RANDOMIZED LIFESTYLE INTERVENTION IN OVERWEIGHT AND OBESE PREGNANT HISPANIC WOMEN

PROTOCOL

NCT01868230

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Approach & Methods

D1. Study Overview

The overall goal of this randomized controlled trial is to test the efficacy of a culturally and linguistically modified, individually tailored lifestyle intervention to reduce excess gestational weight gain (GWG), increase postpartum weight loss, and improve maternal metabolic status among overweight/obese Hispanic women. Specific aims are to evaluate the impact of the intervention on 1) GWG and postpartum weight loss, 2) pregnancy and postpartum biomarkers of insulin resistance (i.e., glucose, insulin, HbA1c, HOMA, leptin, adiponectin), 3) postpartum biomarkers of cardiovascular risk (i.e., blood lipids, blood pressure), 4) offspring outcomes (i.e., anthropometric measures and biomarkers of insulin resistance), and 5) to evaluate the cost-effectiveness of the intervention per average incremental improvement in the outcome variables. Overweight/obese Hispanic women will be recruited in early pregnancy (around 10 wks gestation) and randomly assigned to a Lifestyle Intervention (n=150) or a Comparison Health and Wellness (control) Intervention (n=150). The intervention will utilize exercise (R01NR011295) and dietary intervention materials (R18DK067549) culturally adapted for Hispanics and shown to be efficacious in our previous controlled trials in this ethnic group. Multimodal contacts (i.e., in-person, telephone counseling, and mailed print-based materials) will be used to deliver the intervention during pregnancy (~12 wks gestation to delivery) continuing into postpartum (~6 wks to 6 mos postpartum); follow-up will continue for one year postpartum. Targets of the intervention are to achieve Institute of Medicine Guidelines for GWG and postpartum weight loss; ACOG guidelines for physical activity through increasing walking and developing a more active lifestyle; and reduction in total calories by following a balanced healthy diet in compliance with American Diabetes Association guidelines. The intervention draws from Social Cognitive Theory and the Transtheoretical Model and includes strategies for partner and/or family support to address the specific social, cultural, and economic challenges faced by underserved Hispanic women. Measures of compliance will include actigraphs and Hispanic food frequency questionnaires. The proposed project builds upon the expertise of the investigative team in conducting randomized controlled trials of exercise interventions among Hispanic pregnant women (R01 DK074876) and dietary interventions among low-income Hispanics with type 2 diabetes (R18 DK0658850) and can readily be translated into clinical practice in underserved and minority populations.

D2. Study Population & Eligibility Criteria

The study will be based at the ambulatory obstetrical practices of Baystate Medical Center, a large tertiary care facility in Western Massachusetts that serves a socioeconomically diverse population; 4,300 infants are delivered annually, 57% are Hispanic (predominantly from Puerto Rico with ~58% having income <$15,000 per year). Eligible women will be Hispanic, overweight or obese (BMI >25 kg/m2), and 16-45 years of age. We will exclude women with 1) prepregnancy BMI<25 kg/m2, 2) history of type 2 diabetes, heart disease, or chronic renal disease, 2) contraindications to participation in moderate physical activity or to a low-fat/high-fiber diet (e.g., Crohn's disease, ulcerative colitis), 3) inability to read English or Spanish at a 6th grade level, 4) <16 or >45 yrs of age, 5) >20 wks gestation, 6) current medications which adversely influence glucose tolerance, 7) not planning to continue to term or deliver at the study site, or 8) pregnant with twins or triplets. Women who have a very early preterm birth (<34 wks), a miscarriage, or a still birth after enrollment or a stillbirth will be excluded Women who become pregnant again in the year following delivery will be censored at the time of their positive pregnancy test.

D3. Recruitment, Baseline Assessment, and Sample Size

Bilingual (Spanish and English) and bicultural health educators will recruit women at the first prenatal care visit (~10 wks gestation). Women will be informed of the aims/procedures of the project, sign an informed

consent, and complete a screening form to determine eligibility. The baseline assessment will be collected via standardized questionnaire and the pregnancy blood sample will be taken (see Figure 1). Expectations for the study and a contacts schedule (face-to-face meeting, mailings, booster telephone calls) will be reviewed. Each assessment and interview completed is associated with a gift card for a total of up to $360, to be handed out after completing the study component.

Based on observed rates in our 2 trials (R01DK074876 and ASPH/CDC S3948), we conservatively expect to 333 women over the 24 mos recruitment period. We expect 10% of women to leave the New England area, deliver elsewhere, or withdraw during pregnancy, and therefore expect 300 participants (150 in each intervention arm) at the time of delivery. We calculate that 4% of women will be excluded for very early preterm birth (<34 wks), miscarriage, or stillbirth resulting in 288 children at delivery. Over the following 1 yr, we conservatively project that an additional 8% of women will be lost to follow-up due to withdrawal or movement out of the New England area. Women who become pregnant again will be censored. Therefore, we expect 264 women and children at 1 yr postpartum.

