Title: Examining the effect of hyper-personalized nutrition advice for OBGYN patients on health and wellbeing outcomes during and after pregnancy

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Summary and Significance: Dietary quality and total energy intake during pregnancy significantly influences the mother's health during pregnancy and that of the fetus as well as decade long influences on the health outcomes of the child. However, a one size fits all approach to nutritional guidance is far from ideal given the unique biological, lifestyle, demographic, and health condition differences of expecting mothers. This research proposal will examine the effect of precision nutrition on the health and wellbeing outcomes of mothers during pregnancy, at the time of delivery, and post-delivery. Personal nutritional guidance is based on personal biological, behavioral, and health data.

Hypothesis. Personalized nutrition advice, monitoring, and feedback provided during prenatal care will result in improved cardiometabolic profiles during pregnancy, gestational weight gain within targeted goals, improved wellbeing as reported by the mother and greater satisfaction with prenatal care as well as birthweight for gestational age in the optimal range.

Target Population and exclusions: Pregnant patients of Maimonides Medical Center less than 20 weeks gestation at the time of randomization. Exclusions are: High-risk patients with severe obesity (BMI >35), existing pre-conditions such as diabetes, hypertension, cardiac abnormalities, and need for special medical attention

Population power required: A minimum of 75 participants per group (total 150) will be required for a continuous endpoint measure for independent outcome measures for an expected 20% reduction in complications expected in the intervention group with a 25% of mean standard deviation, alpha=0.05, beta=0.1, and power of 80%.

Intervention and control group assignments: Patients consenting to participation will be randomly assigned with the control group receiving the usual nutrition consultation process in the hospital whenever available. The intervention group will go through a personalized nutrition assessment including DNA-based predisposition analysis for micronutrient, macronutrient, and metabolic needs as well as a baseline health-based lifestyle screening questionnaire. Intervention group participants will then receive personalized nutrition advice during regular OBGYN visits. All participants will be asked the same health questionnaires during their regular OBGYN visits and in post-delivery follow-ups.

Data Collection

Data collection will include the standard clinical and patient intake form data, as well as data collection done at regular OBGYN visits for both groups. For the intervention group, DNA test data and nutrition-focused health questionnaire data will be collected. For both groups additional data on energy and mood levels, pregnancy-related symptoms, activity levels and nutritional intake data will be collected. Additionally, clinical outcome data on birth and post-birth complications for both groups will be used in the final analysis.

STUDY OBJECTIVES

Research Question. What is the impact of continuous personalized nutrition advice, monitoring, and feedback on objective and self-reported health and wellbeing measures and outcomes for healthy women during pregnancy, at childbirth, and post-delivery?

HYPOTHESIS

Hypothesis. Personalized nutrition advice, monitoring, and feedback provided during prenatal care will result in improved cardiometabolic profiles during pregnancy, gestational weight gain within targeted goals, improved wellbeing as reported by the mother and greater satisfaction with prenatal care as well as birthweight for gestational age in the optimal range.

Background / Significance:

INTRODUCTION

Dietary quality and total energy intake during pregnancy significantly influences the mother's health during pregnancy and that of the fetus as well as decade long influences on the health outcomes of the child . However, a one size fits all approach to nutritional guidance is far from ideal given the unique biological, lifestyle, demographic, and health condition differences of expecting mothers. This research proposal will examine the effect of precision nutrition on the health and wellbeing outcomes of mothers during pregnancy, at the time of delivery, and post-delivery. Personal nutritional guidance is based on personal biological, behavioral, and health pre-condition data.

BACKGROUND AND SIGNIFICANCE

According to the CDC, between 1993 and 2014 the number of pregnant women with hypertensive disorders increased by 100%. A significant portion of that comes with obesity and BMI issues before and during pregnancy.

And postpartum hemorrhage rates have increased 6 folds in the same timeframe, and there is a strong linkage with antenatal iron−folic acid use. Therefore, there is little doubt that healthy and targeted nutrition can help reduce many of these complications. However, the actual influence of

personalized nutrition, i.e., nutritional advice that is customized and tailored to the individual's biology, preexisting health conditions, physiology, and lifestyle has not been adequately studied.

Source: Center for Disease Control, Pregnancy Complications Bulletin
https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-complications.html

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STUDY DESIGN

The proposed study design is a randomized controlled trial (RCT) with a one arm treatment group compared to a control group. Pregnant women visiting the hospital (subject to exclusion criteria) will be assigned randomly to an intervention group receiving personalized nutrition guidance and a control group receiving the standard nutrition advice during their visits.

Subjects/Target Population: Pregnant patients of Maimonides Medical Center less than 20 weeks gestation at the time of randomization.

Eligibility Requirements/Exclusions: High-risk patients with severe obesity (BMI >35), existing pre-conditions such as diabetes, hypertension, cardiac abnormalities, , and need for special medical attention

Sample Size/Population power required: A minimum of 75 participants per group (total 150) will be required for a continuous endpoint measures for independent outcome measures for an expected 20% reduction in complications expected in the intervention group with a 25% of mean standard deviation, alpha=0.05, beta=0.1, and power of 80%.

Intervention and control group assignments: Patients consenting to participation will be randomly assigned to either control group or an intervention group. All participants will be asked the same health and wellbeing outcome questionnaires during their regular OBGYN visits and in post-delivery follow-ups.

