Distribution Agreement

In presenting this thesis as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis in whole or in part in all forms of media, now or hereafter known, including display on the World Wide Web. I understand that I may select some access restrictions as part of the online submission of this thesis. I retain all ownership rights to the copyright of the thesis. I also retain the right to use in future works (such as articles or books) all or part of this thesis.

Signature:

_____

Saumeth D. Cardona **Date**

LOLA
LIFESTYLE INTERVENTION FOR THE PREVENTION OF GESTATIONAL DIABETES IN PREGNANT OVERWEIGHT/OBESE LATINAS
GRANT PROPOSAL

BY
Saumeth D. Cardona
Degree to be awarded: M.P.H.
Executive MPH

_____

Linelle M. Blais, PhD, CPF Date
Committee Chair

_____

Guillermo E. Umpierrez, MD, CDE, FACP, FACE Date
Committee Member

_____

Laurie Gaydos, PhD Date
Associate Chair for Academic Affairs, Executive MPH program

LOLA
LIFESTYLE INTERVENTION FOR THE PREVENTION OF GESTATIONAL DIABETES IN PREGNANT OVERWEIGHT/OBESE LATINAS GRANT PROPOSAL

By
Saumeth D. Cardona
Doctor of Medicine
Zaparozhye State Medical University, Ukraine
1995

Thesis Committee Chair: Linelle M. Blais, PhD, CPF

An abstract of
A thesis submitted to the
Faculty of the Rollins School of Public Health of Emory University
In partial fulfillment of the requirements for the degree of
Master of Public Health
Executive Master of Public Health
2016

Abstract

LOLA
LIFESTYLE INTERVENTION FOR THE PREVENTION
OF GESTATIONAL DIABETES
IN PREGNANT OVERWEIGHT/OBESE LATINAS
GRANT PROPOSAL

By

Saumeth D. Cardona

This thesis develops a public health grant proposal to prevent Gestational Diabetes Mellitus (GDM), which is a form of diabetes that develops during pregnancy, usually during the second trimester and resolves after delivery. Women with GDM are at risk of future development of type 2 diabetes, with about half of patients developing diabetes during the next 10 years. Overweight, obesity and excessive gestational weight gain are among the most important risk factors associated with GDM, in particular in minority populations. In the United States the prevalence of overweight and obesity is increasing among pregnant women and recent CDC data estimate that more than one-third of women of reproductive age are overweight and two thirds of women gain more weight than the Institute of Medicine (IOM) recommendations.

Latina women are 30% more likely to be overweight than non-Hispanic white women. Hispanic women with GDM are at higher risk of developing diabetes within 5 year of index pregnancy, indicating the need for intensive screening and interventions to prevent excessive weight gain and GDM-associated maternal and fetal complications.

Increasing evidence indicates that lifestyle intervention programs based on diet and exercise can prevent the development of diabetes in high risk populations. Such programs have reported mixed results in Caucasians, with some studies reporting positive effects of increasing exercise and improved nutrition, and reduction in excessive weight gain in Caucasian and African American women. Few lifestyle intervention studies have been conducted in Latino women at risk of GDM.

This proposal will determine if a culturally-grounded lifestyle intervention program started in early pregnancy in overweight/obese Latina women will result in higher compliance with IOM weight gain guidelines when compared to women receiving standard obstetrical care. We hypothesize that lifestyle modifications will prevent excessive weight gain during pregnancy and may reduce risk of GDM and maternal and neonatal complications. By limiting excessive gestational weight gain, this lifestyle intervention program may prevent the burden of obesity-related complications during pregnancy and reduce risk of subsequently developing overt diabetes.

LOLA
LIFESTYLE INTERVENTION FOR THE PREVENTION OF GESTATIONAL DIABETES IN PREGNANT OVERWEIGHT/OBESE LATINAS GRANT PROPOSAL

By
Saumeth D. Cardona
Doctor of Medicine
Zaparozhye State Medical University, Ukraine
1995

Thesis Committee Chair: Linelle M. Blais, PhD, CPF

An abstract of
A thesis submitted to the
Faculty of the Rollins School of Public Health of Emory University
In partial fulfillment of the requirements for the degree of
Master of Public Health
Executive Master of Public Health
2016

ACKNOWLEDGEMENTS

First off, I would like to thank my family, especially my husband, son, and mother for their continued patience over the past years. I could not have completed this program without their support and understanding. My success is also yours!

I also want to thank my committee chair Dr. Linelle Blais, who provided me with valuable expertise, guidance, and instruction during the development of this thesis. I am extremely grateful for her support and encouragement.

Second, thank my advisor and expert in the field, Dr. Guillermo Umpierrez. He not only provided valuable insight, but helped me remain enthusiastic and passionate about the topic of gestational diabetes prevention.

Many thanks to my volunteer expert reviewers: Dr. Nelson Atehortua, Dr. Catherine Barnes, Dr. Francisco Pasquel, and Dr. David Ziemer. Thank you for unselfishly providing your time, insights, and encouragement.

Lastly, many thanks to Britt Rotberg, my friend and past co-worker who helped polish my English.

During my time at Rollins School of Public Health I met wonderful classmates who I am now proud to call my friends. We shared good times, food, and laughs. I am so grateful and blessed for your friendship and support.

Table of Contents

Definition of Terms:

Gestational Diabetes Mellitus (GDM): is a form of diabetes or glucose intolerance of variable severity that begins or is first diagnosed during pregnancy and usually resolves not long after delivery (American Diabetes, 2016).

HbA1C: It is a form of hemoglobin that is measured primarily to identify the three months average plasma glucose concentration.

Large for Gestational Age (LGA): weight, length or head circumference that lies above the 90th percentile for that gestational age.

Latino/Hispanic: The Office of Management and Budget (OMB) defines Hispanic or Latino as "a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The terms Latino and Hispanic are used interchangeably (CDC, 2013a).

Lifestyle Intervention: Changes in eating regimen of physical activity without medication or surgical procedures.

Oral Glucose Challenge Test: A test that evaluates how the body processes the glucose. No fasting is required. A sweet liquid is given and blood is drawn 1 hour from having the drink.

Oral Glucose Tolerance Test (OGTT): medical test in which glucose is given and blood samples taken afterward to determine how quickly is cleared from the blood. Fasting is required.

Type 2 Diabetes Mellitus (T2D): Type 2 diabetes is the most common form of diabetes. Diabetes is a problem that causes blood glucose (sugar) levels to rise higher than normal.

Chapter I

Introduction

Gestational diabetes mellitus (GDM) is a form of diabetes or a state of carbohydrate intolerance of variable severity that is first diagnosed during pregnancy and usually resolves shortly after delivery (American Diabetes, 2016). Recent data from the Center of Disease Control (CDC) indicates that GDM is a growing health problem affecting about 10 percent of all U.S. pregnancies annually (DeSisto, Kim, & Sharma, 2014), resulting in approximately 200,000 cases a year. After delivery, 5 to 10 percent of women with GDM continue to have type 2 diabetes (T2D), and 20 to 50 percent will develop diabetes within 5 – 10 years after delivery (CDC, 2014).

GDM affects minority populations (African-American, Hispanic/Latino, and American Indian women) more frequently than Caucasians (CDC, 2013b). The prevalence of GDM has increased significantly between 10% and 100% in minority racial-ethnic groups during the past 20 years. Risk factors for GDM are overweight/obesity (Chasan-Taber, 2015), advanced maternal age (Morisset et al., 2010), and minority women with a family history of diabetes (Reece, Leguizamon, & Wiznitzer, 2009). The trends toward older maternal age, the epidemic of obesity (Ehrenberg, et al., 2004; Kim et al., 2007), and the reduction in physical activity (BRFSS, 2014) have contributed to the increasing prevalence of GDM.

Mothers with GDM, when compared to those with non-GDM pregnancies have a seven-fold increased risk of developing future type 2 diabetes mellitus (T2D) (Bellamy et al., 2009). In addition, pregnant women with GDM are at higher risk of maternal complications and their infants are at risk for adverse outcomes such as macrosomia, miscarriage and preterm birth (CDC, 2013b).

Problem Statement

Gestational diabetes mellitus (GDM) is a common complication of pregnancy associated with increased risk of unfavorable outcomes for both mother and infant.

Latinas are 50% more likely than non-Hispanic Caucasian women to have gestational diabetes and a seven-fold increased risk of future risk of T2D (Bellamy et al., 2011). Latina women with GDM are also at higher risk of maternal and fetal complications compared to Caucasian women (CDC, 2013b). The increasing number of GDM cases and associated complications in all ethnic groups, in particular minority populations have a significant impact on healthcare spending and resource utilization. GDM increases hospital costs by 18% ($4,500) while pre-existing diabetes among pregnant women increases hospital costs by 55% ($5,900) compared to hospital costs for deliveries by women who did not have diabetes ($3,800) (Wier, 2006).

Hispanic are the largest minority group in the US (U. S. Census, 2015) and Latina women with GDM have higher risk of developing T2D than Caucasians, even after controlling for pre-pregnancy BMI and other cofounders (Fujimoto, 2013). Hispanic people also are the most physically inactive US ethnic group and have disproportionately high levels of overweight and obesity rates, gestational diabetes and diabetes (Fujimoto, 2013). Hispanic women have worse maternal outcome measures including preterm labor and hypertensive disorders of pregnancy than Caucasians after adjusting for sociodemographic characteristics and comorbidities (Bryant et al., 2005) and about half of Hispanic women with GDM will develop T2D within 5 years of the index pregnancy (Fujimoto, 2013), indicating the need for intensive screening and interventions to prevent GDM and its complications in this group. Few prospective intervention studies have investigated prevention of GDM in Hispanic women. The purpose of

this thesis is to draft a research grant that proposes to conduct a randomized controlled study to determine if a lifestyle intervention program, based on healthy eating and exercise, will reduce the rate of GDM and its complications compared to a standard of care control group in overweight/obese Hispanic women.

Prevalence of Gestational Diabetes in Georgia

In Georgia, approximately 10.5 % or 390.000 women have been diagnosed with diabetes as of 2011 (GDPH, 2013). The incidence rate of GDM was greatest among Hispanic women (37.2 per 1,000 women) compared to White, Non-Hispanic women (31.5 per 1,000 women) (Figure 1). As gestational diabetes affects racial and ethnic minority women, addressing this health issue may help eliminating health disparities for women.

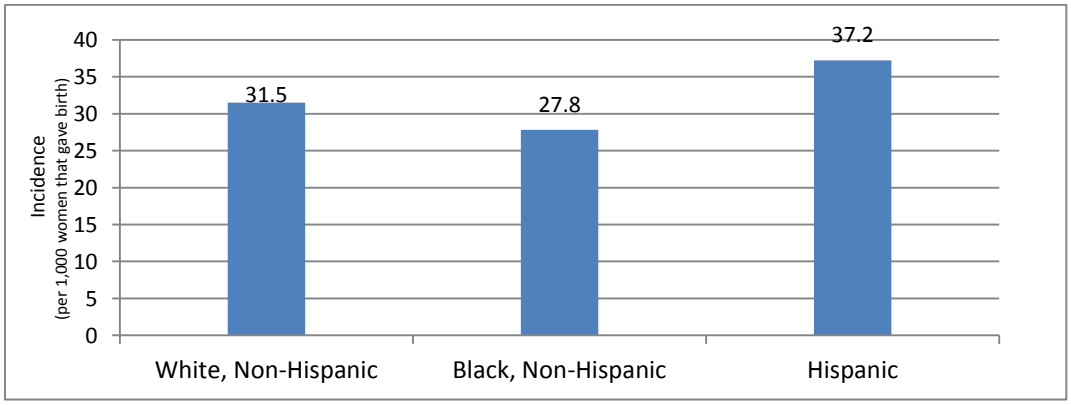


Figure 1. Diagnosed Gestational Diabetes Incidence by Race/Ethnicity, 2011 (Data Source: Georgia Birth Certificates, Georgia Vital Record, Georgia Department of Public Health)

During pregnancy, GDM requires lifestyle modification (weight management) and/or treatment to normalize maternal blood glucose levels to prevent complications for the pregnant women and infants. Experts believe that prevention of GDM can prevent and new cases of T2D (Chasan-Taber, 2015). Given that the pathology of is similar to T2D, it has been hypothesized

that T2D (lifestyle intervention) prevention methods can be effective in preventing GDM (Oostdam et al., 2011). There is increasing evidence on the impact of screening and treatment programs of GDM, however, few studies have focused on the prevention of GDM and its complications in minority populations (Han, Crowther, & Middleton, 2012).

The purpose of this program is to provide culturally and linguistically tailored education to overweight/obese Latino women starting during their first trimester of pregnancy (≤16 weeks). This program's outcomes include 1) weight control to prevent excessive weight gain throughout pregnancy in accordance with the Institute of Medicine (IOM) recommendations (Institute of Medicine Institute of medicine of National Academies, 2009), 2) to compare the occurrence of carbohydrate intolerance and GDM at 24-28 weeks of gestation, and 3) to determine the impact the lifestyle intervention on the development of perinatal maternal and fetal complications.

The lifestyle program is designed to be easily implemented and applicable to everyday life with online resources. It is designed to be a 3 years initiative with a relative low total cost projected to be $486,872

.

Major Components

The major components of this proposal entitled: "Lifestyle Intervention Program for GDM Prevention in Pregnant Overweight/Obese Latinas" - LOLA program are:

1) Education on healthy eating habits,
2) Increase physical activity,
3) Tracking physical activity and healthy eating adherence using a mobile device technology.

Significance Statement

GDM represents a common and serious health care problem in the U.S. and around the world. Increasing evidence from randomized controlled trials (RCT) indicate that lifestyle intervention programs based on promoting good nutrition and physical activity before and early in pregnancy may lower the incidence of GDM (Yin et al., 2014). Some lifestyle intervention studies have reported improvements in risk factors associated with GDM in Caucasian women (Chasan-Taber, 2015); however, the impact of such intervention in Hispanic women has not been investigated. Current guidelines recommend to screen and diagnose GDM at 24-28 weeks of pregnancy to prevent its associated unfavorable outcomes. We believe that screening and intervention programs will have a positive impact in preventing GDM and its complication in overweight/obese Hispanic women.

As mentioned earlier, if T2D can be prevented by modifying risk factors such as weight loss and by increasing physical activity, as has been shown in different randomized trials (Knowler et al., 2002; Pan et al., 1997; Tuomilehto et al., 2001), and programs such as the CDC national diabetes prevention program (NDPP) (CDC, 2011) can be modified and tailored to at-risk Latino women. By limiting gain weight during pregnancy, following appropriate healthy dietary habits, and increasing physical activity as early as in the pre-conception period and/or in the early first trimester, can prevent the development of GDM, and a decrease the negative outcomes associated with maternal overweight and obesity (Bautista-Castano et al., 2013).

This study entitled “Lifestyle Intervention Program for GDM Prevention in Pregnant Overweight/Obese Latinas” (LOLA) proposes a lifestyle intervention program, based on healthy eating and exercise aimed to prevent GDM in Latina women. This proposal includes an early lifestyle intervention program in at-risk overweight/obese women in their first trimester.

LOLA is a culturally tailored innovative program that focuses on traditional public health intervention programs such as the internet Prevent T2 curricula which is a modification of national diabetes prevention program (NDPP). The NDPP is a CDC-recognized lifestyle change program based on research led by the National Institute of Health (NIH). This research showed that people with prediabetes who took part in a structured lifestyle change program can cut their risk of developing T2D by 58%. This finding was the result of the program helping participants achieve a weight loss of 5% to 7% from baseline bodyweight through a healthier eating and at least 150 minutes of physical activity per week (Diabetes Prevention Program Research et al., 2009). Previous type 2 diabetes prevention studies, including the Finnish Diabetes Prevention Study (Tuomilehto et al., 2001) have shown that the prevention of type 2 diabetes is possible and feasible by lifestyle intervention. However, these interventions have been criticized for being too labor intensive and therefore not directly applicable to a primary health care setting (Kahn & Davidson, 2014).

Evidence suggests that pregnancy provides an opportunity to promote positive health behaviors. This opportunity has been branded as a 'teachable moment' in a woman's life, as perceptions of personal risk are increased (Phelan, 2010). In addition, strong emotional responses and a re-definition of their social role and responsibility occurs during pregnancy results in pregnant women to be more motivated in adopting positive health behaviors, such as physical activity (McBride, Emmons, & Lipkus, 2003; Phelan, 2010).

According to Nielsen's report (2013), Latinas are increasing health awareness for both themselves and their families making them more conscientious about weight, preventive health measures, rank health and nutrition as a primary concern. Latinas are also discovering the benefits of untethered entertainment and savoring a multitude of mobile activities at rates

consistently and sizably ahead of non-Hispanic white females. Online Latinas are more likely than their non-Hispanic white counterparts to own smartphones at 77 percent (vs 55 percent). Latinas seem to be bypassing laptops and desktops in favor of mobile technology (Nielsen, 2013). For this reason, we hypothesize that the use of mobile technology will help to better track dietary habits and physical activity.

The LOLA proposal tailors specific components of the Prevent T2 modified CDC program to be adapted to pregnant Latino women who are at risk of developing GDM and future T2D. The program will combine two proven lifestyle interventions delivered in monthly in – person group classes - healthy eating habits and increased physical activity - added to the traditional prenatal care program. In addition, our program encourages the use of mobile technology to track both eating habits and physical activity. As discussed in the following chapter II-literature review, there have been several clinical randomized trials that indicate that dietary counseling, advice on low glycemic diet (LGD), and exercise programs can be beneficial in the prevention of GDM, but very few of these trials include minority Latina women.

Target Audience

The general target population of the LOLA intervention program is at-risk Latino women who are pregnant in their first trimester, between 18-45 years at Centro Internacional de Maternidad (CIMA) and the ambulatory obstetric clinics at Grady Health System (GHS), Atlanta, Georgia.

CIMA is a clinical center that works with Northside Hospital in Atlanta, Georgia that provides care to women during pregnancy regardless of health insurance and income. CIMA performs about 120 deliveries per month. More than 95% of their population is Hispanic

(majority non-English speaking). Incidence of gestational diabetes in their population is around 10% (information provided by CIMA staff).

GHS works to improve the lives of those in Atlanta Georgia, with a mission of serving the poor and uninsured and those suffering from health disparities. At its center, Grady Memorial Hospital is the Southeast's largest public hospital, and has been the public hospital for the city of Atlanta. It is one of six regional perinatal centers in the state of Georgia and serves as the primary referral center for high risk patients in the 40-county North Georgia area. It also accepts maternal transports from outside of our 40-county referral base, from other perinatal centers and their affiliated hospitals that are not equipped to care for high acuity or complexity pregnancies. GHS serves patients with highly diverse racial (>90% minority subjects) and socioeconomic profiles.

Recruitment

Overweight and/or obese (BMI>25 Kg/m^2) pregnant Latino women with ≤ 16 weeks of pregnancy will be identified at their 1^{st} OB clinic visit. CIMA personnel will be trained regarding the program components and enrollment. Our research team and CIMA staff will promote enrollment and adherence to the LOLA program.

Enrollment

Enrollment and program registration for the intervention program will be performed by the research staff. Once consented and registered, the participants will receive free messages and phone calls with educational tips about their pregnancy and caring for themselves on a weekly basis. Upon enrollment, each participant will answer a series of questions to self-qualify for services in their residential County area.

Screening:

Study enrollment will take place at the first or second obstetrical visit but no later than week 16 of pregnancy. Demographic and baseline assessment will be collected and patients will be scheduled for an outpatient visit at the Grady Clinical Research Unit within one week after an overnight fast. An abbreviated history and physical exam will be completed by the PI or co-investigators to collect vital signs, weight, BMI, and assessment of physical activity. Baseline laboratory studies (hemoglobin, hematocrit, biochemistry, HbA1C) and a 75-gram OGTT with measurement of glucose will be drawn to rule out diabetes.

Randomization.

The PI and/or a member of the research team will review medical records and results of OGTT prior to randomization to exclude subjects with contraindications (see eligibility criteria: section IV.B.2). Eligible patients will be randomized into a lifestyle intervention or a standard of care group. A blocked randomization will be based on body weight – overweight (BMI 25-<30 kg/m2) and obese (BMI > 30 kg/m2), using the randomly permuted blocks method in a set of 4 sequential enrolled patients per group.

Content of Educational Sessions**.**

Monthly in-person education sessions are adapted from the Prevent T2, a CDC modified program from the original DPP (Knowler et al., 2002) and will cover the following topics: 1) healthy eating, 2) being active, 3) monitoring weight and physical activity, 4) stress management, 5) problem solving, and 6) healthy coping. Personal and group educational sessions will be led by a bilingual CDC certified lifestyle coach.

Lifestyle Intervention Program.

The linguistically lifestyle intervention will consist of a monthly 60 minutes in-person group educational sessions and biweekly telephone booster calls, which will continue until 3 months after delivery. Participants will attend their regularly scheduled obstetric clinic visits, usually every 4 weeks until the 28th weeks then every 2 weeks until the 35th week of pregnancy and weekly thereafter until delivery. If a participant develops a significant maternal complication, she will be withdrawn from the study and referred for follow up and management by the maternal-fetal specialists. Participants who develop GDM will be referred to the specialist and if specialist agrees, participant will continue participation and followed and monitored until post-delivery period.

Participants will receive information on the appropriate weight gain during pregnancy using the IOM guidelines. At each intervention in-group session, the participant's weight will be measured using a balance beam scale and recorded. The CDC trained lifestyle coach will inform the participant whether her weight gain is at the appropriate recommended level. If her weight gain is within the IOM guidelines, the patient will be encouraged to continue current eating and exercise regimen. If her weight gain is not within the IOM guidelines, the participant's eating and exercise regimen will be reviewed by the coordinator and the lifestyle coach and she will be advised to increase or decrease her intake and increase or decrease her exercise. Final gestational weight will be recorded on arrival to the hospital for delivery.

Ethical Considerations

The program commits to conducting its research consistent with Health and Human Services (HHS) and Emory University Institutional Review Board (IRB) guidelines for the conduct of research involving human subjects. All participants will sign an informed consent

form to participate in the program. For their protection, participants will be de-identified. Participants can withdrawal from participation at any time for any reason.

Chapter II-Literature Review

Introduction

This chapter provides a literature review concerning gestational diabetes, diagnosis, risk factors, complications, and concerning lifestyle intervention programs as a public health intervention. The purpose of this literature review was to substantiate that lifestyle intervention programs in the pre-conception and pregnancy period can reduce the incidence of gestational diabetes.

Pathophysiology of Gestational Diabetes

Gestational diabetes is first detected in pregnancy (Buchanan & Xiang, 2005; Moses, 2010), usually after 20 weeks of gestation. The precise mechanisms underlying GDM remain unknown, though many postulates have been studied. The hallmark of GDM is increased insulin resistance. Pregnancy is a state of physiological insulin resistance, and therefore represents a physiological model of beta-cell stress (Kautzky-Willer & Bancher-Todesca, 2005). In normal pregnancy insulin sensitivity emerges in the second trimester and progresses over the late third trimester, thereby increasing maternal glucose, free fatty acids and amino acids in order to provide adequate energy to the fetus. In normal pregnancy, insulin resistance leads to an appropriate increase of insulin secretion, and blood glucose levels remain in the normal range.

The metabolic/endocrine changes accompanying the second half of gestation induce physiological pregnancy-related insulin resistance and unmask and worsen the underlying pre-existing metabolic disturbances (pre-gestational insulin resistance and relative insulin secretion defect), leading to the full clinical picture of GDM (Catalano, 2010; Xiang et al., 1999).

Impaired first phase insulin secretion, prolonged and increased second phase insulin release, reduced insulinogenic indices, increases hepatic glucose output, changes in insulin kinetics, reduced glucose absorption from the gut (Anderwald et al., 2011) and varying degrees of insulin resistance have been described in women with GDM, as compared to pregnant women with normal glucose tolerance tests.

Gestational Diabetes Risk Factors

Observational studies have helped to identify a multitude of risk factors for GDM; these include maternal body mass index (BMI) of at least 30 kg/m², physical inactivity (Chasan-Taber et al., 2010) advancing maternal age (Morisset et al., 2010), increasing parity, and ethnicity (African-American, Hispanic, and Asian). Diet low in fiber, with a high glycemic load has been shown to increase the risk of GDM (Zhang, Liu, Solomon, & Hu, 2006). Women are also at an increased risk of GDM if they have had a previous macrosomic baby (birthweight 4000 g or more), have had previous GDM (Petry, 2010), have a family history or first-degree relative with diabetes, or have polycystic ovarian syndrome (Reece et al., 2009). Weight gain during pregnancy for women who are overweight or obese has been shown to correlate with GDM risk (Hedderson, Gunderson, & Ferrara, 2010; Morisset et al., 2010).

Excessive weight and a lack of exercise increase insulin resistance. An increased insulin resistance results in an elevated risk of developing prediabetes and Type 2 diabetes. Weight status can be defined using the Body Mass Index (BMI) (Table 1). Compared to women of normal weight, gestational diabetes incidence was greatest in women who were obese (59.6 per 1,000 women that gave birth; 1,564 women) and overweight (35.1 per 1,000 women that gave birth; 877 women) (Figure 2).