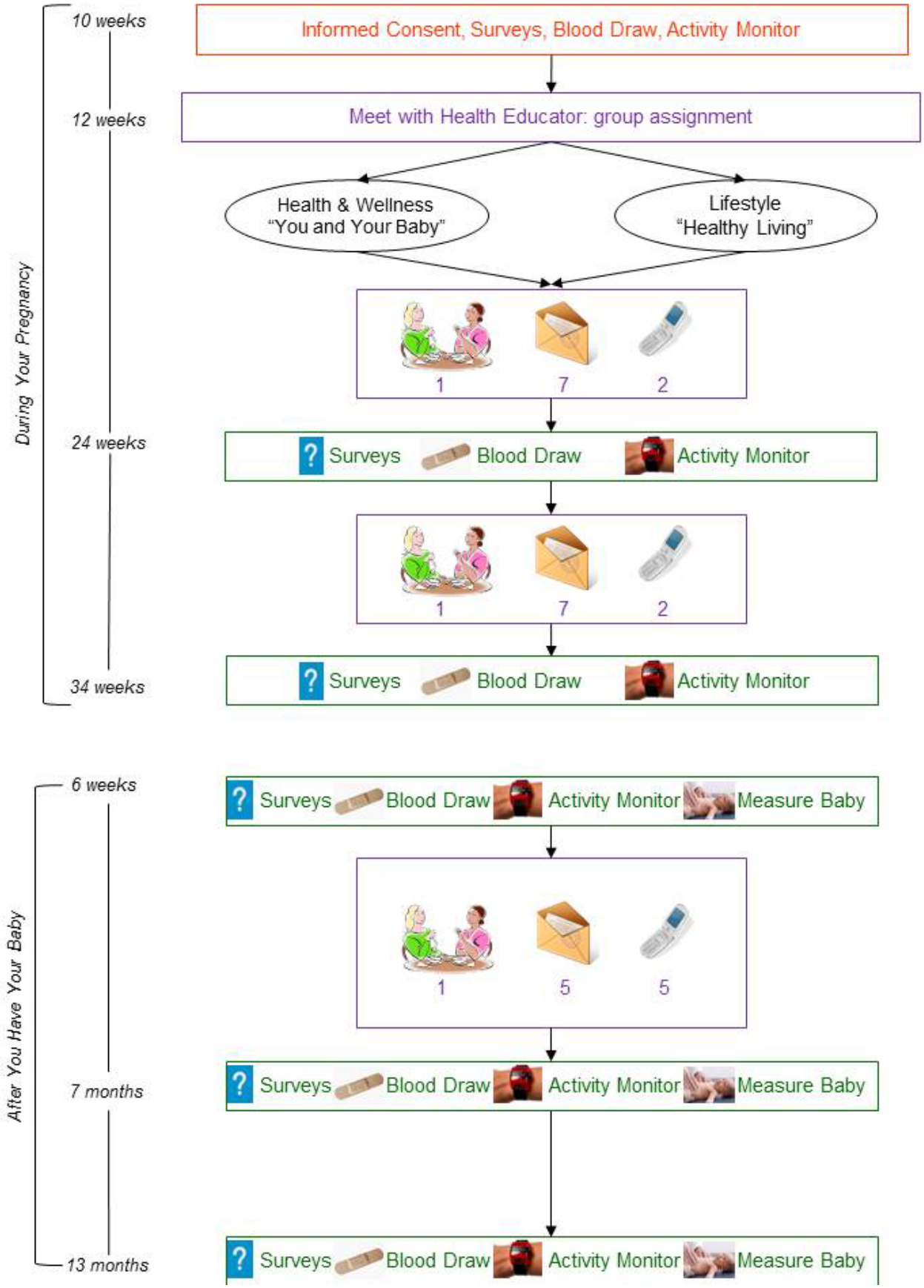
Bilingual (Spanish and English) and bicultural health educators will recruit women at the first prenatal care visit (~10 wks gestation). Women will be informed of the aims/procedures of the project, sign an informed consent, and complete a screening form to determine eligibility.

The recruitment sites will include the Wesson Women's Clinic, Baystate Midwifery and Women's Health, Baystate Maternal-Fetal Medicine and the Baystate Perinatal Diagnostic Center. Screening is done prior to the patient's visit by a research assistant. A Centricity appointment report is reviewed which provides all women with OB appointments in the above locations. This report has the patients' name, medical record number, date of birth, ethnicity, last menstrual period, appointment reason, appointment time and location.

Based on information from the Baystate nutritionist and the Centricity roster, the research assistants will develop a potential participant list. This list will be maintained as a project on the UMASSMED REDCap server. This project will only be accessible to Baystate IRB approved staff. The pre-screened patients are then approached to determine if they are interested in participating in the study. If they are not eligible, the research assistant enters their status and/or reason for ineligibility. If women are eligible and interested, they will be informed of the aims and procedures of the project, sign an informed consent and HIPAA release, and the research assistant will initiate study procedures. If this cannot be completed in person, it will be completed over the telephone.

One purpose of the potential participant list is to create a "Do Not Approach" report which recruiters would be able to review prior to approaching subjects. Prenatal patients have frequent visits and there are several recruiters for this study. A REDCap report will be produced which will be compared with the daily appointment report, so that recruiters can avoid re-approaching subjects who have already been recruited, have refused or have been determined to be ineligible, thereby limiting potential participant burden. In addition, at the conclusion of the study the data from this the potential participant list will be used to provide counts of subjects approached but found ineligible and their reason for ineligibility. The purpose for this data is to better describe the non-participants which will help determine any potential selection bias in this study. After the de-identified counts are tallied, the results will be sent to UMASS and the potential participant list will be destroyed. Only the Baystate PI and research coordinator will have the user rights to export data from the REDCap project. Identified data from this list will never be sent outside of Baystate.

Figure 1 : Study Design and Data Collection Time Points



D.4. Retention

Our team has a strong track record of retaining participants. Central to our retention strategy are bicultural/bilingual health educators that can build rapport with participants as well as materials that are culturally congruent (developed based on focus groups among Hispanic women, 3R01DK074876, R21NR009864, DK0658850). To further ensure retention, prior to randomization, the health educators clearly delineate the requirements of the study. Continued contact with participants over the course of the intervention (e.g., telephone calls, mailings, and assessments) also improves retention. In addition, the proposed study design facilitates high retention:

1) Enrollment occurs prior to delivery, a time period during which we have a track record of success in recruitment.