Control group treatment: The control group will receive the usual nutrition consultation process in the hospital whenever available. This includes basic nutrition guidance provided by the OBGYN during the first visit as well as any referrals to the hospital nutritionist due to gestational diabetes, excessive weight gain, or other nutrition-related complications that may arise during the pregnancy and identified at regular OBGYN visits.

Intervention group treatment: The intervention group will be provided with DNA swab kits to collect samples that combined with and a baseline health and lifestyle screening questionnaire can provide an assessment of the patient's micronutrient, macronutrient, and metabolic needs Intervention group participants will then receive personalized nutrition advice, recipes, and meal plans during regular OBGYN visits and provide information on food intake and adherence in between visits.

Data collection: Data collection will include the standard clinical and patient intake form data, as well as data collection done at regular OBGYN visits for both groups. For the intervention group, DNA test data and nutrition-focused health questionnaire data will be collected. For both groups additional data on energy and mood levels, pregnancy-related symptoms, activity levels and nutritional intake data will be collected. Additionally, clinical outcome data on birth and post-birth complications for both groups will be used in the final analysis.

Data collected for intervention outcome assessment

1. **ICD-9 CM Maternal Morbidity Indicators**

Maternal Morbidity Indicator	ICD-9-CM Codes
Chronic hypertension	642.0x, 642.1x, 642.2x, 642.7x, 401.x, 402.x, 403.x, 404.x, 405.x
Hypertensive disorder in pregnancy (Pre-eclampsia, Eclampsia and Gestational Hypertension)	642.3x, 642.4x, 642.5x, 642.6x, 642.9x
Blood transfusion	99.0x
Cesarean Hysterectomy	'683', '6831', '6839', '684', '6841', '6849', '685', '6851', '6859', '686', '6861', '6869', '687', '6871', '6879', '689'
Obstetric tamponade of uterus or vagina	'758'

Repair of current obstetric laceration of uterus	'7550', '7552'
Uterine artery ligation/embolization	'3979'*, '9929'*, '6825'**, '6824'**
Pulmonary embolism	415.1x, 673.2
Deep venous thrombosis	4534, 453.5x, 453.7x, 453.8x, 453.9x,
Gestational Diabetes	671.3x, 671.4x, 9972
Asthma, Renal Disease Sepsis, and Stroke	

2. Delivery Outcomes

- Preterm Birth
- Miscarriages
- Full-term Vaginal Birth
- Cesarean Section
- Shoulder Dystocia
- Vacuum Assisted Vaginal Delivery
- Intrauterine Fetal Demise
- Low APGAR scores or NICU admission

3. Symptoms during pregnancy

Review of systems form on the SCM

- General
- Neurological
- Breast
- Respiratory
- Gastrointestinal
- Genitourinary
- Musculoskeletal
- Endocrinological
- Gestational Age
- Fundal Height
- Fetal presentation

- Fetal heart rate
- Fetal movement
- Preterm labor
- Blood pressure
- Edema
- Urine protein glucose
- Weight and nutritional screening
- Depression
- COVID-19 status

4. Self-reported pregnancy experience

- Mood measures (Likert scale)
- Fatigue
- Mental health wellbeing (stress, depression, etc.)
- Joyousness
- Satisfaction with prenatal care

5. Social Determinants of Health

While it is not expected that personalized nutrition advice will impact social determinants of health, tracking the actual conditions of the patients will allow for a better understanding of the social environment of the trial.

- Interpersonal Violence
- Barriers to Appointments
- Substance Use
- Unstable housing
- Access to food resources
- Financial Instability

Data Analysis

Data inclusion/exclusion

The table below identifies the data inclusion/exclusion criteria for data analysis.

Statistical Analysis methodology

For each continuous measure of interest, two sample t-test will be performed. For Likert-scale data a non-parametric Mann-Whitney test will be used. For categorical type data, a chi-square test will be employed. A null hypothesis for each measure of interest is that there is no difference between control and precision nutrition (intervention) group at the significance level 0.05. Additionally, we will construct scores for each category: maternal morbidity indicator score, delivery score, symptoms during pregnancy and emotional score. Each score will integrate objective or self-reported measures from each category. The scores will be compared between the intervention and control groups using statistical tests.

10. Expected Outcomes: *Describe specific outcomes or results you expect to see as a result of this study (e.g., treatment group will be higher on outcome measure X than control group).*

It is expected that individuals within the intervention/treatment group will exhibit **at least 20% improved outcomes** (statistically significant change of group average) in the form of risk reduction for risky outcomes, and score improvement for positive outcomes in one or more of the following outcome categories over a 9-month period following the start of the intervention:

Outcome Category A) ICD-9 Maternal Morbidity Indicators (See data collection) (Composite Mortality Index based on all mortality metrics)

Outcome Category B) Pregnancy Symptoms (within the pregnancy period) (Composite Score of Individual Metrics) (See collection data for detailed)

11. Timetable: *Provide an approximate timetable for your study including achievement of key milestones. Include in your timetable any preparatory work needed to carry out the study.*

- IRB Approval Completed (Day 0)
- Protocol refinement (Days 1-14)
- Subject recruitment and consent management (Days 14-74)
- Nutritional needs assessment (DNA testing) for treatment group (Days 15-75)
- Study start date for participants (Days 30-90) (Individuals start the protocol at different times following recruitment)
- Interventions (Physician visit and guidance) (Days 30-334) (Every 4 weeks after starting for those recruited by day 30 for 9 months)
- Year 1 data analysis and hypothesis validation (Days 334-355)
- Start of year 2 study cohort