BMI	Category BMI (kg/m2)
Underweight	Less than 18.5
Normal	18.5 - 24.9
Overweight	25 – 29.9
Obese	Greater than 30

Table 1-Criteria for BMI categories

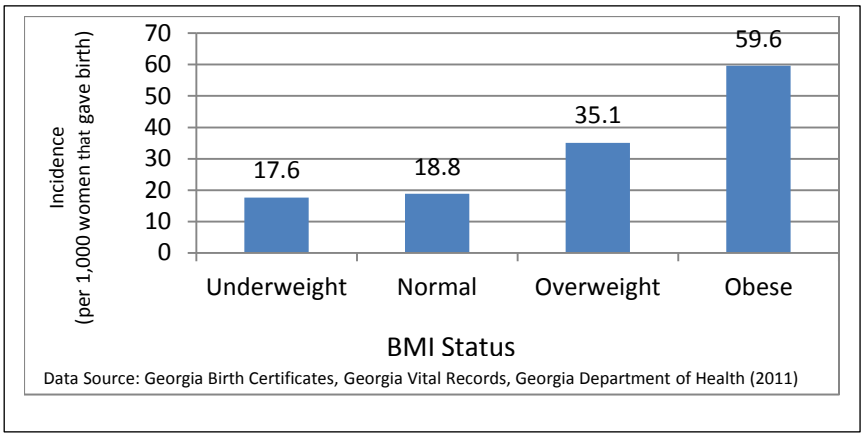


Figure 2. Diagnosed Gestational Diabetes Incidence by BMI

Screening and Diagnosis of Gestational Diabetes Mellitus

Historically, screening for GDM consisted of obtaining the patient's medical history, relying primarily on past obstetrical outcomes and a family medical history of T2D. In 1973, O'Sullivan and Mahan proposed the 50g, 1 hour OGTT test, (O'Sullivan, 1973) which is now widely used in the United States (Berger et al., 2002).

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study was designed to clarify risks of adverse outcomes associated with degrees of maternal glucose intolerance (Coustan et al., 2010). Following this study, a task force of the International Association of Diabetes in Pregnancy Study Group (IADPSG) recommended new criteria for the diagnosis of GDM, which diagnoses GDM if any of the following three 75 g OGTT thresholds are met or exceeded: fasting plasma glucose: 5.1 mmol/L (92 mg/dL), one-hour plasma glucose: 10.0 mmol/L (180 mg/dL) or two-hour plasma glucose: 8.5 mmol/L (153 mg/dL) (IADPSG Consensus Panel, 2010). A number of studies have already revealed higher GDM prevalence when using the IADPSG, compared with other criteria (Moses, 2010; E. P. O'Sullivan, 2011) and some have confirmed an increase in adverse pregnancy outcomes for the diagnosed women (E.

P. O'Sullivan, 2011). Debate surrounding the risks, costs and benefits of use of these diagnostic criteria is ongoing (Langer, 2013).

Below there is a summary of the guidelines used in the United States:

American College of Obstetrician and Gynecologists (ACOG, 2013).

According to ACOG recommendations, all pregnant patients should be screened for GDM, whether by the patient's medical history, clinical risk factors, or laboratory screening test results to determine blood glucose levels.

Screening is generally performed at 24-28 weeks of gestation. Early pregnancy screening for undiagnosed type 2 diabetes is suggested in women with risk factors, including those with a prior history of GDM. If the result of early testing is negative, repeat screening for high-risk women is recommended at 24-28 weeks of gestation. The two-step approach to testing, commonly used in the United States, is based on first screening with the administration of 50 g of an oral glucose solution followed by a 1-hour venous glucose determination. Those individuals meeting or exceeding the screening threshold undergo a 100-g, 3-hour diagnostic OGTT.

The Endocrine Society (TES) (Blumer et al., 2013)

TES recommends that pregnant women be tested for GDM by having a 2-hour, 75-g OGTT performed at 24 to 28 weeks gestation. The 75-g OGTT should be performed after an overnight fast of at least 8 hours (but not more than 14 hours) and without having reduced usual carbohydrate intake for the preceding several days. One or more abnormal values establishes the diagnosis, with the exception that in the case of overt diabetes, but not gestational diabetes, a second test (either a fasting plasma glucose, untimed random plasma glucose, HbA1C, or

OGTT), in the absence of symptoms of hyperglycemia, must be performed and found to be abnormal on another day to confirm the diagnosis of overt diabetes.

U.S. Preventive Service Task Force (USPSTF) (U. S. Preventive Services Task Force, 2014)

USPSTF recommends screening for gestational diabetes mellitus (GDM) in asymptomatic pregnant women after 24 weeks of gestation. The 2-step approach, the 50-g oral glucose challenge test (OGCT) is performed between 24 and 28 weeks of gestation in a non-fasting state. If the screening threshold is met or exceeded, patients receive the oral glucose tolerance test (OGTT). During the OGTT, a fasting glucose level is obtained, followed by administration of a 100-g glucose load, and glucose levels are evaluated after 1, 2, and 3 hours. A diagnosis of GDM is made when 2 or more glucose values fall at or above the specified glucose thresholds. Alternatively, in the 1-step approach, a 75-g glucose load can be administered. GDM is diagnosed if 1 glucose value falls at or above the specified glucose thresholds

In summary, the four guidelines developers agree that pregnant women should be screened for GDM at 24-28 weeks gestation. USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for GDM in asymptomatic pregnant women before 24 weeks.

Maternal and fetal complications

Pregnant women with diagnosed GDM are considered at high risk for maternal complications and their infants are at risk for adverse outcomes such as miscarriage and preterm

birth. GDM increases the potential need for cesarean section (C-section) deliveries due to the risk of giving birth to a large baby (CDC, 2013b).

Poorly controlled GDM is also a significant health risk during pregnancy, affecting both the mother and fetus (CDC, 2013b). Maternal complications associated with uncontrolled GDM include increased risk for high blood pressure during pregnancy (Pregnancy-Induced Hypertension (PIH) (CDC, 2013b). Infants of women who have GDM experience a higher risk of hypoglycemia (low blood sugar), birth defects, and overly large body size which can complicate delivery. These children are also at risk for the future development of both diabetes and obesity (CDC, 2013b).

Prevention Studies

Until recently, research pertaining to gestational diabetes had been largely devoted to its diagnosis and treatment; however, interest in its prevention through modifiable factors such as physical activity and diet is now emerging. There are some studies now which examine the effects of dietary variables, both prior to- (Zhang & Ning, 2011) and during pregnancy (Saldana, 2004), in association with the risk of maternal hyperglycemia. Since dietary counselling during pregnancy has been shown to effectively change maternal food and nutrient intake (Piirainen, 2006), prevention of GDM through the manipulation of dietary factors is a logical approach.

Methodology

The literature review consisted of a comprehensive electronic database search of relevant peer reviewed journal publications including Medline, PubMed, and the American Public Health

Association. Additionally, relevant, government publications of HHS, CDC, NIH, as well as the Kaiser Family Foundation and the Pew Research Center were included.

Publications were limited to the past 10 years and published in English or Spanish. The searches included a combination of the following search terms: gestational diabetes, obesity and pregnancy, healthy behaviors during pregnancy, prevention of gestational diabetes, lifestyle intervention program, maternal weight gain, physical activity and pregnancy, Latina, Hispanics. In the final analysis, the following articles were selected which generally summarized the substantial foundation of evidence around the effectiveness of lifestyle intervention in pregnant women.

Relevant Studies.

There have been several reviews over the past decades that have looked at different lifestyle intervention for prevention of GDM. The majority of these reviews included primarily Caucasian women with interventions that vary in terms of delivery and outcomes, but a common conclusion is that quality of studies is low. Different RCTs have looked at diet intervention only, physical activity or a combination of both diet and physical intervention, and the use drug intervention with different outcomes not limited to GDM.

Diet Only Interventions:

Diet only interventions are strategies to modify dietary intake using a nutritional regimen that followed country dietary guidelines or similar to those used in the treatment of GDM and providing counseling recommendations for eating a healthy diet.

There have been several randomized controlled trials (RCT) that have targeted women with a BMI$\geq$25kg/m^2 with an intervention focused on modifying dietary intake suggesting healthier dietary choices. In some studies, the dietary advice was provided by dietitian or food

technologist. Wolff et al. (2008), conducted a trial with dietary consultations targeting weight gain in obese women with a goal to assess the impact of dietary restrictions in the in glucose metabolism caused by pregnancy-induced changes. In this trial, non-diabetic Caucasian obese pregnant women were randomized to an intervention group with 10-h dietary consultations vs. control group (regular antennal care). In this RCT the intervention group successfully limited their energy intake, and restricted the gestational weight gain when compared to the control group. Results from this trial show that a restriction of weight gain in obese women can be achieved and that it also reduces the deterioration in the glucose metabolism (Wolff, 2008).

A systematic review conducted by Tieu et al. (2008) to assess the effects of dietary advice in preventing gestational diabetes mellitus looked at quasi-randomized and randomized studies of dietary intervention for preventing glucose intolerance in pregnancy. Three trials (107 women) were included in the review. One trial analyzed high-fiber diets, but did not include any outcomes showing statistically significant differences. Two trials assessed low glycemic index (LGI) versus high glycemic index diets for pregnant women. Women on the LGI diet had fewer large for gestational age infants, infants with lower ponderal indexes and lower maternal fasting glucose levels. According to this analysis, the results for women on the LGI diet on neonatal birth weight were not conclusive; however, women on the LGI diet gave birth to lighter babies. Results from this review were inconclusive and no conclusions could be drawn from the high-fiber versus control-diet comparison since the trial involved did not report on many of the outcomes authors had pre-specified (Tieu, Crowther, & Middleton, 2008).

Another RCT in obese women were randomized to an intervention group with a balanced nutritional regimen or control group, who received conventional prenatal dietary management. Women were between 12-28 weeks of gestation with a single pregnancy and pre-pregnancy

BMI>30 kg/m^2. This study found statistically significant differences between the study and control groups regarding 3 variables: (1) gestational hypertension, $p < .46$; (2) mother's last weight before delivery, $p < .001$; and (3) mother's 6-week postpartum weight, $p < .001$. An important finding of this study was that obese pregnant women may be placed on a healthy, well-balanced, monitored nutritional program during their antepartum course without adverse perinatal outcomes (Thornton, 2009).

Other studies have looked at gestational weight gain and how weight management through nutritional prevention strategies could prove successful in reducing the risk for GDM. Most of the studies included Caucasian women only. These reports suggest that maternal obesity assessed by pre-pregnancy BMI is associated with an increased risk of GDM, and that gestational weight gain is also associated with an increased risk for GDM (Morisset et al., 2010). Higher dietary fat and higher carbohydrate intakes during pregnancy appear to be associated with a higher risk for GDM, independent of pre-pregnancy BMI. Weight management through nutritional prevention strategies can be successful in reducing the risk of GDM, but further studies are required to identify the most effective diet composition to prevent GDM and excessive gestational weight gain. However, a firm conclusion on the most effective nutritional intervention for the control of gestational weight gain and glycemic responses could not be reached based on available studies.

In Australia, 124 obese pregnant women were randomized to a 4-step multidisciplinary prenatal care program or to standard obstetric care. This trial included an intervention with a brief dietary counseling and education including itemization of the food consumption of the previous day with a focus on reducing consumption of fast foods, sports drinks, carbonated drinks, and commercial fruit juices and increasing the consumption of fruit and vegetables.

Compared with the standard obstetric care group, women randomized to the intervention group had a significant reduction in the incidence of gestational diabetes mellitus and reduced weight gain in pregnancy, although the number of cases was small (21 cases) (Quinlivan, Lam, & Fisher, 2011).

Physical Activity Intervention

The Diabetes Prevention Program (DPP) study and its translation to community setting show the importance of diet and physical activity in the prevention to T2D in at-risk populations (Knowler et al., 2009). As with prevention of type 2 diabetes, exercise in pregnancy may reduce the risk of gestational diabetes by increasing the sensitivity of skeletal muscle to insulin, decreasing oxidative stress, increasing beta-cell function, and by changing body composition (Han et al., 2012; Hawkins et al., 2015).

Callaway et al. conducted a feasibility controlled trial among 50 obese pregnant women in Australia. Women were randomized to an individualized exercise program with an energy expenditure goal of 900 kcal/wk. or to routine obstetric care. Although insulin resistance did not differ between the 2 groups, the intervention arm experienced a modest increase in physical activity. A total of 73% of women in the intervention group achieved >900 kcal/wk. of exercise-based activity at 28 wk. compared with 42% in the control arm ($P = 0.047$) (Callaway et al., 2010).

Sanabria-Martinez et al. (2015) looked at several RCT (2873 pregnant women) with sedentary healthy women or with low levels of physical activity, with singleton pregnancies randomized to a low to moderate intensity exercises-compared to control group with no type of physical activity. Main outcomes observed were GDM and maternal weight gain (MWG).

According to their findings, physical exercise programs during pregnancy decreased the risk of gestational diabetes, particularly when the exercise program was performed throughout pregnancy. Furthermore, decreases were also observed in maternal weight and no serious adverse effects were reported (Sanabria-Martinez et al., 2015). These findings show that a structured moderate physical exercise programs during pregnancy decrease the risk of gestational diabetes mellitus (31%) and diminish maternal weight gain, and seem to be safe for the mother and the neonate. Some of the limitations of this review include that some studies included different diagnosis criteria for GDM. These findings support that practicing physical exercise from early pregnancy is associated with a higher reduction of GDM. This study has important clinical and public health implications, because it provides support for the recommendation to advise mothers to engage in PA programs as an effective and safe strategy to experience healthier pregnancies because they will have less risk of GDM and they will avoid excessive weight gain and, as a consequence, improve the health status of their offspring.

One of the few studies conducted in Latino women was conducted by Hawkins et al. (2015). This trial was conducted to pilot the feasibility of a prenatal lifestyle intervention to modify physical activity and diet among pregnant overweight and obese Hispanic women, with the aim of reducing risk factors for gestational diabetes mellitus. Women were randomized either to a lifestyle intervention (n = 33, 48.5%), consisting of a culturally and linguistically modified, motivationally targeted, individually tailored 6-month prenatal program, or to standard care (n = 35, 51.5%). Bilingual and bicultural health educators encouraged women to achieve guidelines for physical activity (at least 30 minutes every day for most of the days of the week) and decrease saturated fat and increase dietary fiber. The lifestyle intervention attenuated the pregnancy-associated decline in moderate-intensity physical activity, but differences between

groups were not significant. Hawkins et al. findings suggest that a motivationally matched lifestyle intervention is feasible and may help attenuate pregnancy-related decreases in vigorous physical activity in a population of overweight and obese Hispanic women and that the intervention protocol can readily be translated into clinical practice in underserved and minority populations (Hawkins et al., 2015). This study proves to be a good model for future intervention in Latina women, given its retention during follow-up.

Combined Interventions

Dodd et al. (2010) reviewed nine randomized controlled trials involving 743 women who were overweight or obese during pregnancy comparing dietary and/or lifestyle or other interventions compared no treatment for overweight or obese women. This meta-analysis evaluated the benefits and harms associated with the provision of antenatal dietary and/or lifestyle intervention in overweight and obese pregnant women. The primary outcome of the trials was a large-for-gestational-age infant (birthweight >4000g). Women who received an antenatal intervention gained significantly less weight during pregnancy but with no statistically significant differences between women who received an antenatal intervention and those who did not for the large-for-gestational infant outcome or mean gestational weight gain. There was no statistically significant difference identified for other reported outcomes which included mean gestational weight, hypertension, preeclampsia, gestational diabetes, preterm birth (<37 weeks of gestation) (Dodd et al., 2010). Some of the limitations were the uncertainty of both the effect of an antenatal intervention and its optimal intensity significantly limiting the ability to generate reliable recommendation relating to care in clinical practice (Dodd et al., 2010).

Ootsdam, Van Poppel et al. (2011) reviewed previously published data from RCT's to assess the effectiveness of interventions to prevent GDM. Their review summarized data from nineteen studies evaluating six types of interventions (13 evaluated the effects of a dietary intervention, 3 evaluated an intervention with metformin, and 3 evaluated an exercise training program) with a primary outcome of GDM, and relevant secondary outcomes such as maternal fasting blood glucose and large-for-gestational age (LGA) or macrosomia. Low glycemic index (LGI) diet advice and an exercise program significantly reduced the risk of macrosomia. Their results indicate that there may be some benefits of dietary counseling, a low glycemic index (LGI) diet advice, or an exercise program. Ten studies were combined interventions, focused on changing both dietary intake and physical activity. The majority of studies provided healthy eating advice based on national recommendations or nutrition guidelines in general. Two studies provided advice to follow the Dietary Approaches to Stop Hypertension (DASH) diet or Mediterranean diet and two studies targeted certain nutrient components (decrease consumption of high glycemic index and glycemic load of foods). Only one study used a culturally tailored intervention, specifically for pregnant overweight and obese Hispanic women.

A recent systematic review and meta-analysis of diabetes prevention programs (DPP) in the US, conducted by Mudaliar et al., found that such programs targeting lifestyle modification achieved clinically significant weight and cardiometabolic health improvements and were also very cost-effective. These findings confirm that adaptation of diabetes prevention programs in community settings can be achieved, helping a large number of people decrease their risk of diabetes, can be cost-effective and help people live healthier lives (Mudaliar et al., 2016). See table 2 for a summary of studies targeting different lifestyle interventions in pregnant women.

Need for Intervention Programs in obese/overweight Hispanic women

Preventing and managing gestational diabetes is critical to improve the health of mothers and their infants. Latino women are specifically vulnerable to developing this condition because of genetic, social, and environmental factors are at a higher risk. Gestational diabetes has serious and long term consequences for both mother and the baby. These outcomes include, but are not limited to a predisposition to obesity, metabolic syndrome, and diabetes in later life. As with pre-diabetes, early detection and intervention can improve outcomes for women at-risk and their babies. Lifestyle modifications programs have shown to be successful in preventing type 2 diabetes in at-risk populations and are effective in controlling hyperglycemia in women with established gestational diabetes. Given the epidemic of obesity in the U.S. and the relationship between obesity and increased levels of glycaemia, these findings suggest the need for lifestyle interventions targeting maternal pregravid obesity and mildly increased levels of pregnancy glycaemia in order to improve the health of the next Latino generation.

Summary:

The majority of studies have been performed in non-Hispanic white women, thus these cannot be generalized to minority populations, which are disproportionally affected by gestational diabetes. Ethnic minority groups are more likely to experience poorer health outcomes, including higher rates of obesity and GDM. Furthermore, research in the United States suggests that black and Hispanic women are inclined to have excess GWG (Headen et al., 2012).

This review highlights the need and the importance of targeted research on GDM prevention and management in high-risk populations such as Latinas, in hopes that this knowledge will guide interventions that will reduce the incidence of GDM, adverse perinatal

outcomes, and subsequent T2D mellitus in Latina women. Therefore, culturally tailored lifestyle interventions can add to the scant literature on the impact of maternal obesity and ethnic group on pregnancy outcomes. In addition, a tailored intervention targeting the reversal of postpartum weight retention with the aim of reducing pregnancy complications such as GDM in subsequent pregnancies may be a promising in future studies.

Table 2- Studies targeting lifestyle interventions

Reference	Country	Study Type	Intervention	GA-weeks	Population	Outcomes	Results
Barakat, 2009	Spain	RCT	light-intensity resistance exercise training second and third trimester	12-13	Sedentary women N=160 I: n=80 C: n=80	Type of delivery GDM	NS differences
Callaway et al., 2010	Australia	RCT	feasibility of an individualized exercise program to prevent GDM in obese pregnant women	12	N-41 I: n= 22 C:n= 19	GDM	Modest changes in PA. NS differences in GDM
Dodd et al., 2014	Australia	RCT	Does antenatal lifestyle advice improve maternal and health outcomes in OW-obese women	10-20	N=2202 I: n=105 C: n=1097	LGA infants	NS GWG and NS differences in neonatal outcome
Guelinckx, 2010	Belgium	RCT	Does lifestyle intervention on a brochure or active education improve dietary habits, ↑ PA and ↓ GWG in obese pregnant women	<15	N=122 I-passive: n=37 I-active: n=42	Diet, PA, GWG	NS differences in neonatal outcome (macrosomia) between groups
Harrison, 2013	Australia	RCT	Optimize GWG and ↑adherence to IOM recommendations	12-15	N=228 I: n=121 C: n=107	GWG	Maternal: P<0.05 I: 6.062.8 kg C: 6.963.3 kg Neonatal: NS differences
Hawkins, 2015	USA	RCT	Feasibility of lifestyle intervention among OW-obese pregnant women	<18	N=68 I: n=33 C: n=30	Changes in diet and PA	NS maternal outcome or neonatal differences
Price, 2012	USA	RCT	benefits and possible risks of aerobic exercise during pregnancy,	12-14	N=62 I: n=31 C: n=31	GDM	NS difference of GDM, improved delivery outcomes in I group.
Quinlivan et al., 2011	Australia	RCT	Does a 4-step multidisciplinary approach ↓ incidence of GDM in obese pregnant women	1st antenatal visit	N=124 I; n=63 C: n=61	Prevalence of combined decreased GGT and GDM	Maternal: P<0.001 I: 7.0 kg C: 13.8 kg Neonatal: NS differences

Rakhshani, 2010	India	RCT	Effects of yoga in prevention of pregnancy complications in high-risk pregnancies	12	N=68 I: n=30 C: n=38	GDM	Significantly fewer PIH, GDM and IUGR in the I group
Renault et al., 2014	Denmark	RCT	Assess a PA intervention with or without dietary intervention on GWG in obese pregnant women	<16	N=425 I: PA+diet: n= 142 I: PA only: n=142 C: n=141	GWG, obstetrical, and neonatal outcomes	NS between I groups. Intervention reduced GWG in both groups. NS in neonatal outcomes
Stafne et al., 2012	Norway	RCT	Does exercise in second half of pregnancy can prevent GDM and improve insulin resistance in women with normal BMI	18-22	N=702 I: n=375 C: n=327	GDM	NS difference
Thornton, 2009	USA	RCT	Does an active nutritional and behavioral intervention improve perinatal outcomes in obese pregnant women	12-28	N=232 I: n=116 C: n=116	Perinatal outcomes	GDM, 9.5% vs. 16.4% I: n = 116, C: n = 116 Macrosomia (> 4500g), 7.8% vs. 3.4%
Wolff et al., 2008	Denmark	RCT	Does dietary counseling restrict GWG and ↑changes in glucose metabolism in obese women		N=50 I; n=23 C; n=27	GWG, glucose metabolism	Reduced fasting blood glucose in Intervention group vs. control.

Abbreviations: C: control; D: diet; GA: gestational age; GDM: gestational diabetes mellitus; GGT: gestational glucose tolerance; GWG: gestational weight gain; I: intervention; IOM; Institute of Medicine; IUGR: intrauterine growth restriction; OW: overweight; PA: physical activity; PIH: pregnancy induced hypertension; RCT: randomized controlled trial.

Chapter III: Proposal Review Methodology

Introduction

There is no universal method or standard used to evaluate, score, and fund grant proposals (Hinman, 2015; Miner, 2008). There are different types of funding agencies including, but not limited to governmental, non-governmental, non-profit, industry, and others. Despite significant variance among agencies and approaches, a body of best practice knowledge has emerged which can guide funding agencies and researchers regarding the most effective methods for judging funding worthiness regardless of where funding may originate (Hinman, 2015; Miner, 2008). The National Institutes of Health (NIH). NIH is an operational division of the U.S. Department of Health and Human Services (HHS) and acts as a focal point to advance objective grant evaluation, external compliance with policy and legislative mandates. NIH enhances compliance oversight by recipient institutions (HHS, 2016a, 2016b, 2016c). NIH is the largest public funder of biomedical research in the world, investing more than $32 billion a year to reduce illness and disability.

Funding for public health- related grant program sponsored by HHS is done on a competitive basis. In support of its mission, HHS awards grants for more than 300 programs and is the largest grant-awarding agency in the Federal government. Information forecasting grant funded is programs is provided by HHS and is available through Internet access (HHS, 2016c).

Potential Funding

The LOLA proposal included in this thesis will be submitted in response to the funding opportunity announcement-Pragmatic Research in Healthcare Settings to Improve Diabetes and

Obesity Prevention and Care (R18) (http://grants.nih.gov/grants/guide/pa-files/PAR-15-157.html).

The purpose of this Research Demonstration and Dissemination Projects (R18) Funding Opportunity Announcement (FOA) is to encourage research applications to test approaches to improve diabetes and obesity prevention and/or treatment in routine healthcare settings designed to test practical and potentially sustainable strategies to improve processes of care and health outcomes for individuals who are overweight or obese or at risk for becoming overweight or obese and/or at risk for or have type 1 or type 2 diabetes. This FOA seeks research to test the effectiveness of implementable and potentially scalable and sustainable strategies for healthcare delivery to prevent type 2 diabetes in at-risk individuals, improve care for individuals with type 1 and type 2 diabetes, and reduce associated long term complications, or to test the effectiveness of obesity prevention and treatment strategies that can be implemented in primary care settings.