2) the postpartum face-to-face meeting takes place at the routine 6 wk postpartum visit and adherence is facilitated by bus passes, cafeteria vouchers, and the 2006 Mass insurance reform law providing free health care insurance for residents earning <150% of the federal poverty level. However, if a woman does not intend to attend this visit, the health educator will meet the women at locations outside the hospital, with consideration for the participant's and the health educator or assessors level of comfort (i.e., their pediatrician's office, their home, a community center). Locations will be selected for privacy (for example, an unused exam room at a pediatrician's office) and only staff who have experience making home visits will be permitted to complete home visits.

3) The 6 mos and 1 yr postpartum assessments will be conducted in the hospital or at a location outside the hospital with consideration for the participant's and the health educator or assessors level of comfort

4) Approximately 5% of participants in our prior pregnancy cohorts left the Springfield area after delivery; however, travel funds are budgeted for assessors to travel to the broader tri-state area (MA, NY, CT) if necessary.

5) Delivering the intervention does not rely upon women remaining in the immediate area during the postpartum year as it is based upon tested mailed print-based materials and telephone contacts. In addition to providing home/cell/work numbers, women will be asked to provide the contact information for a person close to them. Pre-paid cell phone time will be provided as an additional incentive.

D.5. Randomization

Immediately prior to randomization (~12 weeks GA), participants will be evaluated for study inclusion by answering if their provider has restricted their physical activity during this pregnancy. If they answer yes, their medical records will be reviewed by Dr. Markenson (Co-Investigator, and Director of Maternal/Fetal Medicine at Baystate). Eligible patients will be randomized into either the Lifestyle Intervention vs. the Health and Wellness Comparison Group. Randomization will be stratified based on age (<30, >30 years) and pre-pregnancy BMI (overweight >25-<30 kg/m2 vs. obese >30 kg/m2). Within each strata, a blocked randomization will be used such that both treatment groups will be assigned an equal number of times in each set of 4 sequentially enrolled patients.

D.6. Intervention

The Lifestyle Intervention is an evidence-based approach utilizing culturally modified, motivationally targeted, individually-tailored intervention materials tested in our randomized controlled trials. These programs capitalize on behavioral strategies common to effective interventions which have resulted in short and long term weight loss.[122, 123] The intervention is based on Social Cognitive Theory (SCT)[124] and the Transtheoretical Model (TTM)[125] and includes strategies for partner and/or family support to address the specific social, cultural, and economic challenges faced by underserved Hispanic women. Based on findings from our research group, the intervention addresses culture-specific beliefs concerning safe and appropriate foods, physical activity during and after pregnancy and how family may influence adherence to recommended gestational weight gain guidelines.[107,126-128]. The intervention begins in early pregnancy (~12 weeks gestation) and continues through a year postpartum. It consists of 3 in-person sessions, 9 phone calls and 14 mailings (see Figure 1).

Overall Goals: are to achieve IOM Guidelines for gestational weight gain, postpartum weight loss, and improve maternal metabolic status by achieving and maintaining 1) gestational weight gain within guidelines based on pre-pregnancy BMI;[75] 2) postpartum weight reduction to pre-pregnancy weight if pre-pregnancy BMI was in the normal range, or achieve a 5% reduction from pre-pregnancy weight if pre-pregnancy BMI was overweight/obese, 3) at least 150 min per week of moderate intensity physical activity such as brisk walking, as recommended by ACOG,[129] and 4) reduction in total energy intake by following a balanced healthy diet as recommended by ADA.[130]

D.7. Theoretical Framework

The intervention draws from Social Cognitive Theory and the Transtheoretical Model and takes into account findings by our research group on the specific social, cultural, economic, and environmental resources as well as challenges faced by women of Hispanic backgrounds.

The Transtheoretical Model was originally developed by Prochaska et al. to help understand how and when individuals make behavior change.[111] According to this model, individuals adopting a new behavior move through a series of stages: Precontemplation (not intending to make changes), Contemplation (considering a change), Preparation (making small changes), Action (actively engaging in the behavior) and Maintenance (sustaining the change over time). Also included in this model are processes of change which constitute strategies that individuals use to help make changes in their behavior.

Theory-driven interventions using the Stages of Motivational Readiness for Change Model and Social Cognitive Theory have been shown to be effective for exercise adoption and dietary change.[13] Interventions matched to the individual's stage of motivational readiness for physical activity adoption have been recommended and utilized[106, 107] and have been found to be more effective than non-targeted interventions.[15]

Using Social Cognitive Theory, the intervention will target patients' perceptions/beliefs as well as their behavioral patterns. Central to Social Cognitive Theory is the construct of self-efficacy, an individual's belief in his/her ability to perform a specific behavior in a specific situation (e.g., selecting low-fat food for lunch during a stressful day). Social Cognitive Theory posits that individuals develop self-efficacy for specific behaviors through their own ability to perform the behavior in a given situation (mastery experiences), watching others perform the behavior in specific situations (modeling), and by verbal persuasion from people in their environment that are able to perform the behavior.

Our intervention will provide a variety of opportunities for mastery experiences, modeling and verbal persuasion to enhance self-efficacy for self-management.

