the case meets the minimum criteria for expedited reporting.

Inconveniences participants may experience include time spent to participate in the research. This includes time to complete study assessments, and, for women randomized to the M4M condition, time to learn and monitor activity and weight. We have planned study

team members not involved in the conduct or analysis of the interviews will not have access to the audio recordings or private identifiable information about participants.

Data from uninterested or ineligible potential participants: Contact information will be stored in a password protected file (REDCap project) with an indication that they are not eligible and reason(s) for ineligibility.

Confidentiality of Data

The study team will protect the confidentiality of the information participants provide. However, confidentiality cannot be guaranteed.

The following security protocols will also be applied to all data: physical protections - all data will be stored on secure servers behind firewalls (e.g., REDCap hosted by UCHC, password-protected UConn/UCHC drives such as OneDrive or InCHIP research drive). All hard copy files will be locked in secure cabinets; logical protections –data will be password protected and/or encrypted; and access protections – access will be granted to data on a need-to-know basis only. All records consisting of personal identifiers will be destroyed upon completion of the study by shredding of the hard paper copy, redacting the PHI/PII from the hard paper copy, and/or destruction of the electronic files. Only relevant study staff will have access to participant PHI/PII. Analytic datasets will not include PHI/PII. Interview recordings will be deleted after transcription.

Budget/Resources

Funding for the Meals 4 Moms study has been provided by the Clinical Research and Innovation Seed Program (CRISP).

Dissemination

We plan on disseminating study results via publication of scientific articles, presentation at scientific conferences, and/or dissemination to the public (e.g., social media posts, infographics for a general audience).

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