The LOLA grant proposes to identify at-risk Latino women who are pregnant and in their first trimester and start an early lifestyle intervention program. Risks here is defined as women who have one or more predisposing factors to develop gestational diabetes as a measure to further prevent Type 2 diabetes; and these include BMI >25 Kg/m^2. LOLA is designed to be a culturally tailored innovative program that focuses on traditional public health intervention programs such as the Prevent T2 program that is a modification of the national diabetes prevention program (NDPP), which is a CDC-recognized lifestyle change program based on research led by the National Institute of Health (NIH), focused on people with prediabetes who cut their risk of developing T2D. The purpose of this program is to provide education to Latino women starting during their first trimester of pregnancy (≤16 weeks). The main outcome is to limit weight gain throughout pregnancy according to the Institute of Medicine (IOM) guidelines.

This outcome should be achieved with the help of lifestyle changes which include healthy eating and increased physical activity. The lifestyle advice provided is designed to be easily implemented and applicable to everyday life. As a result, GDM and other complications associated with weight gain during pregnancy should be reduced. LOLA will continue to provide education and follow-up in the post-partum period up to 6 months after delivery to determine the longer effects of the intervention as a measure to prevent T2D in Latino women and their offspring.

Five Expert Reviewers

Five highly qualified individuals were selected to be the expert reviewer for the LOLA grant proposal. Their names and titles are summarized in the table below. Dr. Blais is part of the thesis committee.

LOLA Expert Reviewers

Nelson A. Atehortua De la Pena MD., PH.D., MPH. MS.

Department of Public Health and Community Health

College of Science and Health-Utah Valley University

Dr. Atehortua is a bilingual-bicultural public health professional and physician, who after combining clinical, administrative, and academic work; received a Master of Science degree in healthcare management and began his experiences with public health interventions. His passion for public health became manifest after realizing that community-level health education, health promotion, and disease prevention approaches can do more to save lives and spare suffering than clinical approaches. Dr. Atehortua is currently an Assistant Professor in the Department of Public and Community Health at Utah Valley University and a fellow of the Utah Regional Leadership Education in Neuro-developmental and Related Disabilities (URLEND) program.

Catherine Barnes. Ph.D.

Research Associate-Emory University School of Medicine

Dr. Barnes is the co-director of the Diabetes Management Feedback Program (DMFP) at Grady Health System. The DMFP supports diabetes-related performance feedback and decision support flowsheets to providers in the Grady Primary Care Clinics. Dr. Barnes is a Research Grant Reviewer for both the American Diabetes Association and American Heart Association since 2011. She is currently working on hypoglycemia and provider inertia /feedback.

Linelle M. Blais, Ph.D.

Research Associate Professor- Rollins School of Public Health

Dr. Blais is the Executive Director of the Emory Centers for Training and Technical Assistance, and Associate Research Professor in the Department of Behavioral Sciences and Health Education at the Rollins School of Public Health at Emory University. As a health psychologist and certified professional facilitator, her professional goals are to translate science into practice that works through professional development of people, programs and practices. Emory Centers is a CDC recognized training site for the delivery of CDC's National Diabetes Prevention Program's lifestyle change program.

Francisco Pasquel, MD., MPH.

Assistant Professor of Medicine-Emory University School of Medicine

Medical Director, Grady Endocrine Clinic

Dr. Pasquel is an Assistant Professor of Medicine at Emory University. He serves as Medical Director of the Endocrinology Clinic at Grady Hospital. He provides clinical care in the inpatient and outpatient settings. His research focuses on translational studies on primary prevention of type 2 diabetes by lifestyle intervention. Dr. Pasquel is a research reviewer for the NIH and also

participates as an affiliated investigator in the HCHS/SOL (Hispanic Community Health Study/Study of Latinos) study.

Guillermo Umpierrez, MD., CDE

Professor of Medicine-Emory University School of Medicine

Dr. Umpierrez is a member of the National Board of Directors for the American Diabetes Association and the American Association Clinical Endocrinologists, as well as a member of the Endocrine Society Clinical Guideline Committee and American Association Clinical Endocrinologists Diabetes Scientific Council. His research interests include mechanisms for Beta-cell dysfunction in minority populations and the management of inpatient hyperglycemia. He is a national and international leader in the field of hospital management of diabetes and has published several landmark papers and guidelines in the field of inpatient diabetes. His research program is currently funded by the National Institutes of Health and American Diabetes Association, and by investigator-initiated research trials aiming to determine best insulin protocols for the management of hospitalized patients with diabetes. He heads the Emory Latino Diabetes Education Program, a nationally accredited Spanish Diabetes education program dedicated to providing diabetes education to Latinos.

David C. Ziemer, MD., MPH.

Associate Professor of Medicine-Emory University School of Medicine

Dr. Ziemer developed the Grady Diabetes Patient Tracking System, a relational database which has contributed to improving diabetes management and care in the diabetes clinic and, even more importantly, to translating this improved care into the much larger primary care clinic setting at Grady. This clinical relational database has allowed performance feedback and decision-support

recommendations to improve ongoing clinical diabetes care as translated from evidence-based medical studies. Dr. Ziemer is also a research reviewer for the NIH.

Review Criteria and Scoring

Each reviewer will be asked to read, score, and independently comment on all the aspects of the grant proposal, consistent with the guidelines that are contained in the appendix A: LOLA Grant Proposal Scoring Instrument. This appendix was developed to provide reviewers with the detailed instructions, review criteria, and scoring instrument for the LOLA Grant Proposal.

HHS/NIH grant proposals are evaluated according to a Scored Review Criteria (SRC) that has been published in advance of the grant approbation process. This process has some consistency over a number of common elements. In accordance to the funding opportunity announcement procedure, Appendix A was created to score for 1) overall impact; 2) significance; and 3) the specific and additional SCR criteria review factors.

Usually, the Funding Opportunity Announcement (FOA) has five score review criteria: significance, investigator qualification, innovation, approach and environment, and in addition, there are additional non-scored review criteria which are also specified: protections for human subjects, inclusion of women, minorities, and children. In accordance with Appendix A, reviewers will review, as well as score and comment on each element of the grant proposal. All three of these criteria are considered when making funding decisions (HHS, 2016a, 2016b, 2016c; HHS/NIH, 2016).

Although variations are possible, many of the HHS/NIH grant applications use a nine-point scoring system scale for the overall impact/priority score and individual scores for (at least) five scored criteria (HHS, 2016b, 2016c, 2016d; HHS/NIH, 2016). It should be noted that for

many HHS/NIH, the scoring system is somewhat counter-intuitive in that a score of 1 indicates an exceptionally strong application with essentially no weaknesses; whereas a score of 9 indicates an application with serious and substantive weaknesses with very few strengths. Five (5) is considered an average score (HHS, 2016b, 2016c, 2016d; HHS/NIH, 2016).

Determination of scores is purely a reviewer decision. No formula is used to derive the overall impact/priority score from the individual criterion scores, and reviewers are instructed to weigh the different criteria as they see fit in deriving their overall scores and rating in whole numbers only (no decimal ratings permitted (HHS, 2016b, 2016c, 2016d; HHS/NIH, 2016). Also, in terms of scoring system procedures, reviewers score a grant proposal as presented in its entirety, and may not modify their scores on the assumption that a portion of the work proposed will be deleted or modified or revised based upon review guidance (HHS, 2016b, 2016c, 2016d; HHS/NIH, 2016).

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria. In addition to the overall score, reviewers will be asked to provide a paragraph summarizing the factors that informed their overall impact score. NIH indicates that a grant proposal does not need to be strong in all scored categories to be judged likely to have major scientific impact. In their written critique, reviewers will be asked to use bullets to note strengths and weaknesses for each of the scored review criteria. Additionally, reviewers will be asked to write a paragraph summarizing the factors that informed their overall impact score (HHS, 2016b, 2016c, 2016d; HHS/NIH, 2016).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

GDM represents a common and serious health care problem in the U.S. and around the world. Increasing evidence from randomized controlled trials (RCT) indicate that lifestyle intervention programs based on promoting good nutrition and physical activity before and early in pregnancy may lower the incidence of GDM (Yin et al., 2014). Some lifestyle intervention studies have reported improvements in risk factors associated with GDM in Caucasian women (Chasan-Taber, 2015); however, the impact of such intervention in Hispanic women has not been investigated. We believe that screening and intervention programs will have a positive impact not only in limiting weight gain during pregnancy, but also in preventing GDM and its complication in overweight/obese Hispanic women.

Innovation

The LOLA research grant proposes to conduct a randomized controlled study to determine if a linguistically and culturally tailored program that focuses on a modified version of the CDC's National DPP's lifestyle intervention program will result in a higher compliance with the IOM guidelines for weight gain during pregnancy and reduce the rate of GDM and perinatal complications when compared to a standard of care control group in overweight/obese Hispanic women.

The innovative element of this intervention is the implementation of a culturally sensitive lifestyle intervention during pregnancy as an opportunity to promote healthy behaviors with the use of minimally intrusive electronic monitoring of physical activity in pregnancy is not standard practice but could be easily implemented cellular devices or Fitbit as a tool to track progress of eating behavior and physical activity, which have been proven to be a powerful predictor of behavior change.

Moreover, women are often the keepers of culture, the family members who pass on cultural practices, such as what foods are served for holiday celebrations or what activities family members are encouraged to engage in. This responsibility to maintain cultural practices and pass them on to younger generations can make it difficult for a mother to successfully make lifestyle changes. Since evidence suggests that pregnancy provides an opportunity to promote positive health behaviors, which has been branded as a 'teachable moment' in a woman's life, as perceptions of personal risk are increased (Phelan, 2010). In addition, strong emotional responses and a re-definition of their social role and responsibility occurs during pregnancy results in pregnant women to be more motivated in adopting positive health behaviors, such as physical activity (McBride et al., 2003; Phelan, 2010). This proposal seeks to take advantage of this moment to start long-term improvements in both nutrition and physical activity that can impact Hispanic families.

We need to increase screening and education among high-risk groups and institute culturally appropriate interventions that will enhance change in the pre-diabetes years, particularly early adulthood with a focus on interventions that target lifestyle changes—in particular, proper nutrition and adequate exercise.

We need to educate and empower Hispanic women to take control of their own health since overweight/obese Hispanics women are at particularly high risk for GDM and diabetes as a consequence.

Approach

The Lola grant proposal plans to approach patients at both obstetric clinics at Grady Memorial Hospital (GHS) and Centro Internacional de Maternidad (CIMA) where there is a majority of Hispanics patients. Patients will be identified by their obstetric provider and referred to our research team. All participants must have an approval from their regular obstetric provider prior to participation. This will increase awareness among providers to identify at-risk patients.

The program commits to conducting its research consistent with Health and Human Services (HHS) and Emory University guidelines for the conduct of research involving human subjects. All participants will sign an informed consent form to participate in the program. For their protection, participants will be de-identified. Participants can withdraw from participation at any time for any reason.

Environment

Recruitment and retention of patients in the intervention and control group represent the most important challenge; however, based on the large number of patients seen by CIMA and GHS Obstetrics, we anticipate no problems recruiting participants. Our group has previously conducted clinical randomized trials, and educational programs at both facilities, thus, we expect no problems in recruiting patients for this program. To facilitate recruitment and retention, the PI, lifestyle coach, coordinator, and dietician are bilingual professionals with extensive experience in educating and treating minority populations.

Additional Review Criteria

As applicable for this proposed project, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Protections for Human Subjects

The reviewers will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

Inclusion of Women, Minorities, and Children

A total of 120 overweight/obese Hispanic women will be invited to participate into the lifestyle intervention program at their first prenatal care visit. Only women between 18-45 years of age will be invited to participate in this lifestyle intervention education program.

Review and Scoring Procedures

The procedures for reviewing this proposal were developed to conform to the general HHS/NIH grant review guidelines. The HHS/NIH scoring system was designed to encourage more consistent and reliable scoring of applications (HHS, 2016c, d, e; HHS/NIH, 2016). To help ensure process uniformity, reviewers will receive a written copy of review instructions along with a copy of the proposal one week in advance of their rating and comments due date/time. Reviewers will also be given detailed instructions regarding how to conduct the review. Reviewers will carefully consider the rating guidance provided in determining their

scores. Reviewers will also provide comments to improve the communication of scientific and operational information.

Reviewers were asked to spend no less than four and no more than eight hours on their review tasks. No advance or additional preparation was required on their part. Reviewers were instructed that critical, constructive comments were welcomed and expected. Reviewers were also informed that highly rating all sections of the grant—unless warranted—would greatly diminish the ability of author to improve the proposal. No group meeting was be held to arrive at a consensus—as may be typical of the actual grant review processes conducted by HHS or NIH.

Criterion Scoring

Reviewers provided evaluation scoring and written comments relative to three areas: Overall impact; overall significance; and, specific Scored Criteria Review (SCR) review factors. The specific and additional SCR criteria were developed to ensure that the grant proposal contained all of the proper mechanics required to comply with representative grant requirements.

Reviewers used common directions, scoring criteria, and score sheets to provide their ratings and comments. Reviewers independently read and reviewed the proposal, followed all reviewing directions. Each aspect of the grant contained in the score sheet received numerical impact, significance, and the overall impact score based on each individual reviewer‘s assessment. The overall impact score includes significance and SCR criteria. SCR criteria were scored; additionally, reviewers were asked to provide bulleted discussion notes explaining each rating. Reviewers were instructed that providing scores without providing comments in the review critique is discouraged—the rational for rankings and notations regarding strengths, weaknesses and areas for improvement need to be clearly indicated.

Reviewers were instructed that they were free to use the full range of the rating scales values, as appropriate, to better discriminate the strengths and weakness of each section. Reviewers were to feel free to assign the score that they believed best represents the impact of the application, and not feel constrained to limit their scores to the upper half of the score range if they did not feel such a score was warranted.

Reviewers were asked to score each review criterion based on how important they feel each review criterion is to the work as being proposed. Per the typical HHS/NIH guidance, a reviewer may give only moderate scores to some of the review criteria, but still give a high overall impact/priority score. A proposal does not need to be strong in all categories to be judged likely to have major impact, e.g., a project that by its nature is innovative may be essential to advance a field. Conversely, a reviewer could give mostly high criterion ratings, but rate the overall impact/priority score lower because, based upon their experience, they found one criterion critically important to the proposal. Table 4: HHS/NIH New Grant Scoring Rubric illustrates the criteria used by the reviewers to score the grant proposal.

Table 4: HHS/NIH New Grant Scoring Rubric

Impact	**Impact/Priority Score**	**Descriptor**	**Additional Guidance on Strengths/Weaknesses**
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Moderate	4	Very Good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but with at least one major weakness

	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths and numerous major weaknesses
Definitions			
Minor: easily addressable weakness that does not substantially lessen the impact of the project. Moderate: weakness that lessens the impact of the project. Major: weakness that severely limits the impact of the project			

Reviewers were asked to consider if the proposal appropriately translates technical terms and processes for non-experts in any specialized areas discussed in the proposal. Of particular note is the ability to demonstrate how this proposal was relevant to limit weight gain during pregnancy and prevent the development of gestational diabetes. Other aspects included judgments regarding the capabilities of the overall capabilities represented in the proposal.

Chapter IV: Proposal Review Results

I would like to express my sincere thanks to the expert reviewers who had taken their time and commitment to provide scientific and excellent critiques of the LOLA grant proposal. Their diligent assessment and feedback is as valuable as they are experts in this topic area and provided comments to improve this proposal. Thanks to their input I was provided an immense opportunity for professional growth and learning.

Scores provided by the reviewers for the overall significance ranged from one (1) to six (6), overall innovation from one (1) to seven (7) and for overall impact from one (1) to six (6). In the Master Scoring Rubric, a score of one (1) indicates an exceptionally strong response with essentially no weaknesses; whereas a score of nine (9) indicates an application with serious and substantive weaknesses with very little strength. Five (5) is considered an average score. All of their critiques and recommendations which are described below were taken into consideration to improve this proposal.

Reviewer 1 comments:

Significance

Comment 1: *The proposal of Dr. Cardona is very well written and addresses a major public health problem. Diabetes is a major epidemic and Hispanics are at higher risk of pre-diabetes and diabetes. An approach tailored to prevent gestational diabetes in very high-risk women does not only have a short-term impact potential but could also prevent or delay diabetes following delivery. The implementation of CDC's PreventT2 curriculum for high-risk pregnant women in a RCT, with the aid of low-cost technology is a major strength.*

The randomized nature of the study with the included inclusion exclusion criteria can limit the generalizability of RCTs when the aim is to "translate what works", however the included criteria in the proposal would likely exclude only a minority of pregnant women.

Response to Comment 1: No response required.

Comment 2: *No major weaknesses identified.*

Response to Comment 2: No response required.

Innovation

Comment 1: *The proposal includes a program to address a public health problem in very high-risk individuals (overweight Hispanic women) implementing a culturally sensitive lifestyle intervention with the use of cell phones or Fitbits to track performance.*

Response to Comment 1: No response required.

Comment 2: *No major weaknesses identified.*

Response to Comment 2: No response required.

Approach

Comment 1: *A randomized controlled trial will allow balancing potential confounders in both groups. Recruitment and implementation seem very feasible.*

Response to Comment 1: No response required.

Comment 2: *Clarify in assessment measures of compliance section how often compliance will be measured. Revise inclusion criteria in section VII to match criteria previously described. Instead of withdrawing patients from the study if GDM is diagnosed (as mentioned in Section IV.D.), consider continuing tracking performance and evaluating after delivery to evaluate the proportion of patients that regress to normoglycemia. Include in the appendix a summary overview of CDC's PreventT2 curriculum*.

Response to Comment 2: Compliance measure will take into consideration how often the tracking devise (Fitbit) was used, we will also take into consideration the questionnaires (food and physical activity). This has been further clarified in the proposal.

Inclusion criteria in section VII was removed, instead, in the human subjects section a sentence now refers to section in methods V.B.2 describing eligibility criteria. To make the intervention more translational in the selected population, the inclusion criterion of sedentary lifestyle was removed.

In section V.D. of methods, the research design was modified by removing the sentence that if patient developed GDM would be withdrawn from the study. Patients who develop GDM will be referred to maternal-fetal specialists, and if specialist agrees that patient can continue participation, we will continue to follow and monitor remission in the post-partum period. A summary of current Prevent T2 program has been added to section V.D.

Environment

Comment 1: *This is a major strength of the proposal as it proposes to take advantage of an established program (Emory Latino Diabetes Program) and recruitment will be conducted at centers with an expected number of pregnant Hispanic patients*.

Response to Comment 2: No response required.

Overall Impact

Comment 1: *The proposal aims at reducing the risk of gestational diabetes in high-risk women, and will reduce disparities with a culturally sensitive approach in Hispanic women (who commonly experience disadvantages related to diverse socio-economic, language and cultural factors).*

Response to Comment 1: No response required

Additional Criteria Strengths:

Comment 1: *The proposal is designed to address a major public health problem in minority women.*

Response to Comment 2: No response required.

Reviewer 2 comments:

Significance

Comment 1: *The data provided to support the public health problem of gestational diabetes in Hispanic women in overweight/obese women, their babies and their increased risk of type 2 diabetes adequately demonstrates the significance of the area of study.*

Response to Comment 1: No response required.

Comment 2: *The argument for using evidence based lifestyle intervention for weight control, physical activity in this population is discussed.*

Response to Comment 2: No response required.

Comment 3: *Perhaps some language around potential estimated impact of proposed intervention on population, cost-benefits, or other assumptions might have strengthened this section.*

Response to Comment 3: The reviewer's comment is a valid point in order to establish if a potential intervention provides cost-effective benefits, there should also be information about implementations costs and benefits. Unfortunately there are no studies reporting on cost related to perinatal complications associated with pre-pregnancy overweight/obesity and excessive GWG. A post-hoc cost-analysis can be performed in this cohort of patients and analyze resource utilization and hospitalization costs and determine if there is a difference among intervention and

control groups. The objective of this proposal is to determine if a lifestyle intervention program started in early pregnancy will increase the percentage of pregnant overweight/obese Latina who adheres to IOM recommendations for weight gain during pregnancy when compared to standard of care. Adherence to IOM GWG guideline would result in a decrease of perinatal complication associated to pre-pregnancy obesity and excessive gestational weight gain such as gestational diabetes, pre-eclampsia, preterm labor and delivery, the need of cesarean delivery, translating in a decrease in health costs. It is well known that the obesity epidemic which affects millions of Americans (including Latinos), contributes to increasing health costs (Cawley & Meyerhoefer, 2012; Finkelstein, Trogdon, Cohen, & Dietz, 2009; Teuner et al., 2013). We hypothesize that if the lifestyle intervention is successful, especially in the post-partum period, the benefits will extend beyond pregnancy in decreasing health costs associated to overweight/obesity.

Innovation

Comment 1: *The innovation here is the application of evidence based lifestyle change program tailored and targeted at a specific high risk audience – overweight/obese Latinas at high risk for gestational diabetes, and the addition of mobile technology as a tool to track progress. Tracking eating behavior, physical activity and weight change has been proven to be a powerful predictor of behavior change. Counselor calls is also an enhancement to the National DPP lifestyle change program.*

Response to Comment 1: No response required.

Comment 2: *The importance of diet and physical activity in controlling glucose concentrations in women with GDM has been established, however it is not known if similar results can be obtained when such interventions are carried out before onset of impaired glucose, making this a potential value to the field.*

Response to Comment 2: No response required.

Comment 3: *The approach and intervention isn't inherently novel as much as an adaptation of existing intervention methodologies to a needed audience.*

Response to Comment 3: The innovation in this proposal is the translations of the successful Prevent T2 program to a different target population. Patients diagnosed with GDM which is associated with pre-pregnancy overweight/obesity (Chasan-Taber et al., 2010) are a higher risk to develop T2D (C. Kim, 2014) for this reason this thesis proposes to approach these patients and adapt the successful Prevent T2 in a phase of their lives when they can make changes (McBride et al., 2003), have access to and more frequent contact with the healthcare system.

Another innovation is the use of objective, minimally intrusive electronic monitoring of physical activity in pregnancy, which is not standard practice, but could be easily implemented. This can open the door for use of "wearable technology" for other monitoring functions as well if subjects are adherent. The proposal design has been modified to make this clearer in the innovation section.

Comment 4: *Might want to discuss rationale for enhancements to lifestyle change program.*

Response to Comment 4: Prevent T2 is a modification of the original DPP which is evidence based (Knowler et al., 2002) and focuses on patients with pre-diabetes. The program is tailored to non-pregnant women and requires weekly participation. We understand that during pregnancy women will require to keep their regular obstetric appointments which may interfere with their regular work, school or family schedule, for this reason we will adapt the Prevent T2

program to have biweekly phone calls to participants in the intervention group, to encourage participants to keep engaged in the lifestyle intervention. Another modification is to have a nutritionist who will also be trained as a lifestyle coach. The nutritionist will meet and counsel participants in the intervention group about the caloric requirements taken into consideration for fetal growth and development. In the intervention group participants will see a nutritionist when enrolling the program and as needed during pregnancy if weight gain goals have not been met. Our hypothesis is that the adherence to IOM weight will prevent excessive GWG and result in fewer complications.

Approach

Comment 1: *The investigator demonstrates appropriate partnerships with CIMA and Grady Health Systems for making recruitment and research implementation feasible*.

Response to Comment 1: No response required

Comment 2: *Randomized control clinical trial design seems strong.*

Response to Comment 2: No response required.

Environment

Comment 1: *The clinical environment supports similar programs in past and would seem most convenient to the patient for participating in the study.*

Response to Comment 2: No response required.

Overall Impact

Comment 1: *Prevention impact on those Latinas at risk for GDM is high and will have potential impact on their incidence of type 2 diabetes in the future and on the health of their children.*

Response to Comment 1: No response required.

Comment 2: *Enhancement of additive components of the intervention over and above the National Diabetes Prevention Program to include counselor calls and mobile tracking.*

Response to Comment 2: No response required.

Comment 3: *Need to address issue of patients enrolling in group program such that all start within the same window of time so that the intervention is the same for each patient.*

Response to Comment 3: We anticipate that we will be able to recruit 2-4 participants per week. Since patients will be approached during their first obstetric visit, we anticipate that participants will be at similar gestational age and will be able to know each one other better and establish a support group throughout their pregnancy.

Comment 4: *Need to consider what dose of the intervention is minimal to say the intervention was delivered.*

Response to Comment 4: The plan is to conduct an intention to treat analysis. All patients who participate in at least one in-person class will be considered in the analysis. A sensitive analysis will allow determining the minimum intervention required to successfully adhere to IOM guidelines in regards to gestational weight gain.

Comment 5: *Potential costs related to group based programs plus counselor calls plus tracking device may not be scalable due to costs (as was found in the original National DPP studies).*

Response to Comment 5: Reviewer is correct that there is an additional cost when recommending using Fitbit devices and the extra counselor calls. For this reason we also propose to use cellular devices. Many cellular devices have built in applications that allow to track physical activity among other activities, and since many participants have a cellular device

instead of a landline. There may be an advantage to teaching them how to use these built in applications to track not only physical activity, but eating habits, sleeping hours, etc. It is known that resource requirements severely restrict widespread implementation of lifestyles interventions in primary care practices and for this reason our intervention will be a modification of the Prevent T2 program. There has been recent a publication from a RCT suggesting that weight loss in some individuals can be achieved and maintained by the use of novel written material with brief nurse follow-up, but more people can maintain clinically important weight reductions with a web-based behavioral program and brief remote follow-up with no increase in health service costs (Little et al., 2016). In the future, a combined online intervention can be planned and assessed in this target population.