D.8. Intervention: Pregnancy Phase (~12 weeks gestation – delivery) (Figure 1)

The intervention will start with a face-to-face session building upon the usual prenatal care received by patients during this time period (see "Usual Care" below). Goal setting will emphasize strategies to mobilize family and social support. As one example, themes identified in focus groups among Latinas identified the need for partner support and, in response, our print-based materials incorporate partner and/or family negotiations strategies from the marital therapy field.[131, 132] The session includes administration of questionnaires that facilitate tailoring the intervention. The session will target knowledge and attitudes regarding gestational weight gain, physical activity and nutrition during pregnancy, with the goal of moving women over the continuum of pre-contemplation to contemplation and preparation. Women will be advised in accordance with the IOM guidelines for gestational weight gain, ACOG guidelines for pregnancy physical activity, and ADA guidelines for diet. This session will be followed over the remainder of pregnancy (Figure 1) by culturally modified, individually-tailored, motivationally targeted Mailed Print-Based Intervention Materials and Booster Telephone Counseling Sessions which will address gestational weight gain management. Each mailed component is in Spanish and English and is written at a 6th grade reading level. Quality control procedures ensure that stage of change and social cognitive constructs are consistently represented in all intervention materials. Systems created

in our pilot study, "Estudio VIDA," ensure that all mailings (i.e., physical activity and dietary intervention materials) are synchronized such that participants receive them at the same time. Telephone sessions facilitate review of progress toward the weight gain goal and provide 1) motivationally-based individualized feedback (i.e., problem-solving of challenges such as balancing caregiver/household responsibilities, cultural norms of self-sacrifice, social support, partner/family negotiation, and neighborhood safety), 2) review of weight gain grids and activity and dietary logs to evaluate progress toward behavioral goals, and 3) new goal setting. At ~34 wks gestation a face to face session, with the goal of preparation for the Postpartum Phase, will target knowledge and attitudes regarding postpartum weight loss and type 2 diabetes prevention.

D.9. Intervention: Postpartum Phase (~6 wks postpartum - ~7 months postpartum) (Figure 1)

The postpartum phase will start with a face-to-face session. Counseling will include the development of individualized postpartum weight loss, physical activity, and dietary goals as described above. This session will be followed by culturally modified, individually-tailored, motivationally targeted Mailed Print-Based Intervention Materials and Booster Telephone Counseling Sessions. Each mailed component is in Spanish and English and is written at a 6th grade reading level. Quality control procedures ensure that stage of change and social cognitive constructs are consistently represented in all intervention materials. Systems created in our pilot study, "Estudio Vida," ensure that all mailings (i.e., physical activity and dietary intervention materials) are synchronized such that participants receive them at the same time. Telephone sessions facilitate review of progress toward the weight loss goal and provide 1) motivationally-based individualized feedback (i.e., problem-solving of challenges such as balancing caregiver/household responsibilities, cultural norms of self-sacrifice, social support, partner negotiation, and neighborhood safety), 2) review of weight loss grids and activity and dietary logs to evaluate progress toward behavioral goals, and 3) new goal setting.

D.10. Curriculum

At the outset of the intervention, the health educator will set a gestational weight gain goal based on pre-pregnancy BMI and explain the importance of meeting weight gain guidelines. The weight-based curriculum will focus on periodic weight monitoring, graphing and education. Participants will be provided with a digital scale and be encouraged to weigh themselves at home daily and chart their weight on a grid weekly. Emphasis will be placed on using the scale as an important feedback and learning tool for how to better regulate personal diet and exercise behaviors. The postpartum weight loss goal of a 5% reduction from pre-pregnancy weight if pre-pregnancy BMI was overweight/obese is based on a modified version of the Diabetes Prevention Program[134] and prior postpartum weight loss interventions.[62] Participants will be encouraged to work toward this postpartum weight loss goal by focusing on a reduction of 1-2 lbs/wk. The health educator will utilize a checklist of motivators for wanting to lose weight specific to new mothers to highlight benefits of weight loss and reinforce engagement. Mailed Stage Matched Manuals and Tip Sheets during the postpartum period include strategies to elicit family and social support for weight loss and tips for managing fluctuations in weight loss motivation over time.

Physical Activity Change will be targeted via individualized week-by-week physical activity goals which focus on increasing, by 10%, the time spent in moderate activity as well as steps. Women will choose what form of safe activity they enjoy the most or can most readily fit into their lifestyle, from dancing to walking in a shopping mall to yard work. The accumulation of short bouts (i.e., 10 min episodes) will be encouraged. Mailed Stage-Matched Manuals matched to the participants' current level of motivational readiness for change focus on the benefits of exercise, building social support for new behavioral patterns, and strategies for overcoming barriers to exercise specific to Hispanic women. Based on responses to the tailoring questionnaires, individually-tailored computer Expert-System Feedback Reports[98, 99, 101, 135] draw particular messages from a library of approximately 296 messages regarding motivation, self-efficacy, and cognitive and behavioral strategies for exercise adoption. Mailed Tip Sheets include topics such as "We all need a little support", and

"Stretching and exercising with baby" (e.g., walking while pushing a stroller). Pedometers (Omron) and activity logs are provided for women to as a motivational tool to increase their activity. Prior studies support the use of pedometers as a motivational tool for walking.[136]

Dietary Change will be targeted via individualized week-by-week dietary goals determined in conjunction with the participant from an individualized dietary target goals checklist and based upon the woman's caloric intake, breastfeeding status (during the postpartum period), and stage of change for a variety of dietary changes. Calories are targeted through the identification of high-calorie, high-frequency food items in the woman's diet. Participants are provided with a Food Calorie Guide for culturally relevant foods. Actionable behavioral substitutions will emphasize what to eat and what not to eat, and steps to trying healthier methods for preparing traditional ethnic recipes. Mailed Tip Sheets cover the range of eating triggers in this population and strategies to manage these challenges, tips on meal planning, healthy recipes and grocery shopping lists, food label reading instructions with attention to cultural preferences. Participants will be provided with measuring cups and instruction in tracking caloric intake on a dietary log. The primary focus during pregnancy will be on decreasing high fat foods through limiting intake of energy dense foods (i.e., fast food, high-fat snacks and sugar-sweet beverages) and substituting them with healthier alternatives (e.g., fruit and vegetables). Women will be encouraged to decrease saturated fat intake while maintaining a balance of monounsaturated fats (up to 20% of calories) and polyunsaturated fats (up to 10% of calories); increase fiber through increasing whole grains, adding bran, nuts, seeds, and fruits and vegetables; replace refined grain products with whole grain products; and control portion size as recommended by the American Diabetes Association.[130] The primary focus in the postpartum period is reduction in total caloric intake via reduced consumption of popular calorie dense foods (e.g., fast food, high fat snacks, fried foods and sugar-sweetened beverages), reduced portion size, appropriate modifications in ethnic recipes, and higher fruit and vegetable intake, as recommended by the American Diabetes Association.[130]

D.11. Comparison Health & Wellness Intervention

To ensure retention and to control for contact time, the Comparison Health & Wellness arm receives mailed materials and telephone booster calls on the same schedule as the Lifestyle Intervention arm (Figure 1). In this way, we control for contact time, while keeping the content of the two interventions distinct. These booklets represent high-quality, standard, low-cost, self-help material currently available to the public which focus on non-exercise and non-dietary topics in both English and Spanish. These include the ACOG series of informational booklets on general issues related to health and wellness during pregnancy (e.g., Alcohol and Drug Use during Pregnancy, Easing Back Pain) and the American Academy of Pediatrics booklets on parent resources (e.g., Parenting your Infant). Hispanic control-arm participants in our prior studies (R01DK074876, R01NR011295, R21NR009864) reported that these materials were of interest[149] and differential dropout did not occur between study arms.

D.12. Outcome Variables

D.12.1. Biomarkers of Insulin Resistance and Other CVD Risk Factors

Fasting samples will be collected at a Baystate Reference Laboratory at baseline (~10 weeks gestation), 24-28 wks, and 32-34 wks gestation during routine prenatal care visits, and at 6 wks, 6 mos, and 1 yr, and among children at ~1 yr postpartum (coordinated with timing of the routine lead/CBC screen) (termed "blood draw"). Samples will be stored at -80 degrees Celsius in a freezer at Baystate with temperature monitoring, alarm and a back-up power system. Samples will be shipped periodically to the assaying lab. Residual blood samples will be stored at Dr. Rafai's lab to resolve potential data validation questions related to this study, and will be destroyed 7 years after study completion, unless the participant agrees to storage for future studies (included as "opt-in" in the informed consent form). Quality control for specimen handling will be performed monthly by the head lab technician. Samples will be assayed by Dr. Nader Rifai (Department of Laboratory Medicine, Harvard University) at Children's Hospital, Boston, MA.

Fasting Glucose (FG) will be measured enzymatically on the Roche P Modular system using Roche Diagnostics reagents (Indianapolis, IN).[155] Glucose at the concentrations of 90 and 312 mg/dL are determined in Dr. Rifai's laboratory with a day-to-day variability of 1.7 and 1.6%, respectively. Fasting Insulin (FI) will be measured by an electrochemiluminescence immunoassay on the Roche E Modular system. The lowest detection limit of this assay is 0.2 uU/mL and the day-to-day imprecision values at concentrations of 6.36, 20.9 and 747 uU/mL are 2.6, 2.8 and 2.5%, respectively. HOMA: Homeostasis model assessment will be calculated as [(FI x FG)/22.5] on a scale of 1-8. The Hemoglobin A1c (HbA1c) determination on the Roche P Modular system will be based on turbidimetric immunoinhibition using packed red cells. The day-to-day variability at values of 5.5 and 9.1 are 1.9 and 3.0%, respectively. Total Adiponectin (Multimeric) will be measured using an ELISA method from ALPCO Diagnostics Inc. (Salem, NH); day-to-day variabilities at concentrations of 9130 and 3930 are 9.8, 10.2%, respectively. Leptin will be measured by an ultra-sensitive ELISA assay, an enzymatically amplified "two-step" sandwich-type immunoassay (R&D Systems, Minneapolis, MN); day-to-day variability at concentrations of 65.7, 146 and 581 pg/mL are 5.4, 4.2 and 3.5%, respectively. Lipoprotein Profile: will be simultaneously performed on the Roche P Modular system. Dr. Rifai's laboratory is certified by the CDC/NHLBI Lipid Standardization Program.[156] Total Cholesterol will be measured enzymatically.[157] At cholesterol concentrations of 132.8 and 280.4 mg/dL, the day-to-day reproducibility are 1.7% (SD=2.4 mg/dL) and 1.6%, respectively. Triglycerides will be measured enzymatically with correction for endogenous glycerol.[158] Triglycerides at concentrations of 84.0 and 201.8 mg/dL have a day-to-day reproducibility of 1.8% (SD=1.6) and 1.7% (SD=3.5), respectively. The concentration of High Density Lipoprotein Cholesterol will be determined using a direct enzymatic colorimetric assay.159 HDL-C at the concentrations of 27.0 and 54.9 mg/dL have a day-to-day reproducibility of 3.3 (SD=0.9) and 1.7% (SD=0.9), respectively. Low Density Lipoprotein Cholesterol will be determined by a homogenous direct method;160 day-to-day variabilities at concentrations of 90, 106, and 129 mg/dL are 3.01, 2.34 and 2.18%, respectively. The concentration of High Sensitivity CReactive Protein (hsCRP) will be determined using an immunoturbidimetric assay on the Roche P Modular system using reagents and calibrators from DiaSorin (Stillwater, MN); day-to-day variabilities of the assay at concentrations of 0.91, 3.07 and 13.38 mg/L are 2.81, 1.61 and 1.1%, respectively.