Additional Review Criteria

Comment 1: *Inclusion/Exclusions seem appropriate.*

Response to Comment 1: No response required.

Comment 2: *Minimal risks and precautions provided, including DSMC*.

Response to Comment 2: No response required.

Reviewer 3 comments:

Significance

Comment 1: Aims are feasible and achievable**,** addresses an important problem for Hispanic mothers, Public Health and Health Education will be improved and successful completion might be favorable impact preventative interventions in this area.

Response to Comment 1: No response is required.

Comment 2: *Aims need to be refined linking them more specifically with hypothesis and expected changes. It is not clear what amount of change would be considered significant.*

Response to Comment 2: Aim 1 in the proposal has been modified to express that we would like to achieve an increase of at least a 50% of women who adhere to IOM GWG recommendations. This was taken into consideration when calculating the sample size calculation in the power and sample size of proposal.

Innovation

Comment 1: *A proposal to improve current practice by culturally translating an existing program. Utilization of a validated approach and instrumentation.*

Response to Comment 1: No response required.

Comment 2: *Needs to describe the existing program in a clearer way.*

Response to Comment 2: Addressed in response to comment 4 in the approach section of first reviewer. Section V.D has now a summary of current of the Prevent T2 program in the proposal.

Approach

Comment 1: *Overall strategy, methodology, and analysis are appropriate, with appropriate partnerships. Resources and infrastructure are adequate. There is a proper description of subjects, inclusion and exclusion criteria.*

Response to Comment 1: No response required.

Comment 2: *Letters from support from partners should be included.*

Response to Comment 2: At this stage of the grant proposal preparation**,** the only document provided to experts for review is the research design. The applicant organization will supply the required letters of support and endorsement at time of grant application.

Comment 3: *Sustainability in the long run has to be addressed.*

Response to Comment 3: If positive results are observed, a policy that addresses the implementation of this strategy should be considered. Policy should address coverage and reimbursement by health insurance as there are current reimbursement and/or coverage for referral of patients with pre-diabetes to a certified diabetes prevention program. A key factor to the sustainability of the program is to implement a protocol to provide proper training of medical personnel involved in patient's care. Requirements by CDC are to undergo specific training to become a lifestyle coach. All obstetric and primary care clinic providers should be able to deliver prevention messages and behavior change supports for gestational weight gain, gestational diabetes, and diabetes prevention. This can be done through narrative, supportive, and educational messages combined with a short follow-up health coaching by trained bilingual (if needed) staff and referrals to community-accessible resources (social networks, health coaches, and other community resources). Short phone follow-up calls for re-enforcement of the prevention message. This intervention should extend to the post-partum period to encourage women to continue proper lifestyle changes.

Environment:

Comment 1: *Scientific environment is a plus. There seems to be experienced personnel at all levels. There is a cultural and linguistic support already in place.*

Response to Comment 1: No response required.

Overall Impact:

Comment 1: *Define changes as to what would be considered significant to modify existing standard of practice.*

Response to Comment 1: Only 30% of pregnant women adhere to current IOM GWG recommendations; about the same percentage of women achieve pre-pregnancy weight at approximately 6 weeks post-partum. A clinically significant change can be defined as at least 50% of women in the intervention group achieving recommended IOM guideline and return to their pregnancy weight at 3 months post-delivery. If this percentage is achieved and it is associated with positive findings, it would be considered a clinically significant change which can suggest modifying existing standard of practice.

Additional Review Criteria

Comment 1: *Protections for an especial group clearly outlined. Benefits for subjects and others in the study, if successful, benefits for Hispanic mothers down the road and knowledge to be obtained is important.*

Response to Comment 1: No response required.

Reviewer 4 comments:

Significance

Comment 1: *There are many strengths in this proposal:*

- *Specific Aims are clear. Hypotheses serve as a starting point for further investigation.*
- *The 6-point headings in significance section cover important and comprehensive issues.*
- *The table, study design algorithm and data collection visits tables are all helpful in better understanding the proposal.*
- *CDC and IOM population facts / references are up-to-date.*
- *Settings appear excellent sources for study population recruitment and intervention.*

- *IPAQ-L and General Nutrition Knowledge Questionnaire are well validated.*
- *Statistical plans seem well thought-out.*

Response to Comment 1: No response required.

Comment 2: *My question is "is this a current problem?" These references are over 10 years old. What research has been completed recently (or not)? If there is no published data, this represents a definite need (a plus for the need for the study) – but this should be explained and clarified.*

Response to Comment 2: GDM constitutes a major health problem which affects 9.2% of all pregnancies (DeSisto et al., 2014) and is associated with a significant increase in both maternal and perinatal morbidity (CDC, 2013b). In addition, women with GDM have increased risk of developing T2DM after pregnancy (Bellamy et al., 2009). Most of the current available literature on prevention of GDM has been conducted in Caucasians and limited studies have included Hispanics (Fujimoto, 2013; Oostdam et al., 2011; Streuling, Beyerlein, & von Kries, 2010; Tieu et al., 2008). Few studies have been performed on the feasibility of lifestyle intervention in Latinas to prevent GDM (Chasan-Taber et al., 2011). Research that has been done on this topic is not generalizable to this specific group. There is literature available in Latinas once they have been diagnosed with GDM and how to prevent diabetes in patients with previous history of GDM (Chasan-Taber, 2012, 2015; Perez et al., 2015). Hispanic people also are the most physically inactive US ethnic group (C. Kim, 2014) and have disproportionately high levels of overweight and obesity rates (U. S. Census, 2015), gestational diabetes and diabetes (Fujimoto, 2013); however, despite the increasing Hispanic population and the observed health disparities, relatively few prevention studies have included Hispanic women. This information has been further clarified in the proposal with citations.

Innovation

Comment 1: *Addressing the needs of this high risk Hispanic population is important and needed. Using pregnancy as an opportunity for promote healthy behaviors is certainly a great idea.*

Response to Comment 1: No response required.

Comment 2: *The ideas presented in this proposal are interesting and potentially helpful, but the case is not made that the intervention is new or original. Have lifestyle interventions for GDM been investigated in the past 10 years? Is there any information to show impact or breakthrough ideas? It is stated (Innovation) that "increasing evidence indicates that modification of exercise and nutrition is safe and effective in controlling excessive weight gain during pregnancy…", but this information is not referenced.*

Response to Comment 2: The references for this statement have been added to the proposal (Sanabria-Martinez et al., 2015; van Poppel, Ruchat, & Mottola, 2014)

Comment 3: *What interventions make this study novel?*

Response to Comment 3: Addressed in response to comment 3 of reviewer 2 in the innovation section. The innovation in this proposal is the translations of the successful Prevent T2 program to a different target population. Patients diagnosed with GDM which is associated with pre-pregnancy overweight/obesity (Chasan-Taber et al., 2010) are a higher risk to develop T2 (C. Kim, 2014) for this reason this thesis proposes to approach overweight/obese pregnant patients and adapt the successful Prevent T2 in a phase of their lives when they can make changes (McBride et al., 2003), have access to and more frequent contact with the healthcare system.

Another innovation is the use of objective, minimally intrusive electronic monitoring of physical activity in pregnancy, which is not standard practice, but could be easily implemented.

This can open the door for use of "wearable technology" for other monitoring functions as well if subjects are adherent. The proposal design has been modified to make this clearer in the innovation section.

Approach

Comment 1: *Preliminary data: Except for graphs, this section was well written and clear.*

Response to Comment 1: No response required.

Comment 2: *Randomization: Well thought out; blocked randomization will ensure a better comparison based on weight.*

Response to Comment 2: No response required.

Comment 3: *Methods / Experimental Plan: Study Design Algorithm and Schedule of Data Collection Visits helpful charts.*

Response to Comment 3: No response required.

Comment 4: Recruitment: *Very little information about how subjects will be recruited. More recruitment detail needed – step-by-step.*

- *How / where will the subject be approached? In the waiting room? In the office? Called beforehand?*

Further clarifications were added to the proposal. A standardized process will be put in place to screen and recruit patients. Clinic schedule will allow for study personnel to pre-screen and identify possible participants in advance. We will notify provider of participant's eligibility to participate in the study. We will only approach participants after they have seen their provider to ensure that they are able to participate in this trial and not interfere with the regular clinic flow.

- *How long will the consent and preliminary questionnaires take? Will this impede the clinic flow?*

The consent will depend on the participants' health literacy. We anticipate that this process can take a maximum of 30 minutes to answer all the participants' question. Participants will only be approached after patients have seen their provider to make sure there are no limitations that would prevent participation from in the lifestyle intervention.

- *How will the study staff be trained?*

Personnel providing study intervention, including nutritionist, will undergo the required CDC training provided by the Diabetes Training and Technical Assistance Center (DTTAC) at Emory University to become a CDC certified lifestyle coach.

To ensure retention the control group participants will get mailed material focus on non-exercise and non-dietary topics and booklets from ACOG and American Academy of Pediatrics (English or Spanish).We will also offer incentives, such as grocery gift cards, gifts, cash, food, recipe books, and exercise equipment for intervention attendance or completion at each data collection point. We are committed to also establish a program bonds with participants by building staff–participant relationships, and regular communication with participants, such as thank-you notes, postcards, or program newsletters. If needed, we'll also provide assistance to transportation to and from intervention activities or data collection, make-up sessions for missed intervention sessions, and optional days or call visits for data collection. To facilitate tracking participants, complete contact information will be collected from participants at baseline and a tracking database established. We will send personalized letters to participants who are difficult to reach, to schedule data collection appointments.

Environment

Comment 1: *The Grady Health System and the CIMA both show accessibility of personnel, facilities and infrastructure required to conduct the research. Environment is excellent. It does appear that the applicant can accomplish the research as proposed, based on her access to needed resources. In addition, the ELDEG program, supported and accredited by the AADE, offers an excellent foundational source for data and outreach for this proposal.*

Response to Comment 1: No response required.

Comment 2: *Letter of support from both agencies is needed to make sure they are available settings.*

Response to Comment 2: At this stage of the grant proposal preparation**,** the only document provided to experts for review is the research design. The applicant organization will supply the required letters of support and endorsement at time of grant application.

Overall Impact:

Comment 1: *Overall Impact Hypotheses are explicit. The project seems feasible; a timeline would be helpful. Reviewer was engaged. Compelling reasons were given and interest in the project was peaked. There is potential for a significant contribution to the improvement of Hispanic's health in Atlanta / Georgia to the development of more effective health services and products.*

Response to Comment 1: A project timeline has been added to proposal.

Comment 2: *It is not clear, from reading this proposal, that GDM is <u>currently</u> a significant problem or a represents a gap in health research and the health care system.*

Response to Comment 2: Previously addressed in the response to comment 2 of this reviewer in the innovation section.

Comment 3: *Appropriateness and adequacy of the proposed plan for knowledge dissemination and exchange was not discussed.*

Response to Comment 3: This section has been added with the plan for dissemination of results and findings. Dissemination of findings will focus primarily on communicating research results by targeting and tailoring the findings and the message to the particular target audience. As we move along we will send periodic results to the Prevent T2 program since we will be modifying their curriculum. The program investigators will submit abstracts for presentation at regional and national meetings. We will share all lessons learned with both GHS, CIMA personnel. We will submit abstracts sharing our results at local and national meetings. We will also submit manuscripts to peer-reviewed journals.

Additional Review Criteria:

Comment 1: *The inclusion of women and minorities is clearly addressed in the proposal. Subjects under 18 years of age will not be included in the study.*

Response to Comment 1: No response required.

Reviewer 5 comments:

Significance

Comment 1: *Development of gestational diabetes and weight gain have potential for severe complications and long-term development of diabetes with its costs and complications. Success with this intervention could reduce the near term GDM consequences but also prevent*

future diabetes. This intervention may have benefit of creating long-term behavioral changes and possibly changes in family as well that may have wider impact than just the current pregnancy. This is a higher risk population where absolute effects for a given fractional change will be higher.

This is cast as pilot study; this improves significance. Proving feasibility will strengthen an application for a fully powered study with more robust measures. This to large extent obviates concerns about power discussed below.

Choice of excluding those after 16 weeks is a two edged sword. It gives maximal exposure to the intervention and optimizes chance of demonstrating efficacy and optimizes the study cost to potential effect ratio.

The use of objective electronic physical activity monitoring is affordable and scalable to large populations. If successful this could be a fully generalizable intervention for pregnancy to all populations with benefits to multiple populations.

Response to Comment 1: No response required.

Comment 2: *Choice of excluding those after 16 weeks decreases the potential reach and impact of the intervention (effectiveness).*

Response to Comment 2: The goal of this proposal is to begin a lifestyle intervention as early as possible during pregnancy with a better chance of longer exposure to the intervention and most likely better results. It could be modified to start intervention up to 20 weeks of gestational age, and document results of lifestyle intervention depending on (exposure and length) gestational age at which program was started. Later than 20 weeks of gestational age would probably not have such impact as, screening for GDM usually takes place between 24-26

weeks of pregnancy; at this point the effect of the intervention will be lower and patient has less time left in pregnancy to access healthcare.

Innovation

Comment 1: *While not justified by the narrative, linguistically and culturally competent interventions are in short supply and very much needed. Such programs themselves are not new as evidenced by the ELDEP, but use in pregnancy is not common. The use of objective, minimally intrusive electronic monitoring of physical activity in pregnancy is not standard practice but could be easily implemented. It opens the door for use of "wearable technology" for other monitoring functions as well if subjects are adherent.*

Response to Comment 1: No response required.

Comment 2: *Such programs themselves are not new as evidenced by the Emory LDEP, but use in pregnancy is not common.*

Response to Comment 2: The program is an adaptation of the online Prevent T2 program**.** The purpose of this proposal is to translate into practice a program similar to ELDEP tailored to pregnant overweight/obese Latina women with the goal to educate and empower these women and to prevent a gestational risk which would also be an additional risk for future development of T2D. In addition, we are taking advantage and opportunity to intervene during pregnancy which is considered as a teachable moment (McBride et al., 2003) and opportunity to start healthy habits. It is also a period where women have access to healthcare and more frequent encounters with the health system.

Approach

Comment 1: *Intervention has high likelihood of success given the extensive support in non-pregnant populations who already had linguistically and culturally appropriate interventions. Starting early in pregnancy is a wise compromise to maximize chances for effect. Choosing an easily measured, standard outcome measure of weight is good. Supplementing that with an objectively measured mediating behavior (physical activity) is also an excellent choice.*

Response to Comment 1: No response required.

Comment 2: *Choice of excluding those after 16 weeks decreases the potential reach and impact of the intervention (effectiveness).*

Response to Comment 2: Previously addressed in response to comment 2 in significance section of this reviewer. Proposal has been modified to include women up to 16 weeks of gestational age; further gestational age will decrease the length and exposure to intervention that will probably reduce the effect of intervention (less exposure time).

Comment 3: *I was unable to find compliance with wearing of the Fitbit as a measure. Ideally the control group would wear Fitbit that recorded but did not provide data to the subject. Compensation for inconvenience would improve adherence with this measure.*

Response to Comment 3: Each participant's Fitbit will be linked to the Fitabase analytics system (Small Steps Labs, San Diego, CA, USA), which will enable the investigators to remotely monitor physical activity. Fitabase daily totals for steps and intensity-specific minutes of physical activity (PA) will be downloaded periodically. Fitabase data allows gathering data in near real time as devices sync and updating your Fitabase dashboard. This clarification has been added to the proposal in section V.H.-Assessment of physical activity.

Comment 4: *Dose of the intervention is diminished compared to the original DPP. Given the short-term for the effectiveness of the intervention a more intense intervention would* be *a better test of the concept. This is especially important given the small sample size and implications of negative outcomes on future application for this very promising intervention.*

Response to Comment 4: This will be an adaptation of the Prevent T2 program which will allow patients to have additional resources and work on their own. We understand that during pregnancy women will require to keep their regular obstetric appointments which may interfere with their regular work, school or family schedule and for this reason we will adapt the Prevent T2 program to have biweekly phone calls for participants to keep engaged in the intervention lifestyle. Information collected by participants during these weeks will be reviewed by lifestyle coach during the face to face visit. There has been recent a publication from a RCT suggesting that weight loss in some individuals can be achieved and maintained by the use on novel written material with brief nurse follow-up, but more people can maintain clinically important weight reductions with a web-based behavioral program and brief remote follow-up with no increase in health service costs (Little et al., 2016).

Comment 5: *Choice of withdrawing those who progress to GDM is questionable move. Continuing the intervention (with approval of Special OB) would give chance to observe an increase in DM remission post-partum among those in intervention and to observe weight and complication effects. While this number is likely to be small it will still add to what is likely going to be a crippling attrition rate. Overall weight changes are likely to be small and non-durable based on interventions in other populations. Incidence of GDM is small so Aim 2 is likely to be underpowered. For those with excess weight gain complication rates are likely dose*

dependent and complication rates a fraction of those with weight gain; this will make Aim 3 underpowered as well.

Response to Comment 5: In section V.D. of methods, the research design was modified by removing the sentence that if patient developed GDM would be withdrawn from the study. Patients who develop GDM will be referred to maternal-fetal specialists, and if specialist agrees that patients can continue participation, we will continue to follow and monitor remission in the post-partum period.

Comment 6: *Training and assurance of quality and consistency of life coaches is not described. Will dietitian and exercise expert be involved in training?*

Response to Comment 6: Participants in the intervention group will be seen by a dietitian as described in the healthy eating section (page 10). In order to aim for weight maintenance during gestation and at the same time allowing sufficient caloric intake for fetal growth and development, calorie goals of 25 kg/cal per day will be set. Participants in the intervention group will meet with a dietitian (trained also as a lifestyle coach) during first visit for a nutrition assessment. Further monitoring and evaluation will also be performed by the nutritionist. In addition, a clarification has been added in the design that lifestyle coaches are CDC trained lifestyle coaches. The training to the study team will be provided by the Diabetes Training and Technical Assistance Center (DTTAC) at Emory University. Dietitian will also be trained in by DTTAC.

Comment 7: *Food questionnaires are notoriously inaccurate. It appears different measures will be used in the control and intervention groups. This will weaken comparisons.*

Inclusion of dietitian assessments should be considered to strengthen nutritional mediator assessment.

Response to Comment 7: In order to aim for weight maintenance during gestation and at the same time allowing sufficient caloric intake for fetal growth and development, calorie goals of 25 kg/cal per day will be set. Participants in the intervention group will meet with a dietitian (trained as lifestyle coach) during first visit. Questionnaires will be same for both the intervention and control group. They will be provided at the same time points (beginning, mid-pregnancy and during last trimester) and the intervention group will complete the questionnaire prior to each in-person session. Questionnaires will be provided in advance and participants will be reminded to complete it prior to their visit. The monitoring and evaluation will be performed by the nutritionist. This clarification has been added to the proposal.

Environment

Comment 1: *The environment is exceptional. There is an established educational group that is linguistically and culturally appropriate. The educators are high quality and experienced. There is a well-trained, experienced research team who are used to quality data collection and analysis. The population is already in a clinical setting of trust with whom the team has already been working. The size is of the appropriate population is more than adequate to the study requirements. Resources of dietitian and life coaches are readily available if desired (to address prior questions)*

Response to Comment 1: No response is required.

Overall Impact:

Comment 1: *Potential impact is very high given the significance and high theoretical likelihood of intervention's success and the very high likelihood of the team being able to demonstrate that success. The high risk population to be studied is growing rapidly in this country and has been underserved in general which increases the complication rate and subsequent societal costs.*

Response to Comment 1: No response required.

Comment 2: *Magnitude of weight changes is not likely to be dramatic thus limiting the downstream effects. Future implementation of successful intervention will be limited by delayed access of this population to care, financial limitations that will limit healthy food access, and shortage of teams and trainers for teams to deploy the intervention widely. Thus sustainability may be an issue.*

Response to Comment 2: The primary aim is the percentage of women who adhere to IOM gestational weight gain guidelines; additional aim will be the percentage of women who can achieve pre-pregnancy weight at three (3) months post-delivery.

The intervention is designed to be implemented during early pregnancy, given that knowledge of pre-pregnancy weight status and perceived value of a healthy GWG can be a predictor of limitation of weight gain during pregnancy (Ledoux et al., 2015). During this time participants will receive frequent education and information about expected gestational weight gain and consequences of excessive weight gain, healthy eating and physical activity. Future policy recommendations should include that all obstetric patients be educated independent of on

expected weight gain and pregnancy complications associated to excessive GWG and its future implications beyond pregnancy.

Sustainability was previously addressed in response to comment 3 in the approach section of reviewer 3.

To address financial limitations that would limit healthy food access, we plan to connect women to free community programs and services, and also referral to the Women, Infant, and Children's (WIC) programs.

Additional Review Criteria:

Comment 1: *Need for linguistically and culturally appropriate intervention was taken as given, but data to support this need should have been cited.*

Response to Comment 1: Cultural competence strategies which are critical to creating a hospitable setting during the intervention will be leveraged to address behavioral change facilitating health care connections to communities, and creating a safe, nurturing health care environment in which health can flourish. Overall, the more widespread use of cultural leverage interventions is likely to improve racial disparities in health care (Fisher et al., 2007). Linguistically tailored interventions have been shown to be successful in the treatment of certain chronic conditions as it was found by in the *Latinos in Control* trial by Rosa et al., who found that literacy-sensitive, culturally tailored interventions can improve diabetes control among low-income Latinos (Rosal et al., 2011; Rosal et al., 2009). Our group at Emory Latino Diabetes Education Program (ELDEP) has been shown to be a successful education program for low socio-economic Latino patients with diabetes (Rotberg et al., 2016). DTTAC has the advantage

to provide the Spanish-Language Lifestyle Coaching Training. References supporting this affirmation have been added in the proposal.

Comment 2: *The preliminary data graphs and table are not explained well and nearly undecipherable. What is the significance/meaning of Class 1 Class 2 and "Yes" "No" groups. Are comparisons between these groups pertinent to the application? Little to no use in the text seems to be made of the data in Table 1. Nothing regarding the foods listed is explained o tied into the narrative.*

Response to Comment 2: Previous graphics in the proposal have been removed and replaced by clearer ones; explanations have been provided within the context referring to the graphics.

Comment 3: *Distinction of which measures/procedures are to occur in the two different groups is not easily discerned in the table or text. The aims should be consistent in each spot. Sometimes they include the mediators (PA, nutrition) or follow-up measures. In other spots they do not.*

Response to Comment 3: Procedures were described clearer throughout the proposal. Control group will only receive printed materials during their regular obstetrical care. Intervention group will have biweekly calls, monthly visits, and receive education based on the Prevent T2 curriculum.

Summary:

The purpose of the Specific Criteria Review Factors scoring was to ensure that the proposal was fully compliant with a typical Health and Human Services (HHS) grant proposal content template. There was remarkable consistency in the overall comments relative to template compliance

and content. While the scores varied the overall patterns of observation among reviewers was consistent. The experts reviewers provided overall significance and impact scores ranging from one (1) to six (6). Proposals with this range have a high impact, but also have several minor weaknesses. Comments from reviewers addressing these weaknesses were addressed in previous chapter IV and based on these comments; the LOLA proposal can be improved.

Some of the improvements needed are the support of partners, more clarification on the training of study personnel, modification of the Prevent T2 program applied to the target population, timeline of activities, elements of cost-benefits, and long-term sustainability.

Hispanic pregnant women need to be educated on complications associated with pregravid overweight/obesity and excessive gestational weight gain. More needs to be done in this area to ensure that all pregnant women receive adequate information and education to adhere to IOM guidelines. Science and technology together can be used to accomplish this goal.

All expert reviewers were very helpful providing their critiques. Their thorough review found weaknesses that were addressed and have strengthened this proposal.

Chapter V: Final version of the Proposal

I. RESEARCH OBJECTIVES AND SPECIFIC AIMS

A. Introduction:

Gestational diabetes mellitus (GDM) is a form of diabetes or a state of carbohydrate intolerance diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes (1). GDM occurs more frequently among obese women (2), those with advanced maternal age (3), and women with a family history of diabetes (4). GDM affects African-American, Hispanic/Latino, and American Indian women more frequently than Caucasian women (5) and affects 9.2 % of pregnant women (6). After pregnancy, 5 to 10 percent of women who had GDM continue to have type 2 diabetes and about 20 to 50 percent develop diabetes during follow-up (7).

Hispanics are the largest minority group in the US (8) and Hispanic women with GDM have higher risk of developing T2D than Caucasians, even after controlling for pre-pregnancy BMI and other cofounders (9). In addition, Hispanic women have worse maternal outcome measures including preterm labor and hypertensive disorders of pregnancy than Caucasians after adjusting for sociodemographic characteristics and comorbidities (10). CDC reported that the age-adjusted prevalence of diabetes and pre-diabetes in Hispanics is approximately twice that of the Caucasian population (11). About half of Hispanic women with GDM will develop T2D within 5 years of the index pregnancy (12) indicating the need for intensive screening and interventions to prevent weight gain, GDM and its complications in this group.