D.12.2. Child Anthropometric Measures

Child anthropometric measures will be obtained within 24 hrs of delivery, 6 wks, 6 mos, and 1 yr postpartum and include measured weight on a calibrated scale, length using a measuring board, and subscapular (SS) and triceps (TR) skinfold thicknesses. We will calculate fetal growth as birth-weight-for-gestational-age z-score and ponderal index (PI) as birth weight (g) x 100/birth length $(cm)^3$. Ponderal index in neonates is closely correlated with estimates of total body fat and thus may indirectly reflect neonatal adiposity.[161] We will evaluate change from 0 to 6 mos and from 0 to 12 mos in weight-for-length z score (WFL-z), weight-for-age z score (WFA-z), and length-for-age z score (LFA-z). We will calculate age- and sex-specific scores using U.S.

national reference data (National Center for Health Statistics, CDC Growth Charts). We will use the sum of skinfolds (SS+TR) to estimate overall adiposity, and the ratio of skinfolds (SS/TR) to estimate central adiposity. These anthropometric factors correlate strongly (r=0.84) with estimates using total body electrical conductivity.[162] We will measure waist and head circumference. Every 6 mos the staff will be retrained in the anthropometric measurements.

D.12.3. Maternal Information, Delivery Information

Pre-pregnancy BMI, weight at delivery, and gestational age at delivery will be abstracted from the medical record. Gestational age at delivery is recorded by the obstetrician at the time of delivery based on sonograms, date of last menstrual period (LMP), date the first fetal heart beat was heard with a stethoscope, and fundal height. Pregnancy weight is measured prospectively from all participants at each prenatal visit and postpartum weight will be measured by trained study staff to the nearest 0.1 kg on accurately calibrated standard clinical scales using a standardized protocol. Gestational weight gain will be calculated as the difference between maternal weight at delivery and pre-pregnancy weight. Rate of weight gain will be calculated as the difference between maternal weight at delivery and pre-pregnancy weight, divided by gestational age at delivery in weeks. Compliance with IOM weight gain guidelines will be calculated by comparing the observed weight gain with the 2009 IOM Guidelines[75] at that gestational age. Compliance will be specified as a continuous variable (percent of 2009 IOM Guidelines met) or as a categorical variable: inadequate, adequate, and excessive. Finally, we will measure the area under the gestational weight gain curve (AUC) since the time of randomization.[154] The AUC incorporates in a single statistic not only the final weight but also the trajectory to reach it and has been found to be a predictor of birthweight outcomes.[154] Postpartum weight loss will be calculated as: 1) absolute weight change at 6 and 12 mos postpartum according to pre-pregnancy BMI, 2) percentage who retain a specific amount of weight over pre-pregnancy weight, and 3) proportion whose BMI category changes from pre-pregnancy BMI category as have others.59-61

D.12.4. Covariates

We will consider the following factors as covariates: Social Support for diet and exercise will be measured via the Social Support for Exercise (SSE). The SSE has three subscales (Family, Friends, Rewards/ Punishments) and acceptable internal consistency (alphas .61-.91) and criterion validity.[1] Clinical Characteristics of the Current Pregnancy: will be abstracted from the medical record utilizing customized software developed in our previous studies. Variables include: degree of abnormality on glucose tolerance testing during pregnancy defined as: 1) normal results on the screening 50-g OGTT; 2) failed screening test with normal results on the diagnostic 100-g test; 3) impaired glucose tolerance (IGT) defined as failed screening test and exceeded <1 cutpoints on the 100-g test; and 4) GDM defined as failed 50-g test and exceeded 2 or more cutpoints on the 100-g test;[163] treatment for abnormal glucose tolerance during pregnancy (e.g., diet, oral hypoglycemic and/or insulin); other pregnancy complications (e.g., hypertensive disorders, preterm birth, infection, cesarean delivery, NICU admission, Apgar score). Medical History: will include: personal history of GDM, family history of diabetes, previous infant with anomalies, still birth, or macrosomia, infertility, and parity. Sociodemographic Factors: will include income, level of education, and health insurance; acculturation via the Psychological Acculturation Scale,[164] language preference, and generation in the U.S. Smoking and Substance Use: Alcohol consumption, smoking, and drug use will be collected via questions from the Pregnancy Assessment Monitoring System.[165] Sleep: Pregnancy and postpartum sleep will be collected via The Pittsburgh Sleep Quality Index (PSQI).[166] Depression: Pregnancy and postpartum depression will be assessed via the Edinburgh Postpartum Depression Scale[167] validated in Hispanics.[168] Breastfeeding: History of breastfeeding and frequency and duration of current breastfeeding (i.e., exclusive breast feeding, % of mixed breast and formula feeding, exclusive formula feeding), timing of introduction of solids, and other breastfeeding behaviors and beliefs will be assessed via the validated Infant Feeding Questionnaire.[169] Postpartum Urine

Pregnancy Test and Postpartum Diabetes Screening (using ADA diagnostic criteria[163]) will occur at each postpartum assessment.

D.12.5. Measures of Adherence

Measure of Adherence with Exercise: Women will wear the ActiGraph GT3X-plus activity monitor (Actigraph LLC, Pensacola, FL) on the wrist for a 4 day period at each of the 3 prenatal and 3 postpartum assessments (42 days total). The GT3X-plus actigraph is currently being used to measure activity among pregnant women in NHANES and provides activity counts, steps, MET-min/week, time in sedentary behavior, patterns of active and sedentary behavior, % wear time, subject position, and periods when the device has been removed. Pregnancy cutpoints will be based on our prior studies.[137-139] The GT3X plus can be worn during periods of sleep to measure the amount and quality of sleep. Previous studies have reported reasonable validity under laboratory conditions among pregnant women[140] as well as under free living conditions.[141,6, 7] Assessors, blinded to study arm, will also administer the Pregnancy Physical Activity Questionnaire (PPAQ) at each of the 3 prenatal and 3 postpartum assessments. The PPAQ was developed and validated by our research team in the Baystate Medical Center population (NIH-NICHD R03-39341, PI: Chasan-Taber) and recommended for use in pregnancy and postpartum.[138] Activity-specific measures will be summed to arrive at total daily energy expenditure in MET-hrs/wk and categories of activity type and intensity.

Measure of Adherence with Diet (24-Hour Diet Recalls): Assessors, blinded to study arm, will conduct 3 24-hour diet recalls during each assessment period.

D.13. Measures of Acceptability/Feasibility

After study completion, the assessor will administer a Satisfaction Survey which will assess a variety of factors relevant to the acceptability and feasibility of the intervention. For example, women will be asked what attracted them to the study, what barriers/facilitators enabled them to continue to participate, their response to the intervention materials, their perspectives on the assessment materials as well as the number of measures. Women who drop out of the study will also be contacted for a similar discussion which will include asking women what we could have done to keep them more engaged and barriers to participation. At the end of the study, staff feedback will also be queried using structured satisfaction surveys.

D.14. Staff Training and Quality Control

Recruitment, health education, and telephone assessments will be conducted by trained bilingual (English/Spanish) health educators and assessors. We have built a training course based upon staff feedback and quality control during previous studies (Estudio PARTO, The B.A.B.Y Study and Estudio VIDA) with an accompanying manual which includes instruction on motivational interviewing techniques, role-playing, specific study protocols and scripts. Regular quality assurance and quality control reviews will include observations of the health educator. The observations will be done by asking participants permission to audio record a contact. The recordings will be scheduled so that the same day as the contact, the study coordinator will be available to review the interaction with the health educator, assess the quality of the interaction, and use the time as an opportunity to re-train the health educator as necessary. Assessors will be monitored in the same way. The audio recordings will be (audibly) identified with the participant's study ID and contain no PHI. The recordings will be destroyed once they are reviewed. When not in use, the recorder/memory card will be kept in a locked container in a locked room at Baystate. If a staff person is observed departing from standard protocol, feedback and recommendations for retraining will be provided. The assessor will be blinded to the treatment assignment. The health educator will be blinded to the results of the assessor's assessments. The medical record abstractor will be trained using the Medical Record Abstraction Manual and training program developed as part of our prior studies. The medical record abstractor will be blinded to the treatment assignment.

Our research group has had extensive experience with Baystate medical records over the past 12 years. We have systematically assessed the records for organization as well as completeness through correlations with the hard copy medical record systems and the billing database. Key variables for abstraction have been found to be accurately reported on the electronic system. Reliability of medical record abstraction will be assessed by abstraction of 10% of the medical records twice. The abstractor will be retrained based upon the findings from this assessment. Monthly staff meetings will be attended by the telephone assessor, health educator, medical record abstractor, data analyst, laboratory technician, Project Manager and the Principal Investigator.

D.15. Data Management

All participants will be assigned a Study Identification code (sequentially numbered) which will be used for identification purposes.

Study personnel will have access, on an as-needed basis, to a password protected and encrypted linking file (stored on the network at Baystate and a secure server at the School of Public Health and Health Sciences (SPHHS) at UMASS Amherst) which will allow for the identification of participant by name and include contact information, data collection dates, date of last menstrual period (LMP), and blood specimen locators. This is necessary to allow for women to be identified and approached for follow-up visits and meetings, as well as to be assessed over the phone, and for chart review.

No participant data will be individually identified or released to anyone other than the study investigators.

Data collection, including medical record abstraction, will take place using a dedicated REDCap project on the UMASSMED REDCap server. This project will be controlled and maintained by the Project Manager. Only individuals on the approved Core Data form will have access to the REDCap project. Only the UMass Project Manager and UMass PI will have access to export data from the REDCap project. As required, the UMass Project Manager or PI will export data labeled with a study ID to allow for processing and storage in the secure UMass study database (see below). To enable data management the exported data will include dates, LMP or delivery date, for instance, however there will be no additional identifying information such as name, MRN, or address exported to the UMass database. Note: the REDCap project will not contain data from biomarker testing or activity monitor readout; these data will be merged with data exported from REDCap by UMass staff.

Research staff at University of California, San Diego (UCSD) will analyze coded responses from participants' tailoring questionnaires using states of change analysis from the transtheoretical model. They will then provide UMass Amherst with the tailored intervention that is most appropriate for the participant. The communication between UMass Amherst and UCSD will be via email. UCSD research staff will not have access to any identifiable data.

Dr. Nader Rifal of Children's Hospital Boston will receive specimens labeled by study ID only. Dr. Rifal will send results to Dr. Chasen-Taber's team at UMass Amherst via email. Dr. Chasen-Taber's team will store the lab data on secure School of Public Health and Health Sciences server with access restricted to the study team and will later merge the lab data with the data export from REDCap for analysis.

Data from Activity Monitors is downloaded at UMass Amherst. Activity Monitors are mailed by the study participant to UMass Amherst with an envelope insert with the study ID number, no name or other identifiers. The return address on the envelope is the the Principal Investigator's address at the University of Massachusetts, Amherst. Dr. Chasen-Taber's team will store the activity monitor data on the secure School of Public Health and Health Sciences server with access restricted to the study team and will later merge the lab data with the data export from REDCap for analysis.

All other study information source documents that include identifying information (i.e. Informed Consent document, medical clearance form) will be secured in a locked filing cabinet in the locked Baystate Ob/Gyn office.

All passwords will be at least 8 characters long with at least one number and one capital letter.

Safeguards for Ineligible Subjects Cohort: Using the Potential Participants Form (PPF) a research assistant compiles a spreadsheet with the participants' name, medical record number, date of screening and reason(s) for

ineligibility. This file is password protected per Baystate policy and stored on the Baystate network in a shared folder with access restricted to IRB approved personnel only. After the study is completed, the reasons for ineligibility are counted and the de-identified results will be sent to UMASS and this list will be destroyed. Identified data from this list will never be sent outside of Baystate.

The databases will be maintained and managed by the Project Manager at UMass Amherst.