Observational studies and clinical trials have reported that lifestyle intervention programs during pregnancy: are safe for the fetus and the mother (13-19), lower fasting and postprandial glucose levels and improve insulin sensitivity (20-23). Few prospective intervention studies have investigated prevention of GDM in Hispanic women. We hypothesize that pregnant overweight /obese Hispanic women assigned to, and adopting a lifestyle intervention program will improve eating habits and physical activity resulting in higher compliance with IOM guidelines for gestational weight gain (GWG), than women receiving standard care. In such women, we propose these specific aims:

a) To determine the benefits of a linguistically and culturally tailored lifestyle intervention program based on healthy eating and moderate physical activity in achieving IOM recommendations for weight gain,

b) To compare the occurrence of carbohydrate intolerance and GDM at 24-28 weeks gestation between women in the lifestyle intervention group and women receiving standard care; and,

c) To determine the impact of the lifestyle intervention on the development of maternal and fetal complications during pregnancy and outcomes up to 3 months after delivery.

B. Specific Aims:

1. **To determine whether an early bilingual culturally grounded lifestyle intervention program based on healthy eating and exercise will improve the percentage of women who are compliant with GWG (IOM guidelines) in overweight/obese Hispanic women.**

Hypothesis: Overweight and obese Hispanic women who participate in an early lifestyle intervention program will improve healthy eating habits and physical activity and result in a higher compliance with Institute of Medicine guidelines for GWG, when compared to patients receiving standard care. Intervention should also improve post-partum weight loss.

2. **To compare the occurrence of carbohydrate intolerance and diabetes at 24-28 weeks gestation and at 6 week post-partum between women in the lifestyle intervention group and women receiving standard care.** Oral glucose tolerance test and hemoglobin HbA1C will be assessed at baseline, at mid-pregnancy GDM screening visit (24-28 weeks gestation) and at 6 weeks and 3 months postpartum.

   Hypothesis: The lifestyle intervention program will result in a lower rate of carbohydrate intolerance during gestation and shortly after delivery compared to women receiving standard care. At the first obstetrical visit, overweight/obese Hispanic women with one or more risk factors for developing gestational diabetes will be provided with an individualized instruction on nutrition and physical activity.

3. **To determine the impact of the lifestyle intervention in preventing maternal and neonatal complications compared to women receiving standard care.**

   Hypothesis: By reducing excessive GWG and promoting exercise, women assigned the lifestyle intervention program will experience lower rates of maternal and fetal complications compared to women receiving standard of care. We will explore the impact of the intervention in reducing maternal complications (i.e., need for C-section and pre-term labor, changes in blood pressure and rate of pregnancy-induced hypertension and preeclampsia) and birth outcomes and fetal complications at delivery (fetal weight, rate of macrosomia, shoulder dystocia, respiratory distress, stillbirth, neonatal hypoglycemia, jaundice, and polycythemia).

II. Significance

a. Prevalence of overweight/obesity and weight gain during Pregnancy.

More than one-third of women of reproductive age in the U.S. are overweight or obese (24-27). Pregnancy itself can alter the weight gain trajectory in adulthood, with excessive weight gain a major risk for increasing long-term BMI and subsequent risk for chronic disease (28). According to the NHANES report 45.7% of Hispanics age 18 to 49 were overweight or obese, compared to 35.5% of non-Hispanic white (29, 30). Weight gain during pregnancy for women who are overweight or obese has been shown to correlate with GDM risk (3, 31).

The Institute of Medicine (IOM) published in 2009 the recommendations for total and rate of weight gain during pregnancy (32). Despite continued debate over the optimal range of GWG for obese mothers, too few mothers of all pregravid BMI categories gain within recommended ranges, and excessive gain is more common than inadequate gain (33). This is more evident in Hispanic women, who experience higher rates of overweight/obesity when entering pregnancy as well as a higher GWG (34). There is therefore a need to identify culturally appropriate lifestyle intervention programs for Latino Women to limit weight gain during pregnancy that will decrease the risk of gestational diabetes and associated maternal and fetal complications.

b. Maternal obesity and complications. Maternal obesity during pregnancy increases the risk of complications to both mother and child. Overweight and obese women are at higher risk of spontaneous abortion, hypertension, GDM, and cesarean birth (35-45). Women who gain in excess of the IOM guidelines (32) had higher odds of having large for gestational age neonates ([OR] 1.72, 95% confidence interval [CI] 1.53-1.93), preterm delivery ([OR] 1.30, 95% CI 1.14-1.48), and primary cesarean delivery (OR 1.52, 95% CI 1.26-1.83) than women who gained within the guidelines (46). Maternal obesity is associated with 2.5 times the risk of hypertensive pregnancy and 2.7 times higher risk of preeclampsia compared with normal weight women; and excessive GWG results in a 3-fold increased risk of a hypertensive disorder and a 4-fold risk of preeclampsia compared to women achieving weight gain guidelines (47, 48). In addition, infants of obese mothers are at higher risk of birth trauma (shoulder dystocia), macrosomia (49), neural tube defects and cardiovascular abnormalities (50-53). Obese Hispanic women are more likely to have increased risk of neonatal complications and macrosomic babies compared to obese White women (54-57) and Hispanics with GDM have an increased risk of developing type 2 diabetes (12).

c. Disparities in maternal outcomes among minority populations. The National Health and Nutrition Examination Surveys indicate that Latina women in their childbearing years are significantly more likely to be obese than are other women. Hispanic women have worse maternal outcome measures including preterm labor and hypertensive disorders of pregnancy than Caucasians after adjusting for sociodemographic characteristics and comorbidities (10, 58). Hispanic women are at a higher risk for the development of GDM and more likely to have diabetes compared to Caucasian (59). The Latina Gestational Diabetes Mellitus Study (60), a prospective cohort of 1231 women conducted from 2000 to 2004, reported that pre-pregnancy obesity is associated with 2.5 higher risk of hypertensive pregnancy (95% CI, 1.3-4.8) and 2.7 times the risk of preeclampsia (95% CI, 1.2-5.8), compared to women whose BMI was 19.8 to 26.0 kg/m. These results demonstrated a need for interventions to help Hispanic women avoid obesity by regulating their pregnancy weight gain.

d. Physical activity during pregnancy. Similar to non-gravid women, regular physical activity (PA) during pregnancy has been associated with reduced risk of diabetes and excessive weight gain (61). Clinical studies indicate that PA reduces the risk of diabetes directly by improving insulin sensitivity, and indirectly by producing beneficial changes in body mass and composition (20-22, 62). In women with GDM, regular exercise lowers fasting and postprandial glucose levels and may be a helpful adjunctive therapy (13, 63-65). Exercise increases glucose uptake in the muscle to as much as 40 times its normal rate (14), and improves insulin responses and glucose tolerance for as long as 40 hours beyond the time of last exercise (66). The American College of Obstetricians and Gynecologists (ACOG) recommends 30 minutes of moderate intensity physical activity (brisk walking, recumbent bicycle or arm ergometer) during most days of the week for women without medical or obstetric complications (63, 67). Despite endorsement by professional organizations (63, 67), regular exercise has not been widely accepted during the pregnancy state (68).

e. Medical nutrition therapy during pregnancy. Medical nutrition therapy is the key to weight control during pregnancy. Goals are to provide adequate maternal and fetal nutrition, energy intake for appropriate maternal weight gain, and maintenance of optimal maternal blood

glucose control (69, 70). Diets containing 40-45% of total energy intake from carbohydrate have been shown to reduce postprandial glucose levels (71-74). Most pregnant women need 2,200 to 2,900 kcal a day, but pre-pregnancy body mass index, rate of weight gain, maternal age, and appetite must be considered when tailoring this recommendation to the individual (75). Several reports have indicated that caloric restriction to ~1,600-1,800 cal/day results in reduced blood glucose levels without elevations of free fatty acids and ketonuria (76). More severe energy restriction (~1,200 cal/day) are not recommended because the risk of ketonemia and ketonuria (76). Although clinical studies have established the importance of diet and physical activity in controlling glucose concentrations in women with established GDM, it is not known if similar results can be obtained when such interventions are carried out before the onset of impaired glucose tolerance. Because the risk from such intervention is low and the likelihood that it will be beneficial is high, the position of the Academy of Nutrition and Dietetics recommends that behavioral counseling be provided to all women to improve diet and PA to prevent adiposity and promote physical activity is justified in all overweight/obese women (77).

f. Behavior Intervention Studies and Prevention of Type 2 diabetes. Epidemiological evidence suggests that obese and GDM women are at increased risk for the development of T2DM after pregnancy (7, 63, 78-83). Risk of developing diabetes is 9.6 times greater for patients with GDM and the cumulative risk of developing T2DM for patients with GDM is about 25.8% at 15 years post diagnosis (84). The extent of this risk depends on maternal risk factors, some of which are potentially modifiable. Several prospective and cross-sectional epidemiological studies have indicated that lifestyle and behavior modification programs are associated with a significant reduction in the development of T2DM in individuals with IGT (20-22, 85). In the Diabetes Prevention Program (DPP) (21), 3,234 subjects with impaired glucose tolerance (IGT) were randomized to an intensive lifestyle intervention (goal of ≥7% weight reduction and ≥150 min/week of moderately intense activity), or to a standard diet and exercise program plus a medication treatment group of metformin or placebo. After an average follow-up of 2.8 years, a 58% relative reduction in the progression to diabetes was observed in the lifestyle group compared with control subjects, greater than the 31% relative reduction in the metformin group. The results of these studies have led to a position statement from the American Diabetes Association and National Institute of Diabetes, Digestive and Kidney Disease, which indicated that T2DM can be prevented or delayed, and therefore, recommended behavior changes to achieve healthy lifestyle in populations at risk. The validity of generalizing the results of previous prevention studies to the pregnancy state have shown modest effects on GWG and diabetes suggesting that more successful interventions are possible. Based on the encouraging results of lifestyle modification programs, we hypothesize that this early cultural, linguistically grounded lifestyle intervention program can limit excessive GWG, risks of developing GDM and other obesity-related maternal and fetal complications during pregnancy (84, 86).

III. Innovation.

Increasing evidence indicates that modification of exercise and nutrition is safe and effective in controlling excessive weight gain during pregnancy, thereby, lowering the risk of fetal and maternal complications (87, 88). This proposal will test if a bilingual culturally-grounded lifestyle intervention based on the CDC Prevent T2 program (89) can improve compliance with the IOM guidelines for weight gain during pregnancy in overweight/obese Hispanic women. The more widespread use of cultural interventions is likely to improve racial disparities in healthcare

(84). Linguistically tailored interventions have been shown to be successful in the treatment of certain chronic conditions as it was found by in the *Latinos in Control* trial by Rosa et al., who found that literacy-sensitive, culturally tailored interventions can improve diabetes control among low-income Latinos (86, 90). Preventing excessive weight gain through improved nutrition and exercise program is likely to reduce obesity-related maternal and fetal complications. This is critically important as Hispanics are one of the largest minority groups in the United States (8), and are reported to have higher rates of overweight and obesity when entering pregnancy (34). Moreover, they experience higher rates of excessive weight gain during pregnancy, and as a consequence are at increased risk of having neonatal and maternal complications including preterm labor, hypertensive disorders of pregnancy and GDM after adjusting for socio-demographic characteristics than Caucasian women (10, 48, 58).

The program will build upon the experience of the research team in conducting randomized control clinical trials in obesity, diabetes, and in prevention and screening of low-income minority populations. It will take advantage of the extensive clinical practice at healthcare system for inner city patients in metro Atlanta area. An additional strength is the availability of the bilingual Emory Latino Diabetes Education program, a lifestyle intervention and education program that provides culturally sensitive lifestyle education to minority populations with diabetes in Atlanta and Georgia. We plan to use an adaptation of the Prevent T2 CDC curriculum (89) and mobile technical capability to encourage and track both intervention and weight management (91). We hypothesize that this can be the basis of a lifestyle intervention that can prevent obesity and T2D beyond pregnancy. Evidence suggests that pregnancy is an opportunity to promote positive health behaviors, branded as a 'teachable moment', as perceptions of personal risk are increased (92). In addition, strong emotional responses and a re-definition of their social role and responsibility occurs as a result, pregnant women tend to be more motivated to adopt positive health behaviors, such as physical activity (92, 93).

IV. Preliminary Data

a. Maternal clinical characteristics in women with GDM at Center for International Maternal (CIMA) Health Clinics.

The Emory Latino Diabetes Education for Gestational Diabetes (ELDEG) provides culturally sensitive nutrition and diabetes education program in Spanish to low-income overweight and obese Hispanic women with GDM aiming to improve compliance with the Institute of Medicine (IOM) guidelines for weight gain during pregnancy as a measure to control glycemia through diet and exercise.

b. Gestational Age at Presentation

The mean gestational age at the first antepartum clinic visit in women with GDM is 15±2 weeks. Approximately half of the women presented earlier than 15 weeks of gestation. These findings indicate that in community and inner city programs, women at risk of GDM present early enough during their pregnancy to allow intervention with an education and behavior modification program that might reduce the development of GDM.

Table 1 summarizes the clinical characteristics and assessment of the nutritional knowledge of women with GDM at their first visit with the ELDEG program at CIMA during 2014-2015. We

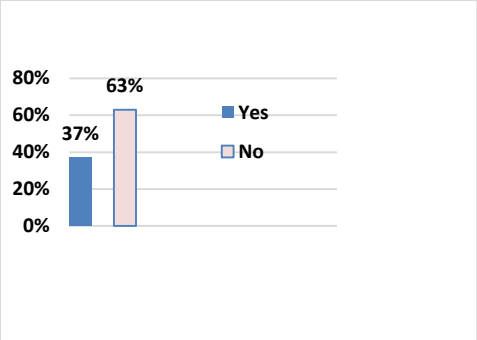
observed that Latina women had a least two of the risk factors associated with GDM such as obesity (mean BMI 32±6) and maternal age > 25 year. As depicted in table 1, majority of participants had limited knowledge about foods that can raise their blood glucose. Among participants, very few patients knew which group of meals could elevate their blood glucose (BG). These are patients with GDM that otherwise would not have been able to get the proper education on management of GDM and would probably end up with complications related to uncontrolled glycemic controls. These findings demonstrate that there is a need for education and/or an intervention to help Hispanic women avoid eating habits that can worsen gestational weight gain and will also increase glycemic values.

Table 1. Clinical Characteristics of Women with GDM in the ELDEG Program in 2014-2015

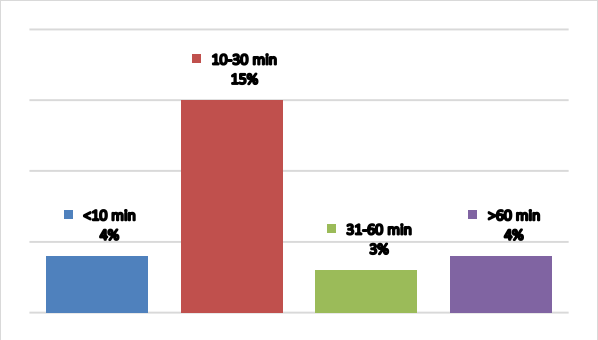
	GDM (n=67)	
Maternal age (yr.)	32±6.7	
Gestational age at diagnosis of GDM (wks.)	26±2	
Body weight before pregnancy (kg)	77±3	
BMI before pregnancy (kg/m2)	32±6	
Systolic blood pressure (mm Hg)	117±13	
Diastolic blood pressure (mm Hg)	71±9	
Knowledge about food raising blood glucose	**Yes**	**No**
Bread/corn patties/tortillas, n (%)	41 (61)	26 (39)
Pasta, n (%)	34 (51)	33 (49)
Vegetables/Legumes, n (%)	0	37 (55)
Beans, n (%)	10 (15)	57 (85)
Fruits, n (%)	12 (18)	55 (82)
Fats/Meats, n (%)	21 (31)	46 (69)
Rice, n (%)	24 (36)	43 (64)
Milk/cheese, n (%)	14 (21)	53 (79)
Sweets, n (%)	47 (70)	20 (30)

d. Physical Activity (PA)

At the time of diagnosis of GDM, only 25 (37%) participants in the ELDEG education program practiced any type of regular PA (Graph 1), among those only 3 (4%) participants reported PA for 31-60 min/day (Graph 2) as recommended by ACOG (67). Usually pregnant women are less likely to incorporate exercise into their daily routine due to pregnancy symptoms, or due child care and work commitments (94). It is therefore even more difficult to implement a physical exercise program with moderate to high intensity 3 times/week for pregnant women as suggested in general ACOG clinical recommendations (95). For this reason, we propose to start education on increasing physical activity as early as the first trimester.



Graph 1: Physical Activity



Graph 2: Length of Physical Activity

Emory Latino Diabetes Education Program (ELDEP): An innovative and successful lifestyle education program for low socio-economic Latino patients with diabetes. In response to the growing number of Latinos in the Grady Healthcare System and the lack of data on Latinos in Georgia, the Emory Latino Diabetes Education program was created in 2006 to provide culturally-competent lifestyle education to patients and educate healthcare providers on how to take care of Latinos with diabetes. The ELDEP program curriculum was created entirely in Spanish and is conducted by native Spanish-speaking professionals (physicians, diabetes educators, nurses and dieticians). To date more than 700 patients and 650 healthcare providers have participated in our program. Education sessions are conducted at 7 different sites in Georgia including hospitals, clinics, and non-medical facilities. The ELDEP is funded in part by education grants from the Georgia Healthcare Foundation and pharmaceutical industry.

The ELDEP education model follows the American Association of Diabetes Educators (AADE) seven self-care behaviors framework (96). The AADE self-care behaviors include healthy eating, being active, monitoring, medication use, problem solving, healthy coping, and reducing risks. Patients attend an initial 3 hour session and then follow-up sessions which we refer to as "Clubes de Diabetes" or diabetes club meetings. Subjects fill out a questionnaire and levels of HbA1C, blood pressure, weight, waist circumference and BMI were measured at each visit. The overall result was an improvement in glycemic control with a mean HbA1C reduction of 0.97% and women experiencing a better glycemic control than men. The HbA1C decreased from 8.8% to 7.9% in females, and 9.7% to 8.4% in males ($p<0.01$).

The Grady Health System (GHS) and Maternal-Fetal Medicine Division.
Grady Memorial Hospital is the Southeast's largest public hospital, and has been the public hospital for the city of Atlanta since 1892 with a mission of serving the poor and uninsured and those suffering from health disparities. The work of the Maternal-Fetal Medicine specialists is integrated with pediatric geneticists, who assist in prenatal diagnoses, neonatologists, and staff Level I neonatal intensive care units at each site. The Division of Maternal-Fetal Medicine also maintains a large, computerized data base that provides information for patient care and research including prenatal records, laboratory data, and obstetrical outcomes. It also serves patients with highly diverse racial (>90% minority subjects) and socioeconomic profiles. Approximately 97% of women who deliver at GHS are in minority ethnic groups (56% Black, 38% Hispanic).

Centro Internacional de Maternidad (CIMA).
CIMA is a clinical center that works with Northside Hospital in Atlanta, Georgia that provides healthcare to women during pregnancy regardless of health insurance and income. CIMA performs about 120 deliveries per month and more than 95% of their population is Hispanic (majority non-English speaking). Incidence of gestational diabetes in their population is around 15% and associated with complications as spontaneous abortion, intrauterine fetal demise, large for gestational age, increased cesarean rate and increased neonatal hypoglycemia.

F. Summary of Facilities and Preliminary results. Obesity and GDM constitute major health problems in minority pregnant women. Data indicate a high prevalence of obesity and a strong relationship between obesity and the development of GDM, and other complications. The Emory Latino Diabetes Education Program (ELDEP) has been shown to be a successful education program for low socio-economic Latino patients with diabetes. The ELDEP improved glycemic control with a mean HbA1C reduction of 0.97% and women engaged in self-management behaviors. The high annual number of deliveries by CIMA and GHS of mostly minority women (> 90%) with a high rate of overweight/obesity (>50%) assures sufficient number of potential patients to be recruited in this prospective randomized trial.

V. Study Design.
We propose to conduct translational research, adapting the lifestyle intervention model of the Prevent T2 CDC modified program of the NDPP in at-risk overweight/obese pregnant Hispanic women in order to:

1) Determine whether the tailored culturally lifestyle intervention program will result in higher (50%) compliance with IOM guidelines for weight gain compared to women receiving standard care;
2) To determine the occurrence of carbohydrate intolerance and GDM at 24-28 weeks gestation and at postpartum between women in the lifestyle intervention group and women receiving standard care; and
3) To explore the impact of the lifestyle intervention on the development of maternal and fetal complications during pregnancy and to explore the reversal of postpartum weight retention with the aim of reducing the risk of T2D.

It is hypothesized that by limiting GWG and increasing exercise during the gestational period, the lifestyle intervention program has the potential to prevent the burden of obesity-related complications and may lower the risk of subsequently developing overt diabetes. We will recruit 120 women who will be randomized to a lifestyle intervention or standard care group. The lifestyle intervention will consist of online access to education, a monthly in-person educational group session and biweekly telephone booster calls, which will continue until delivery.

V.A. Aim # 1
Specific Aim 1. To determine whether a culturally tailored lifestyle intervention program based on healthy eating and moderate physical activity results in higher compliance with Institute of Medicine guidelines for GWG compared to women receiving standard care.

V.A.1 Rationale.

More than one-third of women of reproductive age in the U.S. are overweight or obese (24-27), and two thirds of women gain more weight in pregnancy than is recommended by the IOM guidelines (97). Hispanic people also are the most physically inactive US ethnic group (7) and have disproportionately high levels of overweight and obesity rates (8), gestational diabetes and diabetes (9); however, despite the increasing Hispanic population and the observed health disparities, relatively few prevention studies have included Hispanic women. Lifestyle modification programs have been found successful in preventing GDM in women at risk (98, 99), as well as in preventing T2D in populations at risk (20-22, 85, 100). Observational studies and intervention clinical trials have reported that lifestyle intervention programs during pregnancy are safe for the fetus and the mother (13-15), and result in lower fasting and postprandial glucose levels and improvement in insulin sensitivity (20-22).

Hypothesis: Overweight/obese pregnant Hispanic women assigned to a lifestyle intervention program will improve diet and physical activity and result in a higher compliance with IOM guidelines for weight gain than patients receiving standard care.

V.B. Methods:

V.B.1. Study Population

The study will be conducted at the ambulatory obstetrical clinics at Centro Maternal Internacional (CIMA International Women's Health Services) and Grady Health System, Atlanta, Georgia. The OB/GYN Clinic at Grady Hospital serves an inner city and ethnically diverse population. There were 3,740 deliveries at Grady Hospital in 2014-2015. Of them, 95% of women were from minority ethnic groups (56% Blacks, 38% Hispanics, 3% Caucasians, and 3% other ethnic groups).

V.B.2. Eligibility Criteria

Eligible patients will 1) be overweight and obese (BMI > 25 kg/m^2) Hispanic women, and 2) prenatal care established less than 16 weeks of gestation, 3) with a singleton pregnancy. We will exclude women with 1) age < 18 or > 45 years, 2) > 16 weeks gestation, 3) history of diagnosis of type 2 diabetes, hypertension, cardiovascular disease, chronic renal disease, or active liver disease (AST > 3 ULN), 4) fetal anomaly 5) planned termination of pregnancy 6) history of ≥3 consecutive miscarriages 7) anemia (hemoglobin < 10 g/dl); 8) current medications which adversely influence glucose tolerance (e.g., corticosteroids, metformin), 9) multiple pregnancy, 10) contraindications to participate in regular physical activity, 11) patients with mental conditions rendering them unable to understand the nature, scope, and possible consequences of the study 12) previous bariatric intervention, 13) participation in another interventional study to modify weight 14) previous participation in this trial with a previous pregnancy 15) Unwillingness or inability to commit to 1 year follow-up.

V.B.3. Recruitment

Patients will be pre-screened from the ambulatory obstetric clinic schedule. Patients with a BMI > 25 kg/m^2 will be considered for approach. Women will be recruited by research staff after their first prenatal visit. The research staff will go over study aims and procedures, and if the patient is interested in participating she will sign the consent form (Spanish or English). Study enrollment will take place at the first or second obstetrical visit but no later than week 14 of pregnancy.

Demographic and baseline assessment will be collected and patients will be scheduled for an outpatient visit at the Grady Clinical Research Unit within one week.

V.B.4. Baseline assessment

Patients will be asked to come to the Grady research unit or CIMA (depending on place of obstetric care) after an overnight fast. An abbreviated history and physical exam will be completed by the PI or co-investigators to collect vital signs, weight, BMI, and assessment of eating habits and physical activity.

Baseline laboratory studies: hemoglobin, hematocrit, biochemistry profile, HbA1C, and a 75-gram OGTT with measurement of glucose, to rule out diabetes (see Aim 2).

V.B.5. Demographic questionnaire. A 25 item survey will be collected to elicit age, race/ethnicity, and primary language, education level, place of birth, and duration of U.S. residence, occupation, household income, and number of pregnancies, a history of GDM, and a family history of DM.

V.C. Randomization.

The PI and/or a member of the research team will review medical records and results of OGTT prior to randomization to exclude subjects with contraindications (see eligibility criteria: section IV.B.2). Eligible patients will be randomized into a lifestyle intervention or a standard of care group. A blocked randomization will be based on body weight – overweight (BMI 25-<30 kg/m^2) and obese (BMI > 30 kg/m^2), using the randomly permuted blocks method in a set of 4 sequential enrolled patients per group.

V.D. Lifestyle Intervention Program. The lifestyle intervention will consist of a 60 minutes monthly in-person group educational session adapted from the Prevent T2 program and biweekly telephone booster calls, which will continue until 3 months after delivery.

The Prevent T2 is a modification of the original 2002 DPP trial and follow-up studies that promotes modest weight loss and increased physical activity through a 12 months lifestyle change program that reflects on self-efficacy, physical activity and healthy eating. It consists of 16 modules to be presented in the first 6 months (introduction, get active to Prevent T2, track your activity, eat well to Prevent T2, track your food, get more active, burn more calories that you take in, shop and cook to prevent T2, manage stress, find time for fitness, cope with triggers, keep your heart healthy, take charge of your thoughts, get support, eat well away from home, and stay motivated to Prevent T2). During the last six months of the program consist of 6 modules chosen by the lifestyle coach and participants from the following: when weight loss stall, take a fitness break, stay active to Prevent T2, stay active away from home, more about T2, more about carbs, have healthy food you enjoy, get enough sleep, get back on track, prevent T2-for life!

Participants will attend their regularly scheduled obstetric clinic visits. Participants who develop a significant maternal complication will be withdrawn from the study and referred for management by the maternal-fetal specialists (MFS). Participants who develop GDM will be referred to MFS for evaluation. If specialist agrees, participant will be followed in the study and continued to monitor remission in the post-partum period. Participants will receive information on the appropriate GWG using the IOM guidelines. At each group session, the participant's weight will be measured using a balance beam scale and recorded. Participant will be informed

whether her weight gain is at the appropriate recommended level. If her weight gain is within the IOM guidelines, the patient will be encouraged to continue current diet and exercise regimen. If her weight gain is not within the IOM guidelines, the participant's eating habits and exercise regimen will be reviewed by the dietitian, CDC certified lifestyle coach and/or coordinator and participant will be advised to increase or decrease her intake and/or increase or decrease her exercise. Final gestational weight will be recorded from arrival to the hospital for delivery.

V.E. Content of Educational Sessions. Monthly sixty minute in-person group education sessions which promote increased physical activity through a 12 month lifestyle change program that also reflects on self-efficacy, physical activity, and healthy eating. We will cover the following topics: 1) healthy eating, 2) being active, 3) monitoring weight and physical activity, 4) stress management, 5) problem solving, and 6) healthy coping as described in the Prevent T2 curriculum. Personal and group educational sessions will be led by a bilingual CDC certified lifestyle coach. The focus will not only be on GWG, the lifestyle intervention will emphasize long-term improvements in nutrition and physical activity.

V.F. Healthy eating. The goal is to decrease the intake of saturated fat and sugar consumption, and to increase healthy food choices, fruits and vegetables, whole grains and fibers as recommended by the American Dietetic Association: Nutrition and Lifestyle for a Healthy Pregnancy outcome (75). Specific goals include reduction in saturated fat intake (<30% of calories); increase fibers through whole grains, nuts, seeds, fruit and vegetables, reduce salt intake, avoid alcohol consumption, and monitor portion size. The healthy eating intervention will take into consideration pre-pregnancy weight and BMI, activity level, and recommended weight gain (32). In order to aim for weight maintenance during gestation and at the same time allowing sufficient caloric intake for fetal growth and development, calorie goals of 25 kg/cal per day will be set. Participants in the intervention group will meet with a dietitian (CDC trained lifestyle coach) during first visit and thereafter with a CDC certified lifestyle coach at each study visit. Patients will learn healthier ways of preparing traditional ethnic recipes, easy recipes to cook low fat-low carbohydrate meals, how to avoid products with high content of simple sugars and saturated fat. Evaluation and monitoring of the nutritional part will be conducted by the nutritionist.

V.G. Being active. Patients in the intervention group will be instructed to increase the amount of physical activity, primarily walking, with the ultimate goal of achieving ACOG exercise goals for pregnant women of 30 minutes/day of moderate-intensity activity, such as brisk walking on most days of the week (equivalent to 10 MET-hrs./week) (67). Short episodes (<15 minutes of walking) will be encouraged. Weekly activity goals will be increased by 10% and step goals will be increased by 10-20%. Home-based exercise is encouraged for most sessions, as it has been shown to be as effective in weight loss and risk factor modification as supervised exercise. Participants will be instructed on how to track their physical activity using their mobile phone or a digital Fitbit pedometer to encourage self-monitoring.

The exercise intervention will include a 60 minutes monthly in-person group session (up to 4 participants per group) to establish a support group with similar goals and challenges, review print-based Prevent T2 materials, and set exercise goals. The educational material is available in Spanish and English. Patients will be given a Fitbit (if no mobile phone) to keep track of their

total number of steps. Data from mobile device will be reviewed each month and patients will be provided with a feedback about their physical activity level. The lifestyle coach will review participants' weight gain and mobile data, and if weight is not within the IOM guidelines, the participant's eating and exercise regimen will be reviewed and she will be advised on modifying her intake and exercise level.

V.H. Assessment of physical activity. In this project, we will assess physical activity using patient's mobile devices logs, if the patient does not have one, we will provide a Fitbit Flex. The International Physical Activity Questionnaire Short (IPAQ-SF) form (101) will be assessed at recruitment, at midterm and at the end of pregnancy, and at the post-partum visits. This 27 item self-report instrument measures time spent in occupational, transportation, household, and leisure time physical activities over the past 7 days (101). Patients in both groups will complete the physical activity questionnaire prior to each monthly visit (participant will be reminded to do so prior to visit). Patients in the control group will receive the physical activity questionnaire during the initial visit, at the mid-term visit (24-28 weeks), and at the end of pregnancy.

We will use the mobile device or the Fitbit Flex Charge Wireless Activity Wristband (for those without a mobile device) that accurately tracks all-day stats like steps taken, distance traveled, stairs climbed, active minutes to stay on track, it also syncs stats wirelessly and automatically to a computer and over 150 leading smartphones. Fitabase analytics (Small Steps Labs, San Diego, CA, USA) will enable us to remotely monitor and gather compliance of the Fitbit use. Only women in the intervention group will use a mobile phone application or Fitbit, thus differences in step count between groups will not be assessed in this study.

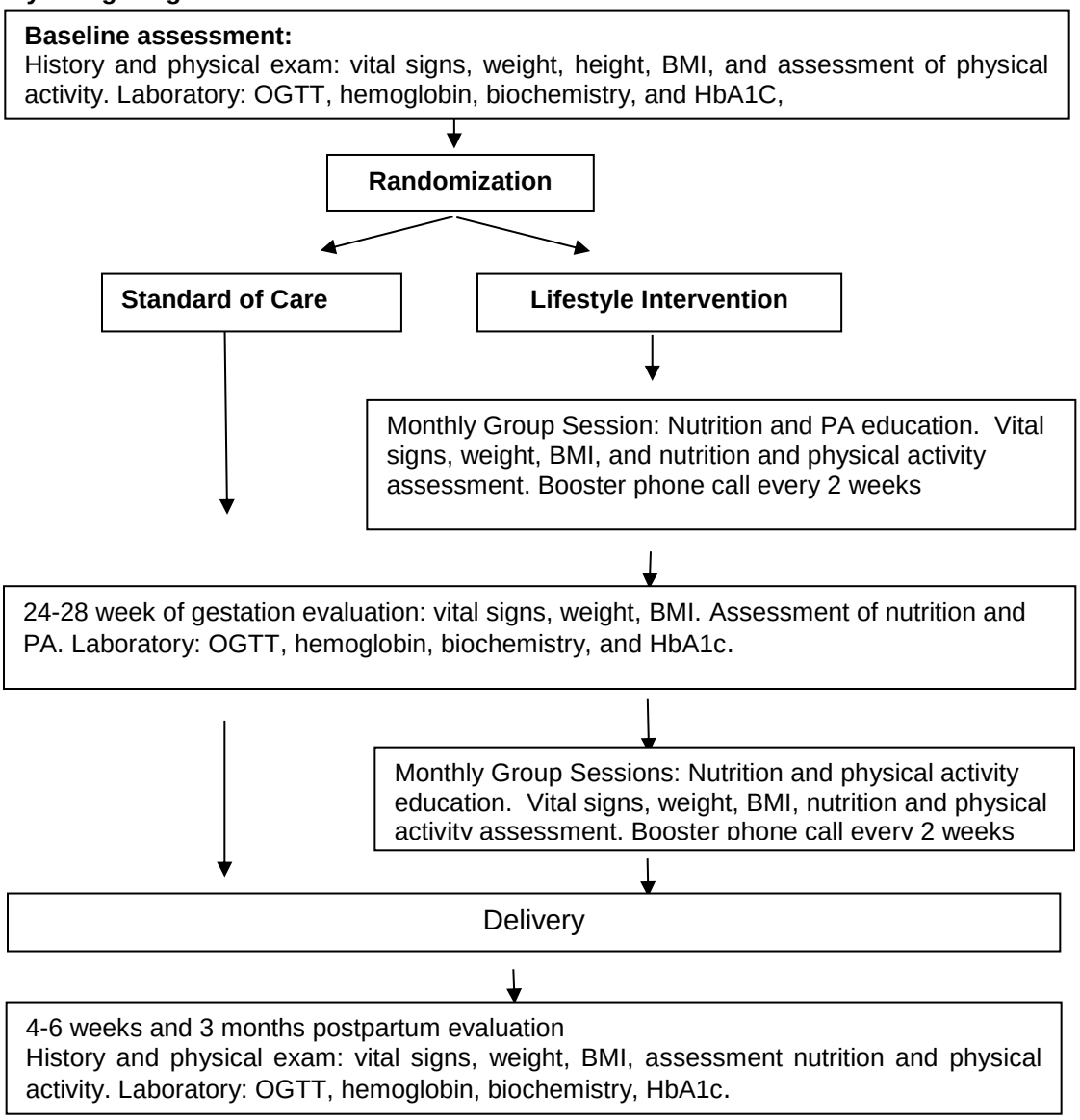
V.I. Nutrition assessment and knowledge. A General Nutrition Knowledge Questionnaire (102) is a well-validated instrument that allows assessment of patient's understanding of healthy eating as well as providing data for examining the relationship between nutrition knowledge and dietary behavior. In addition, participants will be instructed to record all meals, snacks and beverages, including portion size, quantity and methods of preparation consumed from 2 alternating weekdays and 1 weekend day using their mobile device. Patients in the control group will receive the 3-day food diary during the initial visit, at the mid-term visit (24-28 weeks) and at the end of pregnancy; these should be completed prior to the in-person visit. Participants will be reminded by phone to do so. Assessment of these questionnaires will be performed by the research nutritionist.

V.J. Assessment Measures of Compliance. Compliance with use of the Fitbit, healthy eating, and exercise regimen will be conducted in the lifestyle intervention at baseline, during each monthly visits, and post-partum visits. If the lifestyle coach is not able to have a face-to-face contact, the participant will be contacted via telephone to encourage participant to compliant with lifestyle intervention, to answer any questions and to remind upcoming in-person sessions. Data from mobile device can be shared via email. Fitbit compliance will be done through Fitabase.

V.K. Satisfaction Survey. At each assessment period, participants will be asked to complete a satisfaction survey to assess acceptability of the intervention. This survey aims to identify social, cultural, financial and physical barriers to comply with dietary and lifestyle intervention during

pregnancy. We will also collect information on intervention materials, staff and service feedback.

V.L. Study Design Algorithm:



V.M. Anticipated Results and Interpretation. This hypothesis predicts that overweight/obese Hispanic women assigned to the lifestyle intervention program will have higher compliance with IOM guidelines for weight gain than women receiving standard care. In addition, we anticipate that women in the intervention group will increase their PA. We anticipate that by limiting excessive weight gain, appropriated healthy eating habits, and increasing physical activity, the intervention group will reduce the risk of carbohydrate intolerance and GDM (aim 2) and will reduce the risk of maternal and neonatal complications (see aim 3). Results from the intervention group will be sent annually to the CDC Prevent T2 program for evaluation.

V.N. Potential Problems. Recruitment and retention of patients in the intervention and control group represent the most important challenge; however, based on the large number of patients seen by CIMA and GHS Obstetrics, we anticipate no problems recruiting participants. Thus, we expect no problems in recruiting 120 patients (2-4 patients per week). To facilitate recruitment and retention, the PI and lifestyle coaches are bilingual professionals with extensive experience in educating and treating minority populations. To increase retention, we will offer incentives, such as grocery gift cards, gifts, cash, food, recipe books, or exercise equipment for intervention attendance or completion at each data collection point. Assessment of dietary and physical activity is outlined in sections IV.I to IV.K

V.O. Randomization and statistical Analysis.

The study is a two-arm randomized controlled clinical trial. Blocked randomization will be stratified based on body weight – overweight (BMI 25-<30 kg/m^2) and obese (BMI >30 kg/m^2), using the randomly permuted blocks method in a set of 4 sequential enrolled patients per group. The main hypothesis is that the lifestyle intervention will result in higher percentage of women in compliance with IOM guidelines for GWG compared to women receiving standard care. The primary outcome is women with weight gain according to the IOM recommendations. We will conduct an initial comparison of two independent proportions (of women with weight gain following IOM recommendation) based on a two-sided Chi-square test, followed by a Cochran-Mantel-Haenszel test which adjusts for BMI categories (BMI 25-<30 kg/m^2 and BMI > 30 kg/m^2). Logistic regression will be conducted to estimate the effects of intervention, BMI category, and other relevant covariates on the binary primary outcome i.e. complying IOM recommendation vs. not complying IOM recommendation). Similar analyses will be conducted for the binary outcomes measured under Aim 2 and Aim 3. Stepwise, backward, or forward model selection strategy will be adopted to determine the predictors included in the final model. Logistic regression diagnostics will be employed to ensure the resulting logistic model is appropriate.

Power and sample size calculation. The sample size calculation is based on the primary outcome (GWG in compliance with IOM guidelines). After accounting for at a 20% attrition rate, 120 women (60 women per group) will lead to at least 48 subjects for each group. According to data reported by Shieve et al. (103), we conservatively predict that about 30% of patients' in standard care would meet the IOM guideline. Computing power based on the two-sided Fisher's exact test, with alpha=0.05, we expect to achieve 80% power to detect a difference in proportion of 0.19 between the two study groups, which corresponds to 49% compliance in the intervention group to the IOM guideline.

VI. Aim # 2.

To compare the occurrence of carbohydrate intolerance and GDM at 24-28 weeks gestation and after delivery between women in the lifestyle intervention group and women receiving standard care.

VI.A. Rationale GDM constitutes a major health problem affecting 9.2% of all pregnancies (6) and is associated with a significant increase in both maternal and perinatal morbidity (5). In addition, women with GDM have increased risk of developing T2DM after pregnancy (83). Obese Hispanic women have higher rates of chronic hypertension and pre-gestational diabetes,

as well as increased rates of preeclampsia, DGM, fetal macrosomia, cesarean delivery, and operative vaginal delivery compared to non-obese patients (47, 104). Lifestyle modification programs have been successful in preventing T2DM in populations at risk (98, 99), as well as in limiting excessive weight gain during pregnancy. Several clinical trials have reported that lifestyle intervention programs during pregnancy are safe for the fetus and the mother (13-15), lowering fasting and postprandial glucose levels and improving insulin sensitivity (20-22). Therefore, we hypothesize that pregnant overweight/obese Latino women assigned to a cultural linguistically grounded lifestyle intervention program will result in lower rate of carbohydrate intolerance and GDM compared to women receiving standard care.

Assessment of carbohydrate status during pregnancy. In the U.S., screening for GDM is frequently performed at 24 – 28 weeks' gestation with a one hour 50-g oral glucose load (63, 105). If the 1 hour glucose value is > 130 mg/dl, the patient is referred for a 3 hour OGTT (100 gram glucose load). In much of the world and increasingly in the U.S.; however, the diagnosis of GDM is based on the World Health Organization (WHO) criteria for impaired glucose tolerance (IGT) and diabetes using a 2 hour 75-g oral OGTT (63, 106-108). An abnormal 75-g OGTT using WHO criteria has been associated with macrosomia, cesarean section, or both more often than was an abnormal 100-g OGTT (109). Cutoff values to define GDM on the 75-g test were first adapted from a study of Sacks et al in 3,505 pregnant women in the U.S. (110), and more recently by the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study (111, 112). In this study, we propose to use the 75 gram 2-hour OGTT for the diagnosis of carbohydrate intolerance and GDM following the WHO criteria (106-108). The proposed study will allow us to i) determine the prevalence of carbohydrate intolerance at baseline (first trimester) in overweight/obese Hispanic women, and ii) determine the impact of a lifestyle intervention on the occurrence of carbohydrate intolerance and rate of GDM at 24-28 weeks gestation (mid-term evaluation), and iii) determine the impact of the lifestyle intervention on the occurrence of carbohydrate intolerance at 6 weeks and six months after delivery.

VI.B. Methods:

Assessment of carbohydrate status. We will be measure an HbA1c and perform a 75 gram OGTT at baseline (shortly after recruitment), at midterm (24-28 weeks of gestation), and at 6 weeks and 3 months after delivery. Subjects will be asked to come to the clinic after an overnight fast. If the results of the 75-g OGTT are positive (by WHO criteria, fasting BG > 95 mg/dl, 1 hour > 180, and 2-h value > 155 mg/dl) (106, 108, 110) at baseline or at midterm evaluation, the referring physician and participant will be notified of the results. If baseline results are positive, the participant will be excluded from the study and referred to the maternal-fetal service.

VI.C. Anticipated Results and Interpretation. The proposed studies will allow us to determine at baseline (before intervention) the frequency of abnormal carbohydrate metabolism (pre-diabetes and diabetes) in overweight/obese Hispanic women. The proposed studies will determine the impact of a lifestyle intervention on the occurrence of carbohydrate intolerance and rate of GDM at 24-28 weeks gestation (mid-term evaluation) and after delivery (up to 3 months postpartum). We anticipate that women in the lifestyle intervention group will have lower fasting and post-glucose load glycemic values than women in the control group.

VI.D. Statistical Analysis Plan:
The statistical analysis plan for Aim 2 is similar to that for Aim 1. Specifically, we will code the primary outcome for Aim 2, the occurrence of carbohydrate intolerance and GDM at 24-28 weeks of gestation as 1 in presence of carbohydrate intolerance and GDM and 0 otherwise. Model selection and checking will be the same as that proposed for Aim 1. For the secondary outcome, fasting blood glucose and HbA1C values, we plan to compare them between the standard care group and the intervention group using two-sample Wilcoxon test. Linear model will be fitted to account for effects of other relevant covariates on this outcome. Normality assumption will be checked. In case this assumption is violated, standard transformation techniques will be applied. Model selection will use classic stepwise, backward, or forward strategy.

Power. Aim 2 will compare the occurrence of carbohydrate intolerance and GDM at 24-28 weeks gestation and shortly after delivery between the lifestyle intervention group and standard care groups. The results of this exploratory/pilot study aim will serve as the basis for power calculations to support a larger trial designed to investigate the effects of the intervention in prevention of CHO intolerance and GDM in Hispanic women.

VII. Aim # 3.
To explore the impact of the lifestyle intervention in preventing maternal and neonatal complications compared to women receiving standard care.

VII.A. Rationale. Maternal obesity during pregnancy increases the risk of complications to both mother and child. Overweight and obese women are at higher risk of spontaneous abortion, preeclampsia, hypertension, GDM and Caesarean birth (37, 39). Similar to maternal obesity, the development of GDM poses an increased risk of maternal and fetal complications. In addition to maternal complications, obesity is a risk factor for poor fetal outcome. Infants of obese mothers are at higher risk of birth trauma, macrosomia, neural tube defects and cardiovascular abnormalities (38, 50, 52, 113). Maternal obesity is also associated with increased risk of stillbirth (43, 110) and higher mortality during the perinatal period (115) independent of obstetric complications.

VII.B. METHODS

VII.B.1. Maternal outcomes. Maternal outcome measures to be collected in women randomized to both intervention groups include demographics, body weight and BMI, change in body weight and BMI during pregnancy; glycemic control: HbA1C levels and fasting glucose levels; cardiovascular outcome: systolic and diastolic blood pressure and rate of pregnancy-induced hypertension and preeclampsia; rate of pre-term labor and need for cesarean section.

VII.B.2. Fetal outcomes. The following fetal outcome measures will be collected in women randomized to both intervention groups: rate of macrosomia, shoulder dystocia, respiratory distress, stillbirth, neonatal hypoglycemia, jaundice, and polycythemia.

VII.C. Anticipated Results and Interpretation. We anticipate that women participating in the intervention group will result in reduced rate of maternal and fetal complications during pregnancy. Women in the intervention group who gain weight within the IOM guidelines (32)

will experience lower rates of large babies for gestational age, preterm delivery, primary cesarean delivery, preeclampsia compared to women with excessive weight gain.

VII.D. Statistical Analysis Plan: The outcomes of interest for this aim include maternal outcome (such as hemoglobin HbA1C levels, occurrence of C-section) and fetal outcome (such as occurrence of rate of macrosomia, shoulder dystocia). For a continuous outcome, we will follow the same plan proposed for analyzing the secondary outcome in Aim 2. For a categorical outcome that has more than two levels (i.e. non-binary), we will use Chi-square (or Fisher's exact) tests and Cochran-Mantel-Haenszel tests which adjust for BMI categories for group comparisons. Poisson regression or negative binomial regression will be conducted to model the effects of intervention and potential predictors on the categorical endpoint. Model selection and checking will follow the standard procedure for these models.

Power. Aim 3 will explore the impact of the lifestyle intervention in preventing maternal and fetal complications between women in the lifestyle intervention group and women receiving standard care. We anticipate that Aim 3 will be underpowered to assess many of the mentioned clinical outcomes, but the results of this exploratory aim will serve as the basis for sample size calculations to support a larger, future trial designed to investigate the effects of the intervention in prevention of maternal/fetal complications and costs associated with such complications.

VIII. Schedule of Data Collection Visits

Measure	**Baseline**	**Monthly educational sessions and bi-weekly telephone (booster) contacts until end of pregnancy**								**Post-partum**	
		12	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**4-6 Wks.**	**3 mos.**
Lifestyle education (nutritional and exercise) – center visit	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**		**X**	**X**
Telephone – booster-sessions every 2 weeks		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Compliance variables:											
Physical activity	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Nutritional intake	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Fitbit	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Weight and height – BMI	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Seated blood pressure & pulse	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Maternal & fetal outcome									**X**		
Birth weight/gestational age									**X**		
Apgar									**X**		
Complications (VI.b.1 and VI.b.2)									**X**		
Breastfeeding										**X**	**X**
HbA1c, OGTT	**X**					**X**				**X**	**X**
Fasting or random glucose	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**

IX. Human Subjects

IX.A. Study population.

The study will be conducted at the ambulatory obstetrical clinic at the Centro Internacional de Maternidad (CIMA) and Grady Health System (GHS) in Atlanta, Georgia. A total of 120 overweight/obese Hispanic women invited to participate into the lifestyle intervention at their first prenatal care visit or pre-pregnancy visit.

IX.B. Recruitment: a bilingual research staff will recruit women during the pre-pregnancy or first OB visit (up to 18 weeks of gestation). The research staff will go over study aims and procedures, and if the patient is interested in participating she will sign the consent form (Spanish or English). Study enrollment will take place at the first obstetrical visit but no later than week 18 of pregnancy. Demographic and baseline assessment will be collected and patients will be scheduled to come back for the first OGTT and lab work at CIMA or the research unit at GHS.

IX.C. Informed Consent. Informed consent will follow the procedure of Emory University School of Medicine IRB. Participants will be informed in writing and verbally (English/Spanish) about the study protocol.

IX.D. Potential Risks. Medical nutrition therapy is the cornerstone of weight control during pregnancy. Clinical studies have established the safety and efficacy of diet and moderate physical activity in controlling excessive weight gain and in improving glucose concentrations during pregnancy. Severe caloric restriction less than <1200 cal/day may result in ketonemia and ketonuria (76) and will be avoided and in this study. Dietary intervention goal is to decrease the intake of saturated fat and sugar consumption, and to increase healthy food choices, fruits and vegetables, whole grains and fibers as recommended by the American Dietetic Association: Nutrition and Lifestyle for a Healthy Pregnancy outcome (75). Activities with high risk of falling and/or abdominal trauma (running, competitive sports) will not be recommended in this study. We will recommend 30 minutes of moderate intensity physical activity (brisk walking) during most days of the week following the ACOG guidelines (63, 67).

Risks from Blood Draw: The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of dizziness and fainting.

Risks to Privacy: All information and materials will be obtained for research purposes only and the data will be kept in strict confidence. Confidentiality will be assured by the use of subject codes rather than personal identifiers. The study database will be secured, and information will only be entered using subject identifier codes rather than personal identifiers. Electronic communication will involve only coded, unidentifiable information.

IX.F. Potential Benefits to Participants and Society

The benefits of the dietary and exercise intervention will avoid excessive weight gain in overweight/obese pregnant women and will prevent the development of GDM and reduce maternal and fetal complications during pregnancy. The potential benefit to society of this intervention study could be substantial in recognizing the efficacy of a cultural and linguistically grounded lifestyle intervention in reducing maternal and fetal complications in high risk minority populations (84, 86).

IX.G. Data safety and Monitoring Plan

Despite the safety and minimal risk of the proposed intervention, we have established a Data Safety and Monitoring Committee (DSMC) to assure safety of participants and to monitor the progress of the research study. The DSMC will meet every 6 months to assess safety and adverse events, data quality, recruitment, accrual and retention, participant's compliance with the intervention, satisfaction survey results, potential complications, data completeness and preliminary data analysis. The DSMC members will not be involved in the design of the study and will not be directly involved in the conduct of the study.

IX.H. Inclusion of Women and Minority

The study is designed to exclusively evaluate minority gestational (Hispanic) women. No patients under the age of 18 will be included in the study.

IX.I. Inclusion of Children

No subjects under the age of 18 will be included in the study.

IX.J. Compensation for Participation.

Participation in this study is voluntary. Patients will receive fifty dollars gift card after each lifestyle intervention visit and after each OGTT test. The stipend is a token compensation for their time and inconvenience. Patients who lack a mobile device will be provided with at Fitbit Flex to track their physical activity. To ensure compliance wearing the Fitbit, participant will receive a twenty five dollars gift card.

X. Timeline Implementation

The following is the timeline for the implementation of the lifestyle intervention program:

Activity	**Begin Date**	**End Date**	**Responsibility**
To increase percentage of women who adhere to IOM GWG recommendations by 50%	Mar 2017	Jun 2019	Program PI
Introduction of the study procedures to obstetric ambulatory clinics at GHS and CIMA	Jan 2017	Feb 2016	Program PI-Coordinators-
Train coordinators and research staff as CDC certified lifestyle coach	Jan 2017	Jan 2017	Emory Diabetes Training
Recruit participants by research staff (2-4/week)	Mar 2017	Mar 2018	Coordinator
Bi-Weekly calls Monthly meetings with participants in the intervention group.	Mar 2017	Mar 2019	Coordinator, lifestyle coaches
Bi-annual evaluations and analysis of data collection	Jul 2017	Jun 2019	Program PI/Coordinator
Drafting, finalizing and dissemination of project findings/evaluations	Jun 2019	Dec 2019	Program PI/Coordinator

XI. Dissemination of Results

Dissemination of findings will focus primarily on communicating research results by targeting and tailoring the findings and the message to the particular target audience. As we move along we will send periodic results to the Prevent T2 program since we will be modifying their curriculum. The program investigators will submit abstracts for presentation at regional and national meetings. We will share all lessons learned with both GHS and CIMA personnel. We will submit abstracts sharing our results at local, regional and national meetings. We will also submit abstracts with findings to peer –reviewed journals

XII. Rererences

1. American Diabetes A. 2. Classification and Diagnosis of Diabetes. Diabetes Care. 2016;39 Suppl 1:S13-22.
2. Chasan-Taber L. Lifestyle interventions to reduce risk of diabetes among women with prior gestational diabetes mellitus. Best Pract Res Clin Obstet Gynaecol. 2015;29(1):110-22.
3. Morisset AS, St-Yves A, Veillette J, Weisnagel SJ, Tchernof A, Robitaille J. Prevention of gestational diabetes mellitus: a review of studies on weight management. Diabetes Metab Res Rev. 2010;26(1):17-25.
4. Reece EA, Leguizamon G, Wiznitzer A. Gestational diabetes: the need for a common ground. Lancet. 2009;373(9677):1789-97.
5. CDC. Diabetes and Pregnancy: Gestational Diabetes. Atlanta, GA: U.S. Department of Health and Human Services: Centers for Disease Control and Prevention; 2013 2013.
6. DeSisto CL, Kim SY, Sharma AJ. Prevalence estimates of gestational diabetes mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. Prev Chronic Dis. 2014;11:E104.
7. Kim C. Maternal outcomes and follow-up after gestational diabetes mellitus. Diabet Med. 2014;31(3):292-301.
8. U. S. Census. Hispanic Heritage Month 2015 www.census.gov: United Census Bureau; 2015 [Available from: http://www.census.gov/newsroom/facts-for-features/2015/cb15-ff18.html.
9. Fujimoto W, Samoa R, Wotring A. Gestational Diabetes in High-Risk Populations. Clin Diabetes. 2013;31:90-4.
10. Bryant AS, Worjoloh A, Caughey AB, Washington AE. Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants. Am J Obstet Gynecol. 2010;202(4):335-43.
11. CDC. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, . Atlanta: Centers for Disease Control and Prevention; 2014.
12. Fujimoto W. Gestational Diabetes in High-Risk Populations. In: Samoa R, editor. Diabetes Advocay2013. p. 90-4.
13. Bung P, Artal R, Khodiguian N. [Regular exercise therapy in disorders of carbohydrate metabolism in pregnancy--results of a prospective, randomized longitudinal study]. Geburtshilfe Frauenheilkd. 1993;53(3):188-93.
14. Carpenter MW. The role of exercise in pregnant women with diabetes mellitus. Clin Obstet Gynecol. 2000;43(1):56-64.
15. Jovanovic L. Role of diet and insulin treatment of diabetes in pregnancy. Clin Obstet Gynecol. 2000;43(1):46-55.

16. Rauh K, Gabriel E, Kerschbaum E, Schuster T, von Kries R, Amann-Gassner U, et al. Safety and efficacy of a lifestyle intervention for pregnant women to prevent excessive maternal weight gain: a cluster-randomized controlled trial. BMC Pregnancy Childbirth. 2013;13:151.
17. Thangaratinam S, Rogozinska E, Jolly K, Glinkowski S, Roseboom T, Tomlinson JW, et al. Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. BMJ. 2012;344:e2088.
18. Artal R. The role of exercise in reducing the risks of gestational diabetes mellitus in obese women. Best Pract Res Clin Obstet Gynaecol. 2015;29(1):123-32.
19. Currie S, Sinclair M, Murphy MH, Madden E, Dunwoody L, Liddle D. Reducing the decline in physical activity during pregnancy: a systematic review of behaviour change interventions. PLoS One. 2013;8(6):e66385.
20. Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia. 1991;34(12):891-8.
21. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.
22. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344(18):1343-50.
23. Mudd LM, Evenson KR. Review of impacts of physical activity on maternal metabolic health during pregnancy. Curr Diab Rep. 2015;15(2):572.
24. Burstein E, Levy A, Mazor M, Wiznitzer A, Sheiner E. Pregnancy outcome among obese women: a prospective study. Am J Perinatol. 2008;25(9):561-6.
25. Ehrenberg HM, Durnwald CP, Catalano P, Mercer BM. The influence of obesity and diabetes on the risk of cesarean delivery. Am J Obstet Gynecol. 2004;191(3):969-74.
26. Kim SY, Dietz PM, England L, Morrow B, Callaghan WM. Trends in pre-pregnancy obesity in nine states, 1993-2003. Obesity (Silver Spring). 2007;15(4):986-93.
27. American College of O, Gynecologists. ACOG Committee opinion no. 549: obesity in pregnancy. Obstet Gynecol. 2013;121(1):213-7.
28. Amorim AR, Rossner S, Neovius M, Lourenco PM, Linne Y. Does excess pregnancy weight gain constitute a major risk for increasing long-term BMI? Obesity (Silver Spring). 2007;15(5):1278-86.
29. Cogswell ME, Perry GS, Schieve LA, Dietz WH. Obesity in women of childbearing age: risks, prevention, and treatment. Prim Care Update Ob Gyns. 2001;8(3):89-105.
30. Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of Obesity Among Adults and Youth: United States, 2011-2014. NCHS Data Brief. 2015(219):1-8.
31. Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. Obstet Gynecol. 2010;115(3):597-604.
32. WEIGHT GAIN DURING PREGNANCY: REEXAMINING THE GUIDELINES. Institute of medicine of National Academies M, 2009. HTTP://WWW.NAP.EDU/; HTTP://WWW.IOM.EDU/PREGNANCYWEIGHTGAIN.
33. Olson CM. Achieving a healthy weight gain during pregnancy. Annu Rev Nutr. 2008;28:411-23.

34. Hernandez DC. Gestational weight gain as a predictor of longitudinal body mass index transitions among socioeconomically disadvantaged women. J Womens Health (Larchmt). 2012;21(10):1082-90.
35. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, et al. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes Relat Metab Disord. 2001;25(8):1175-82.
36. O'Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of preeclampsia: a systematic overview. Epidemiology. 2003;14(3):368-74.
37. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril. 2008;90(3):714-26.
38. Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, et al. Obesity, obstetric complications and cesarean delivery rate--a population-based screening study. Am J Obstet Gynecol. 2004;190(4):1091-7.
39. Robinson HE, O'Connell CM, Joseph KS, McLeod NL. Maternal outcomes in pregnancies complicated by obesity. Obstet Gynecol. 2005;106(6):1357-64.
40. Bautista-Castano I, Henriquez-Sanchez P, Aleman-Perez N, Garcia-Salvador JJ, Gonzalez-Quesada A, Garcia-Hernandez JA, et al. Maternal obesity in early pregnancy and risk of adverse outcomes. PLoS One. 2013;8(11):e80410.
41. Catalano P, deMouzon SH. Maternal obesity and metabolic risk to the offspring: why lifestyle interventions may have not achieved the desired outcomes. Int J Obes (Lond). 2015;39(4):642-9.
42. Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, et al. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care. 2007;30(8):2070-6.
43. Chu SY, Kim SY, Lau J, Schmid CH, Dietz PM, Callaghan WM, et al. Maternal obesity and risk of stillbirth: a metaanalysis. Am J Obstet Gynecol. 2007;197(3):223-8.
44. Gaillard R, Durmus B, Hofman A, Mackenbach JP, Steegers EA, Jaddoe VW. Risk factors and outcomes of maternal obesity and excessive weight gain during pregnancy. Obesity (Silver Spring). 2013;21(5):1046-55.
45. (ACOG) ACoOaG. Gestational diabetes mellitus. 2013.
46. Cheng YW, Chung JH, Kurbisch-Block I, Inturrisi M, Shafer S, Caughey AB. Gestational weight gain and gestational diabetes mellitus: perinatal outcomes. Obstet Gynecol. 2008;112(5):1015-22.
47. Fortner RT, Pekow P, Solomon CG, Markenson G, Chasan-Taber L. Prepregnancy body mass index, gestational weight gain, and risk of hypertensive pregnancy among Latina women. Am J Obstet Gynecol. 2009;200(2):167 e1-7.
48. Leeman L, Fontaine P. Hypertensive disorders of pregnancy. Am Fam Physician. 2008;78(1):93-100.
49. Gaudet L, Ferraro ZM, Wen SW, Walker M. Maternal obesity and occurrence of fetal macrosomia: a systematic review and meta-analysis. Biomed Res Int. 2014;2014:640291.
50. Rasmussen SA, Chu SY, Kim SY, Schmid CH, Lau J. Maternal obesity and risk of neural tube defects: a metaanalysis. Am J Obstet Gynecol. 2008;198(6):611-9.
51. Guelinckx I, Devlieger R, Beckers K, Vansant G. Maternal obesity: pregnancy complications, gestational weight gain and nutrition. Obes Rev. 2008;9(2):140-50.
52. Robinson H, Tkatch S, Mayes DC, Bott N, Okun N. Is maternal obesity a predictor of shoulder dystocia? Obstet Gynecol. 2003;101(1):24-7.

53. Sebastian Manzanares G, Angel Santalla H, Irene Vico Z, Lopez Criado MS, Alicia Pineda L, Jose Luis Gallo V. Abnormal maternal body mass index and obstetric and neonatal outcome. J Matern Fetal Neonatal Med. 2012;25(3):308-12.
54. Saldana TM, Siega-Riz AM, Adair LS, Savitz DA, Thorp JM, Jr. The association between impaired glucose tolerance and birth weight among black and white women in central North Carolina. Diabetes Care. 2003;26(3):656-61.
55. Kieffer EC, Tabaei BP, Carman WJ, Nolan GH, Guzman JR, Herman WH. The influence of maternal weight and glucose tolerance on infant birthweight in Latino mother-infant pairs. Am J Public Health. 2006;96(12):2201-8.
56. Rosenberg TJ, Garbers S, Lipkind H, Chiasson MA. Maternal obesity and diabetes as risk factors for adverse pregnancy outcomes: differences among 4 racial/ethnic groups. Am J Public Health. 2005;95(9):1545-51.
57. Cavicchia PP, Liu J, Adams SA, Steck SE, Hussey JR, Daguise VG, et al. Proportion of gestational diabetes mellitus attributable to overweight and obesity among non-Hispanic black, non-Hispanic white, and Hispanic women in South Carolina. Matern Child Health J. 2014;18(8):1919-26.
58. Shen JJ, Tymkow C, MacMullen N. Disparities in maternal outcomes among four ethnic populations. Ethn Dis. 2005;15(3):492-7.
59. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care. 2008;31(5):899-904.
60. Gonzalez S, Michalski-rimington AN, Cornbleet A, Stoller NS, Anderson EE, Levy SR. The Latina Gestational Diabetes Mellitus Study: Baseline Data. Hisp Health Care Int. 2005;3(1).
61. Mottola MF. The role of exercise in the prevention and treatment of gestational diabetes mellitus. Curr Diab Rep. 2008;8(4):299-304.
62. Koivisto VA, Yki-Jarvinen H, DeFronzo RA. Physical training and insulin sensitivity. Diabetes Metab Rev. 1986;1(4):445-81.
63. Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care. 2007;30 Suppl 2:S251-60.
64. Horton ES. Exercise in the treatment of NIDDM. Applications for GDM? Diabetes. 1991;40 Suppl 2:175-8.
65. Jovanovic-Peterson L, Peterson CM. Is exercise safe or useful for gestational diabetic women? Diabetes. 1991;40 Suppl 2:179-81.
66. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H. Effect of training on the dose-response relationship for insulin action in men. J Appl Physiol. 1989;66(2):695-703.
67. ACOG Committee Opinion No. 650: Physical Activity and Exercise During Pregnancy and the Postpartum Period. Obstet Gynecol. 2015;126(6):e135-42.
68. Evenson KR, Chasan-Taber L, Symons Downs D, Pearce EE. Review of self-reported physical activity assessments for pregnancy: summary of the evidence for validity and reliability. Paediatr Perinat Epidemiol. 2012;26(5):479-94.
69. Cogswell ME, Serdula MK, Hungerford DW, Yip R. Gestational weight gain among average-weight and overweight women--what is excessive? Am J Obstet Gynecol. 1995;172(2 Pt 1):705-12.

70. Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, et al. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. Diabetes Care. 2003;26 Suppl 1:S51-61.
71. Reader DM. Medical nutrition therapy and lifestyle interventions. Diabetes Care. 2007;30 Suppl 2:S188-93.
72. Shimron-Nachmias L, Frishman S, Hod M. [Dietary management of diabetic pregnancy]. Harefuah. 2006;145(10):768-72, 80.
73. Metzger BE. Diet and medical therapy in the optimal management of gestational diabetes mellitus. Nestle Nutr Workshop Ser Clin Perform Programme. 2006;11:155-65; discussion 65-9.
74. Gunderson EP. Gestational diabetes and nutritional recommendations. Curr Diab Rep. 2004;4(5):377-86.
75. Kaiser L, Allen LH. Position of the American Dietetic Association: nutrition and lifestyle for a healthy pregnancy outcome. J Am Diet Assoc. 2008;108(3):553-61.
76. Knopp RH, Magee MS, Raisys V, Benedetti T. Metabolic effects of hypocaloric diets in management of gestational diabetes. Diabetes. 1991;40 Suppl 2:165-71.
77. Stang J, Huffman LG. Position of the Academy of Nutrition and Dietetics: Obesity, Reproduction, and Pregnancy Outcomes. J Acad Nutr Diet. 2016;116(4):677-91.
78. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care. 2002;25(10):1862-8.
79. Mestman JH, Anderson GV, Guadalupe V. Follow-up study of 360 subjects with abnormal carbohydrate metabolism during pregnancy. Obstet Gynecol. 1972;39(3):421-5.
80. O'Sullivan JB, Charles D, Mahan CM, Dandrow RV. Gestational diabetes and perinatal mortality rate. Am J Obstet Gynecol. 1973;116(7):901-4.
81. Metzger BE. Long-term outcomes in mothers diagnosed with gestational diabetes mellitus and their offspring. Clin Obstet Gynecol. 2007;50(4):972-9.
82. Verier-Mine O. [Outcomes in women with history of gestational diabetes mellitus. Screening and prevention of type 2 diabetes mellitus. Literature review]. J Gynecol Obstet Biol Reprod (Paris). 2010;39(8 Suppl 2):S299-321.
83. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet. 2009;373(9677):1773-9.
84. Fisher TL, Burnet DL, Huang ES, Chin MH, Cagney KA. Cultural leverage: interventions using culture to narrow racial disparities in health care. Med Care Res Rev. 2007;64(5 Suppl):243S-82S.
85. Knowler WC, Narayan KM, Hanson RL, Nelson RG, Bennett PH, Tuomilehto J, et al. Preventing non-insulin-dependent diabetes. Diabetes. 1995;44(5):483-8.
86. Rosal MC, Ockene IS, Restrepo A, White MJ, Borg A, Olendzki B, et al. Randomized trial of a literacy-sensitive, culturally tailored diabetes self-management intervention for low-income latinos: latinos en control. Diabetes Care. 2011;34(4):838-44.
87. Sanabria-Martinez G, Garcia-Hermoso A, Poyatos-Leon R, Alvarez-Bueno C, Sanchez-Lopez M, Martinez-Vizcaino V. Effectiveness of physical activity interventions on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis. BJOG. 2015;122(9):1167-74.
88. van Poppel MN, Ruchat SM, Mottola MF. Physical activity and gestational diabetes mellitus. Med Sport Sci. 2014;60:104-12.
89. CDC. Prevent T2 Lifestyle Program. https://www.cdc.gov/diabetes/prevention/lifestyle-program/curriculum.html: CDC.gov; 2016.

90. Rosal MC, White MJ, Restrepo A, Olendzki B, Scavron J, Sinagra E, et al. Design and methods for a randomized clinical trial of a diabetes self-management intervention for low-income Latinos: Latinos en Control. BMC Med Res Methodol. 2009;9:81.
91. Mattila E, Lappalainen R, Parkka J, Salminen J, Korhonen I. Use of a mobile phone diary for observing weight management and related behaviours. J Telemed Telecare. 2010;16(5):260-4.
92. Phelan S. Pregnancy: a "teachable moment" for weight control and obesity prevention. Am J Obstet Gynecol. 2010;202(2):135 e1-8.
93. McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: the case of smoking cessation. Health Educ Res. 2003;18(2):156-70.
94. Callaway LK, Colditz PB, Byrne NM, Lingwood BE, Rowlands IJ, Foxcroft K, et al. Prevention of gestational diabetes: feasibility issues for an exercise intervention in obese pregnant women. Diabetes Care. 2010;33(7):1457-9.
95. Stafne SN, Salvesen KA, Romundstad PR, Eggebo TM, Carlsen SM, Morkved S. Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial. Obstet Gynecol. 2012;119(1):29-36.
96. Standards for outcomes measurement of diabetes self-management education. Diabetes Educ. 2003;29(5):804, 8-10, 13-6.
97. Robbins CL, Zapata LB, Farr SL, Kroelinger CD, Morrow B, Ahluwalia I, et al. Core state preconception health indicators - pregnancy risk assessment monitoring system and behavioral risk factor surveillance system, 2009. MMWR Surveill Summ. 2014;63(3):1-62.
98. Chasan-Taber L, Marcus BH, Stanek E, 3rd, Ciccolo JT, Marquez DX, Solomon CG, et al. A randomized controlled trial of prenatal physical activity to prevent gestational diabetes: design and methods. J Womens Health (Larchmt). 2009;18(6):851-9.
99. Zhang C, Liu S, Solomon CG, Hu FB. Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. Diabetes Care. 2006;29(10):2223-30.
100. Knowler WC, Fowler SE, Hamman RF, Christophi CA, Hoffman HJ, Brenneman AT, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009;374(9702):1677-86.
101. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. Int J Behav Nutr Phys Act. 2011;8:115.
102. Parmenter K, Wardle J. Development of a general nutrition knowledge questionnaire for adults. Eur J Clin Nutr. 1999;53(4):298-308.
103. Schieve LA, Cogswell ME, Scanlon KS. Trends in pregnancy weight gain within and outside ranges recommended by the Institute of Medicine in a WIC population. Matern Child Health J. 1998;2(2):111-6.
104. Steinfeld JD, Valentine S, Lerer T, Ingardia CJ, Wax JR, Curry SL. Obesity-related complications of pregnancy vary by race. J Matern Fetal Med. 2000;9(4):238-41.
105. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2009;32 Suppl 1:S62-7.
106. Gestational diabetes mellitus. Diabetes Care. 2000;23 Suppl 1:S77-9.
107. ACOG Committee opinion. Number 267, January 2002: exercise during pregnancy and the postpartum period. Obstet Gynecol. 2002;99(1):171-3.
108. Lind T, Phillips PR. Influence of pregnancy on the 75-g OGTT. A prospective multicenter study. The Diabetic Pregnancy Study Group of the European Association for the Study of Diabetes. Diabetes. 1991;40 Suppl 2:8-13.

109. Pettitt DJ, Bennett PH, Hanson RL, Narayan KM, Knowler WC. Comparison of World Health Organization and National Diabetes Data Group procedures to detect abnormalities of glucose tolerance during pregnancy. Diabetes Care. 1994;17(11):1264-8.
110. Sacks DA, Greenspoon JS, Abu-Fadil S, Henry HM, Wolde-Tsadik G, Yao JF. Toward universal criteria for gestational diabetes: the 75-gram glucose tolerance test in pregnancy. Am J Obstet Gynecol. 1995;172(2 Pt 1):607-14.
111. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations with neonatal anthropometrics. Diabetes. 2009;58(2):453-9.
112. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991-2002.
113. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. JAMA. 2009;301(6):636-50.
114. Kristensen J, Vestergaard M, Wisborg K, Kesmodel U, Secher NJ. Pre-pregnancy weight and the risk of stillbirth and neonatal death. BJOG. 2005;112(4):403-8.
115. Salihu HM, Dunlop AL, Hedayatzadeh M, Alio AP, Kirby RS, Alexander GR. Extreme obesity and risk of stillbirth among black and white gravidas. Obstet Gynecol. 2007;110(3):552-7.

Budget justification:

The proposed budget includes fees of the program principal investigator and all associated research staff.

Program Principal Investigator (PI) will devote 30% effort to this project. Program PI will carry out administrative duties, supervise the research coordinator, nutritionist and lifestyle coaches, data managements, and other ongoing aspects such as preparation of abstracts and manuscripts based on the project for presentation on scientific meetings and publications. Program Investigator will meet the research team bi-weekly and with co-investigators monthly. Co-investigators: Guillermo Umpierrez, MD, Professor of Medicine (Endocrinology) and Lisa Flowers, MD, Professor of Medicine (Obstetrics) at Emory University School of Medicine will supervise fellows and the program research staff and will also help with data interpretation and other ongoing aspects such as preparation of abstracts and manuscripts based on the project for presentation on scientific meetings and publications. No salary support is requested. Drs. Umpierrez and Flower's salary is covered by Emory University medicine department and contributions from concurrent research grants department and contributions from concurrent research grants.

This budget includes an estimate of other cost related to training by DTTAC for certification of lifestyle coaches ($750.00 per person) and this grant's needs, including copy, printing, supplies for 120 patients which include baseline studies, mid-gestational and post-partum supplies (HbA1C, oral glucose tolerance test –OGTT). Total participants compensation will be $31,500.

Second and Third Year Costs

There are no structural, systems, experiential, increases proposed for the second and third year costs. Salary amounts are based on actual salaries and include a 3% annual cost of living increase for faculty and staff. The agreements covering all systems and personnel will cover the entire three years of the grant proposal schedule.

Detailed Proposed Award Budget:

	% Effort	Base Salary	1st year	2nd year	3rd year
Program Principal Investigator	25%	$62,896	$15,724	$16,196	$16,682
Program Coordinator-bilingual	100%	$38,400	$38,400	$39,552	$40,739
Nutritionist	50%	$42,000	$21,000	$21,630	$22,279
Statistician	5%	$105,179	-	$5,579	$5,747
Fringe Benefits 30% Salary			$19,387	$21,643	$22,292
Personnel Subtotal			$84,011	$93,785	$96,600
Other					
Information Technology (Data)			$1,500	$1,500	$1,500
Prevent T2 handouts			$500	$500	$500
Patient's Compensation			$7,670	$7,670	$7,670
Lab Costs, OGTT, lab supplies			$1,800	$1,800	$1,800
Other Direct Costs Subtotal			$11,470	$11,470	$11,470
Other Expenses					
Publication					
Travel & education ($2,000 per year)			$2,000	$2,000	$2,000
Subtotal			$13,470	$13,470	$13,470
Local IRB costs			$1,500	-	-

Emory Office of Clinical Research			$5,200	-	-
Total Direct Costs			$108,951	$118,725	$121,540
Indirect Costs (37.5%)			$40,857	$44,522	$45,578
Total per year			$156,508	$163,247	$167,118

ATTACHMENT: GUIDE TO MISSING DOCUMENTS

The following documents are missing from this proposal template and will be supplied by the applicant organization.

- CVs of key personnel named in the grant

- Letters of support and endorsement

REFERENCES:

ACOG. (2013). Gestational diabetes mellitus.

American Diabetes, A. (2016). 2. Classification and Diagnosis of Diabetes. *Diabetes Care, 39 Suppl 1*, S13-22. doi:10.2337/dc16-S005

Anderwald, C., Tura, A., Winhofer, Y., et al. (2011). Glucose absorption in gestational diabetes mellitus during an oral glucose tolerance test. *Diabetes Care, 34*(7), 1475-1480. doi:10.2337/dc10-2266

Barakat, R. (2009). Type of delivery is not affected by light resistance and toning exercise training during pregnancy: a randomized controlled trial. *American Journal of Obstetrics and Gynecology, 201*(6), 590 e591-596. doi:10.1016/j.ajog.2009.06.004

Bautista-Castano, I., Henriquez-Sanchez, P., Aleman-Perez, N., et al. (2013). Maternal obesity in early pregnancy and risk of adverse outcomes. *PloS One, 8*(11), e80410. doi:10.1371/journal.pone.0080410

Bellamy, L., Casas, J. P., Hingorani, A. D., & Williams, D. (2009). Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet, 373*(9677), 1773-1779. doi:10.1016/S0140-6736(09)60731-5

Berger, H., Crane, J., Farine, D., et al. (2002). Screening for gestational diabetes mellitus. *Journal of Obstetrics and Gynaecology Canada. Journal d'Obstétrique et Gynécologie du Canada, 24*(11), 894-912.

Blatt, A. J., Nakamoto, J. M., & Kaufman, H. W. (2011). Gaps in diabetes screening during pregnancy and postpartum. *Obstetrics and Gynecology, 117*(1), 61-68. doi:10.1097/AOG.0b013e3181fe424b

Blumer, I., Hadar, E., Hadden, D. R., et al. (2013). Diabetes and pregnancy: an endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism, 98*(11), 4227-4249. doi:10.1210/jc.2013-2465

BRFSS, B. R. F. S. S. (2014). Physical Activity. Retrieved from http://www.cdc.gov/brfss/brfssprevalence/index.html

Bryant, A. S., Worjoloh, A., Caughey, A. B., & Washington, A. E. (2010). Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants. *American Journal of Obstetrics and Gynecology, 202*(4), 335-343. doi:10.1016/j.ajog.2009.10.864

Buchanan, T. A., & Xiang, A. H. (2005). Gestational diabetes mellitus. *Journal of Clinical Investigation, 115*(3), 485-491. doi:10.1172/JCI24531

Callaway, L. K., Colditz, P. B., Byrne, N. M., et al. (2010). Prevention of gestational diabetes: feasibility issues for an exercise intervention in obese pregnant women. *Diabetes Care, 33*(7), 1457-1459. doi:10.2337/dc09-2336

Catalano, P. M. (2010). Obesity, insulin resistance, and pregnancy outcome. *Reproduction, 140*(3), 365-371. doi:10.1530/REP-10-0088

Cawley, J., & Meyerhoefer, C. (2012). The medical care costs of obesity: an instrumental variables approach. *Journal of Health Economics, 31*(1), 219-230. doi:10.1016/j.jhealeco.2011.10.003

CDC. (2011). *National Diabetes Prevention Program*. Centers for Disease Cotnrol and Prevention Retrieved from http://www.cdc.gov/diabetes/prevention/index.html.

CDC. (2013a). CDC's Healthy Communities Program: Builiding Our Understanding: Communicating with Hispanic/Latinos: cdc.gov.

CDC. (2013b). *Diabetes and Pregnancy: Gestational Diabetes*. Retrieved from Atlanta, GA: U.S. Department of Health and Human Services: http://www.cdc.gov/pregnancy/documents/Diabetes_and_Pregnancy508.pdf

Chasan-Taber, L. (2012). Physical activity and dietary behaviors associated with weight gain and impaired glucose tolerance among pregnant Latinas. *Advances in Nutrition, 3*(1), 108-118. doi:10.3945/an.111.001214

Chasan-Taber, L. (2015). Lifestyle interventions to reduce risk of diabetes among women with prior gestational diabetes mellitus. *Best Practice & Research: Clinical Obstetrics & Gynaecology, 29*(1), 110-122. doi:10.1016/j.bpobgyn.2014.04.019

Chasan-Taber, L., Fortner, R. T., Gollenberg, A., et al. (2010). A prospective cohort study of modifiable risk factors for gestational diabetes among Hispanic women: design and baseline characteristics. *J Womens Health (Larchmt), 19*(1), 117-124. doi:10.1089/jwh.2009.1416

Chasan-Taber, L., Silveira, M., Marcus, B. H., et al. (2011). Feasibility and efficacy of a physical activity intervention among pregnant women: the behaviors affecting baby and you (B.A.B.Y.) study. *J Phys Act Health, 8 Suppl 2*, S228-238.

Coustan, D. R., Lowe, L. P., Metzger, B. E., et al. (2010). The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: paving the way for new diagnostic criteria for gestational diabetes mellitus. *American Journal of Obstetrics and Gynecology, 202*(6), 654 e651-656. doi:10.1016/j.ajog.2010.04.006

DeSisto, C. L., Kim, S. Y., & Sharma, A. J. (2014). Prevalence estimates of gestational diabetes mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. *Preventing Chronic Disease, 11*, E104. doi:10.5888/pcd11.130415

Dodd, J. M., Grivell, R. M., Crowther, C. A., & Robinson, J. S. (2010). Antenatal interventions for overweight or obese pregnant women: a systematic review of randomised trials. *BJOG: An International Journal of Obstetrics and Gynaecology, 117*(11), 1316-1326. doi:10.1111/j.1471-0528.2010.02540.x

Dodd, J. M., Turnbull, D., McPhee, A. J., et al. (2014). Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial. *BMJ, 348*, g1285. doi:10.1136/bmj.g1285

Ehrenberg, H. M., Durnwald, C. P., Catalano, P., & Mercer, B. M. (2004). The influence of obesity and diabetes on the risk of cesarean delivery. *American Journal of Obstetrics and Gynecology, 191*(3), 969-974. doi:S000293780400657X [pii]

10.1016/j.ajog.2004.06.057

Finkelstein, E. A., Trogdon, J. G., Cohen, J. W., & Dietz, W. (2009). Annual medical spending attributable to obesity: payer-and service-specific estimates. *Health Affairs, 28*(5), w822-831. doi:10.1377/hlthaff.28.5.w822

Fisher, T. L., Burnet, D. L., Huang, E. S., Chin, M. H., & Cagney, K. A. (2007). Cultural leverage: interventions using culture to narrow racial disparities in health care. *Medical Care Research and Review, 64*(5 Suppl), 243S-282S. doi:10.1177/1077558707305414

Fujimoto, W. (2013). Gestational Diabetes in High-Risk Populations. In R. Samoa (Ed.), (Vol. 31, pp. 90-94). Diabetes Advocay.

GDPH. (2013). *Georgia Gestational Diabetes Report*. Retrieved from Georgia Department of Public Health: http://dph.georgia.gov/sites/dph.georgia.gov/files/GestationalDiabetes_Final.pdf

Han, S., Crowther, C. A., & Middleton, P. (2012). Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria. *Cochrane Database Syst Rev, 1*, Cd009037. doi:10.1002/14651858.CD009037.pub2

Harrison, C. L. (2013). Optimizing healthy gestational weight gain in women at high risk of gestational diabetes: a randomized controlled trial. *Obesity (Silver Spring), 21*(5), 904-909. doi:10.1002/oby.20163

Hawkins, M., Hosker, M., Marcus, B. H., et al. (2015). A pregnancy lifestyle intervention to prevent gestational diabetes risk factors in overweight Hispanic women: a feasibility randomized controlled trial. *Diabetic Medicine, 32*(1), 108-115. doi:10.1111/dme.12601

Headen, I. E., Davis, E. M., Mujahid, M. S., & Abrams, B. (2012). Racial-ethnic differences in pregnancy-related weight. *Advances in Nutrition, 3*(1), 83-94. doi:10.3945/an.111.000984

Hedderson, M. M., Gunderson, E. P., & Ferrara, A. (2010). Gestational weight gain and risk of gestational diabetes mellitus. *Obstetrics and Gynecology, 115*(3), 597-604. doi:10.1097/AOG.0b013e3181cfce4f

HHS. (2016a). Grant Compliance and Oversight. Compliance Requirements at a Glance. U.S. Department of Health and Human Services

HHS. (2016b). Grant Information for Current and Prospective Grantees. U.S. Department of Health and Human Services.

HHS. (2016c). Grant Review Criteria at a glance: U.S. Department of Health and Human Services.

HHS/NIH. (2016). HHS/NIH Scoring System and Procedures: U.S. Department of Health and Human Services.

Hinman, J. M. (2015). PRS580 Research Design and Grant Preparation Class Materials, . RSPH Course materila.

Institute of Medicine Institute of medicine of National Academies. (2009). WEIGHT GAIN DURING PREGNANCY: REEXAMINING THE GUIDELINES. .

Kahn, R., & Davidson, M. B. (2014). The reality of type 2 diabetes prevention. *Diabetes Care, 37*(4), 943-949. doi:10.2337/dc13-1954

Kautzky-Willer, A., & Bancher-Todesca, D. (2005). Endocrine changes in diabetic pregnancy *Diabetology of Pregnancy* (pp. 18-33): Karger Publishers.

Kim, C. (2014). Maternal outcomes and follow-up after gestational diabetes mellitus. *Diabetic Medicine, 31*(3), 292-301. doi:10.1111/dme.12382

Kim, S. Y., Dietz, P. M., England, L., Morrow, B., & Callaghan, W. M. (2007). Trends in pre-pregnancy obesity in nine states, 1993-2003. *Obesity (Silver Spring), 15*(4), 986-993. doi:15/4/986 [pii]

10.1038/oby.2007.621

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine, 346*(6), 393-403. doi:10.1056/NEJMoa012512

346/6/393 [pii]

Langer, O. (2013). The proposed GDM diagnostic criteria: a difference, to be a difference, must make a difference. *Journal of Maternal-Fetal & Neonatal Medicine, 26*(2), 111-115. doi:10.3109/14767058.2012.734874

Ledoux, T., Van Den Berg, P., Leung, P., & Berens, P. D. (2015). Factors associated with knowledge of personal gestational weight gain recommendations. *BMC Research Notes, 8*, 349. doi:10.1186/s13104-015-1306-6

Little, P., Stuart, B., Hobbs, F. R., et al. (2016). An internet-based intervention with brief nurse support to manage obesity in primary care (POWeR+): a pragmatic, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol, 4*(10), 821-828. doi:10.1016/S2213-8587(16)30099-7

McBride, C. M., Emmons, K. M., & Lipkus, I. M. (2003). Understanding the potential of teachable moments: the case of smoking cessation. *Health Education Research, 18*(2), 156-170.

Miner, J. T. M., L.E. (2008). *Proposal planning & writing.* (4th ed.). Westport, CT: Greenwood Press.

Morisset, A. S., St-Yves, A., Veillette, J., et al. (2010). Prevention of gestational diabetes mellitus: a review of studies on weight management. *Diabetes/Metabolism Research and Reviews, 26*(1), 17-25. doi:10.1002/dmrr.1053

Moses, R. G. (2010). New consensus criteria for GDM: problem solved or a pandora's box? *Diabetes Care, 33*(3), 690-691. doi:10.2337/dc09-2306

Nielsen. (2013). *The Latina Power Shift Report*. Retrieved from http://www.iab.com/wp-content/uploads/2015/08/Nielsen_Latina_Report_2013_.pdf

O'Sullivan. (1973). Screening criteria for high-risk gestational diabetic patients. *American Journal of Obstetrics and Gynecology, 116*(7), 895-900.

O'Sullivan, E. P. (2011). Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria. *Diabetologia, 54*(7), 1670-1675. doi:10.1007/s00125-011-2150-4

Oostdam, N., van Poppel, M. N., Wouters, M. G., & van Mechelen, W. (2011). Interventions for preventing gestational diabetes mellitus: a systematic review and meta-analysis. *J Womens Health (Larchmt), 20*(10), 1551-1563. doi:10.1089/jwh.2010.2703

Pan, X. R., Li, G. W., Hu, Y. H., et al. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care, 20*(4), 537-544.

Perez, A., Alos, V. A., Scanlan, A., et al. (2015). The rationale, design, and baseline characteristics of PREVENT-DM: A community-based comparative effectiveness trial of lifestyle intervention and metformin among Latinas with prediabetes. *Contemporary Clinical Trials, 45*(Pt B), 320-327. doi:10.1016/j.cct.2015.10.011

Phelan, S. (2010). Pregnancy: a "teachable moment" for weight control and obesity prevention. *American Journal of Obstetrics and Gynecology, 202*(2), 135 e131-138. doi:10.1016/j.ajog.2009.06.008

Piirainen, T. (2006). Impact of dietary counselling on nutrient intake during pregnancy: a prospective cohort study. *British Journal of Nutrition, 96*(6), 1095-1104.

Price, B. B. (2012). Exercise in pregnancy: effect on fitness and obstetric outcomes-a randomized trial. *Medicine and Science in Sports and Exercise, 44*(12), 2263-2269. doi:10.1249/MSS.0b013e318267ad67

Quinlivan, J. A., Lam, L. T., & Fisher, J. (2011). A randomised trial of a four-step multidisciplinary approach to the antenatal care of obese pregnant women. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 51*(2), 141-146. doi:10.1111/j.1479-828X.2010.01268.x

Rakhshani, A. (2010). Effects of integrated yoga on quality of life and interpersonal relationship of pregnant women. *Quality of Life Research, 19*(10), 1447-1455. doi:10.1007/s11136-010-9709-2

Reece, E. A., Leguizamon, G., & Wiznitzer, A. (2009). Gestational diabetes: the need for a common ground. *Lancet, 373*(9677), 1789-1797. doi:10.1016/S0140-6736(09)60515-8

Renault, K. M., Norgaard, K., Nilas, L., et al. (2014). The Treatment of Obese Pregnant Women (TOP) study: a randomized controlled trial of the effect of physical activity intervention assessed by pedometer with or without dietary intervention in obese pregnant women. *American Journal of Obstetrics and Gynecology, 210*(2), 134 e131-139. doi:10.1016/j.ajog.2013.09.029

Rosal, M. C., Ockene, I. S., Restrepo, A., et al. (2011). Randomized trial of a literacy-sensitive, culturally tailored diabetes self-management intervention for low-income latinos: latinos en control. *Diabetes Care, 34*(4), 838-844. doi:10.2337/dc10-1981

Rosal, M. C., White, M. J., Restrepo, A., et al. (2009). Design and methods for a randomized clinical trial of a diabetes self-management intervention for low-income Latinos: Latinos en Control. *BMC Medical Research Methodology, 9*, 81. doi:10.1186/1471-2288-9-81

Rotberg, B., Greene, R., Ferez-Pinzon, A. M., Mejia, R., & Umpierrez, G. E. (2016). Improving Diabetes Care in the Latino Population: The Emory Latino Diabetes Education Program. *American Journal of Health Education, 47*(1), 1-7.

Saldana, T. M. (2004). Effect of macronutrient intake on the development of glucose intolerance during pregnancy. *American Journal of Clinical Nutrition, 79*(3), 479-486.

Sanabria-Martinez, G., Garcia-Hermoso, A., Poyatos-Leon, R., et al. (2015). Effectiveness of physical activity interventions on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis. *BJOG: An International Journal of Obstetrics and Gynaecology, 122*(9), 1167-1174. doi:10.1111/1471-0528.13429

Shen, J. J., Tymkow, C., & MacMullen, N. (2005). Disparities in maternal outcomes among four ethnic populations. *Ethnicity and Disease, 15*(3), 492-497.

Stafne, S. N., Salvesen, K. A., Romundstad, P. R., et al. (2012). Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial. *Obstetrics and Gynecology, 119*(1), 29-36. doi:10.1097/AOG.0b013e3182393f86

Streuling, I., Beyerlein, A., & von Kries, R. (2010). Can gestational weight gain be modified by increasing physical activity and diet counseling? A meta-analysis of interventional trials. *American Journal of Clinical Nutrition, 92*(4), 678-687. doi:10.3945/ajcn.2010.29363

Teuner, C. M., Menn, P., Heier, M., et al. (2013). Impact of BMI and BMI change on future drug expenditures in adults: results from the MONICA/KORA cohort study. *BMC Health Services Research, 13*, 424. doi:10.1186/1472-6963-13-424

Thornton, Y. S. (2009). Perinatal outcomes in nutritionally monitored obese pregnant women: a randomized clinical trial. *Journal of the National Medical Association, 101*(6), 569-577.

Tieu, J., Crowther, C. A., & Middleton, P. (2008). Dietary advice in pregnancy for preventing gestational diabetes mellitus. *Cochrane Database Syst Rev*(2), Cd006674. doi:10.1002/14651858.CD006674.pub2

Tuomilehto, J., Lindstrom, J., Eriksson, J. G., et al. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine, 344*(18), 1343-1350.

U. S. Census. (2015). Hispanic Heritage Month 2015. Retrieved from http://www.census.gov/newsroom/facts-for-features/2015/cb15-ff18.html

U. S. Preventive Services Task Force. (2014). Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine, 160*(6), 414-420. doi:10.7326/M13-2905

van Poppel, M. N., Ruchat, S. M., & Mottola, M. F. (2014). Physical activity and gestational diabetes mellitus. *Medicine and Sport Science, 60*, 104-112. doi:10.1159/000357340

Wier, L. M. (2006). Hospitalizations Related to Diabetes in Pregnancy, 2008: Statistical Brief #102. In E. Witt (Ed.), *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD).

Wolff, S. (2008). A randomized trial of the effects of dietary counseling on gestational weight gain and glucose metabolism in obese pregnant women. *International Journal of Obesity (2005), 32*(3), 495-501. doi:10.1038/sj.ijo.0803710

Xiang, A. H., Peters, R. K., Trigo, E., et al. (1999). Multiple metabolic defects during late pregnancy in women at high risk for type 2 diabetes. *Diabetes, 48*(4), 848-854.

Yin, Y. N., Li, X. L., Tao, T. J., Luo, B. R., & Liao, S. J. (2014). Physical activity during pregnancy and the risk of gestational diabetes mellitus: a systematic review and meta-analysis of randomised controlled trials. *British Journal of Sports Medicine, 48*(4), 290-295. doi:10.1136/bjsports-2013-092596

Zhang, C., Liu, S., Solomon, C. G., & Hu, F. B. (2006). Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. *Diabetes Care, 29*(10), 2223-2230. doi:29/10/2223 [pii]

10.2337/dc06-0266

Zhang, C., & Ning, Y. (2011). Effect of dietary and lifestyle factors on the risk of gestational diabetes: review of epidemiologic evidence. *American Journal of Clinical Nutrition, 94*(6 Suppl), 1975s-1979s. doi:10.3945/ajcn.110.001032

Appendix A:

Lifestyle Intervention Program for GDM Prevention in Overweight/Obese Latinas - LOLA Grant

Proposal Scoring Instrument

Name:

Date:

Instructions:

Please type your name and date above. Please read the entire proposal before you begin scoring. Please plan on spending between 4 and 8 hours on this review and evaluation activity.

This grant proposal is to be evaluated using the Scored Review Criteria (SRC) contained in this document.

The application will be scored in the areas described below, including: 1) Significance; 2) Innovation; and, 3) Approach, scored individually, and considered in the Overall Impact.

You will use this document to record all of your scores, make comments, and provide feedback. Please type your responses into the spaces provided in each section.

Please see the Master Scoring Rubric below. For all sections of this grant, a 9-point scoring scale is utilized.

Table A-1: Master Scoring Rubric

Score	Impact	Descriptor	Description
1	High	Exceptional	Exceptionally strong with essentially no weaknesses
2	High	Outstanding	Extremely strong with negligible weaknesses
3	High	Excellent	Very strong with only some minor weaknesses
4	Medium	Very Good	Strong but with numerous minor weaknesses
5	Medium	Good	Strong but with at least one moderate weakness
6	Medium	Satisfactory	Some strengths but also some moderate weaknesses
7	Low	Fair	Some strengths but with at least one major weakness
8	Low	Marginal	A few strengths and a few major weaknesses
9	Low	Poor	Very few strengths and numerous major weaknesses

As shown in the Scoring Rubric Table, a score of 1 indicates an exceptionally strong response with essentially no weaknesses; whereas a score of 9 indicates an application with serious and substantive weaknesses with very little strength. Five (5) is considered an average score. Please note that the scores you record are not additive. You will not total the scores associated with your responses. Your review is to be done independently of others. No group meeting will be held to arrive at a consensus on the evaluation. Your evaluation will stand on its own. Upon completion of your review, please return the completed document (via email only) to: scardon@emory.edu

You are free to use the full range of the rating scales values, as appropriate, to better discriminate the strengths and weakness of each section. Highly rating all areas, if not appropriate, will greatly diminish the future usability of the proposal's content. Please note that in addition to numerical scores, summary comments reflecting areas of strength and weakness are encouraged where appropriate. Critical, constructive comments are welcomed and expected.

Only the review criteria described below will be considered in the review process.

Scored Review Criteria

Reviewers will consider each of these review criteria (significance, innovation, approach, and environment) in the determination of scientific merit.

An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Specific Criteria Review Factors

The purpose of the Specific Criteria Review Factors is to insure that the proposal fully complies with the content template. This is a very detailed area by area review. The scoring outline may or may not follow the proposal outline in a sequential fashion. Accordingly, you may have to use your best judgment regarding the presence or absence of for content and then providing a score relative to its overall strength or weakness.

Significance Scoring

Significance is evaluated and scored independently of the evaluation and scoring of the Specific Criteria Review Factors. The evaluation of significance is a single score representing an overall evaluation of how this proposal will further public health science. The evaluation of significance assumes that the aims of the project will be achieved and/or the project will be successfully completed. Reviewers should evaluate the significance of the project within the context of the research field(s) it addresses. Reviewers should evaluate the significance of the project based upon their overall knowledge of the field(s).

Significant should be gauged around the following types of considerations (HHS, 2016c):

Does the project address an important problem or critical barrier to progress in the field?

Given that the aims of the project will be achieved, how will scientific knowledge, technical capability, and/or public health practice be improved?

How will successful completion of this project change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Table A-2: Overall Significance Worksheet

Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.

Overall Significance Score 1 to 9	
Overall Significant Strengths:	
Overall Significant Weaknesses:	

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Table A-3: Innovation Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.
Innovation Strengths:
Innovation Weaknesses:

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Has the investigator demonstrated appropriate partnerships with the key decision makers and staff in the healthcare setting to justify that the proposed research is feasible? Have the researchers justified the sustainability and dissemination potential of the approach beyond the research period, including appropriate partnerships and consideration of cost and resources such as personnel and infrastructure? If so, was the plan for sustainability compelling--i.e., if successful, would these research findings be likely to improve patient outcomes in routine care settings? Is there a sufficient evaluation of the implementation costs and implementation process to meaningfully inform scalability and sustainability? This evaluation should include, where applicable, issues related to cost, reimbursement, personnel, and other resources.

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of children, justified in terms of the scientific goals and research strategy proposed?

Table A-4: Approach
Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.
Approach Strengths:
Approach Weaknesses:

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Table A-5: Environment Worksheet
Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.
Environment Strengths:

Environment Weaknesses:

Overall Impact Scoring

In judging overall impact, reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved. Reviewers will provide written comments reflecting the proposals overall impact. The overall impact score will be based on each individual reviewer's overall assessment of the proposal. The overall impact score will include all of the considerations that have been previously scored including the Specific Criteria Review Factors, and Significance.

Overall Impact takes into consideration, but is distinct from, the scored review criteria. Overall Impact is the synthesis/integration of the five core review criteria that are scored individually and the Scored Review Criteria which may or may not be scored individually.

Public health related grants which reduce disease risks, add to the existing body of knowledge, reduce disparity, advancing understanding of new intervention methods, and/or to alleviate human disease and suffering are judged to have high overall impact. (Source: http://grants.nih.gov/grants/peer/guidelines_general/scoring_system_and_procedure.pdf)

Reviewers should assign the score that you believe best represents the impact of the application, and not feel constrained to limit their scores to the upper half of the score range if they do not feel such a score is warranted

Reviewers will be asked to score each review criterion based on how important they feel each review criterion is to the work being proposed. Accordingly, per the typical HHS/NIH guidance, a reviewer may give only moderate scores to some of the review criteria but still give a high overall impact/priority score. A proposal does not need to be strong in all categories to be judged likely to have major impact, e.g., a project that by its nature is innovative may be essential to advance a field. Conversely, a reviewer could give mostly high criterion ratings but rate the

overall impact/priority score lower because, based upon their experience, they found one criterion critically important to proposal.

Table A-6: Overall Impact Worksheet Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.	
Overall Significance Score 1 to 9	
Overall Significant Strengths:	
Overall Significant Weaknesses:	

Additional Review Criteria

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Protections for Human Subjects

For research that involves human subjects, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

Inclusion of Women, Minorities, and Children

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of children to determine if it is justified in terms of the scientific goals and research strategy proposed.

Table A-7: Additional Review Criteria Please use your individual knowledge and judgment as a reviewer. Please use bullets to note strengths and weaknesses, where appropriate. You may continue your comments on to additional pages.
Additional Criteria Strengths:
Additional Criteria Weaknesses:

References

HHS. (2016). Grant Review Criteria at a glance: U.S. Department of Health and Human Services.