D.16. Statistical Analysis

Specific Aim #1, 2, 3: Impact of a Lifestyle Intervention on GWG and postpartum weight loss; biomarkers of insulin resistance; postpartum biomarkers of CVD risk. The primary analysis will evaluate differences in the change from baseline in weight gain measures, glycemia and other biomarkers of insulin resistance and cardiovascular risk factors between the groups (an intent to treat analysis). Initial analyses will describe the correlation of factors and investigate simple transformations for normality. The primary analysis will be based on a mixed model with random subject effects, including a common mean at baseline for the intervention groups, a period effect, and an intervention by period interaction.[170] The intervention by period interaction is a measure of the intervention effect, and corresponds to the estimate of an intervention effect in an analysis of covariance. The mixed model analysis will enable inclusion of time varying covariates such as depression, breastfeeding behaviors, and sleep, which may vary between baseline and follow-up for subjects. Equivalence of the intervention groups will be assessed by comparing the distribution of the potential confounders between each group. We will investigate established risk factors for weight gain (e.g., parity) and glycemia as well as degree and treatment for abnormality on glucose tolerance testing during pregnancy (e.g., diet, oral hypoglycemic and/or insulin) as potential confounders or effect modifiers. Generally, we will consider a change in the parameter estimate for the exposure (at least 15%), relative to that observed when not controlling for the variable as reflective of confounding. Effect modification will be evaluated by inspection of stratum specific odds ratios as well as by evaluating the statistical significance of interaction terms via likelihood ratio tests. We will also model the relationship between measured levels of exercise, sedentary behavior, and diet with each outcome, while adjusting for possible confounders using mixed effect linear regression models. We will test hypotheses with 2-sided tests. Finally, we will compare adoption and maintenance of behavior change (i.e., exercise, diet) in the intervention group relative to the control group by adding a fixed treatment group effect.

Specific Aim #4: Evaluate the impact of a Lifestyle Intervention on the outcomes of offspring. We will evaluate the impact of intervention arm on the offspring outcomes using the methods described for Aim #1-3. We will also examine GWG and prenatal glycemic factors as predictors of glycemia and weight gain in early infancy and childhood. Important covariates are listed in the covariate section. In models focused on offspring weight gain as the outcome, we will additionally adjust for fetal growth (i.e., BW/GA z score).

Specific Aim #5: Evaluate the cost-effectiveness of the Lifestyle Intervention. We will use procedures developed in our prior studies examining the cost-effectiveness of our interventions.[171-173] We will calculate the ratio of average dollars spent per average incremental improvement in outcome (i.e., GWG, postpartum weight retention, and biomarkers of insulin resistance and CVD risk). Incremental improvement will be defined as the mean change score from baseline for each group, adjusted for baseline values of the outcome measure and other participant characteristics.

Accounting for Missing Data: Although every effort is made to avoid missing data, we plan to use propensity score techniques[174-176] to evaluate the potential sensitivity of results to missing at random assumptions. Multiple comparisons will be addressed by carefully considering the biologic rationale of observed associations.

D.17. Power

To achieve power to detect clinically significant differences requires 300 participants (150 in each intervention arm) at the time of delivery. Based on observed rates in our 2 trials (R01DK074876 and

ASPH/CDC S3948), we conservatively expect 10% of women to leave the New England area, deliver elsewhere, or withdraw during pregnancy, and therefore will recruit 333 women over the 24 mos recruitment period. For offspring outcomes, we calculate that 4% will be excluded for very early preterm birth (<34 wks), miscarriage, or stillbirth resulting in 288 children at delivery. Over the following 1 yr, we conservatively project that an additional 8% of women will be lost to follow-up due to withdrawal or movement out of the New England area. Women who become pregnant again will be censored. Therefore, we expect 264 women and children at 1 yr postpartum.

We calculated the smallest mean difference in change from baseline in the Lifestyle Intervention vs. the Health & Wellness Control arm which we could detect at 80% power using standard deviations based on our prior studies and the literature[47, 177-180] using 2-sided tests with a significance level of alpha=5% (NCSS PASS 2008 software). For multiple regression models, we assumed that covariates accounted for 20% of the variation. Tables 3 and 4 show we have excellent power to detect even 'small to medium' mean differences, as defined by Cohen,[181] ranging from ~0.30 to 0.35 SDs for a range of representative outcome measures. For example, we have 80% power to detect as small as a 2.4% difference (Table 3) in percent change in HbA1c between treatment arms. A comparable trial among Hispanics observed a 7.1% difference in percent change in HbA1c between treatment arms[182] demonstrating that detecting this difference is well within the capability of the lifestyle intervention. For the categorical outcome of Compliance with IOM GWG guidelines, given our observation that 51% of overweight/obese Hispanic women exceeded guidelines in the study population, we have 80% power to detect a 30% reduction in risk or larger for exceeding IOM guidelines.

Table 3. Power Calculations Corresponding to Aim #1-3.	Projected sample size for analysis	SD for Change from Baseline	Smallest detectable mean difference in change from baseline between arms
Aim #1: GWG & Postpartum Weight Loss			
GWG (kg)	300	7.00	2.3
Postpartum weight loss	264	6.00	2.1
Physical activity (MET-hrs/wk>mod intensity)	300	2.89	0.9
Physical activity (minutes>mod intensity)	300	38.05	12.3
Total Caloric Intake (kcal/day)	300	64.90	22.4
Aim #2: Biomarkers of Insulin Resistance			
Glucose (mg/dl)	300	13.27	4.3
Insulin (pmol/l)	300	14.20	4.6
HbA_{1c}	300	0.26	0.1
HbA_{1c} (percent change)	300	7.4%	2.4%
Adiponectin (µg/ml)	300	3.40	1.1
Leptin (ng/ml)	300	5.50	1.8
HOMA	300	1.00	0.3
Aim #3: Postpartum Biomarkers of CVD Risk			
Total cholesterol (mg/dL)	264	38.38	13.3
Triglycerides (mg/dL)	264	83.06	28.7
HDL-cholesterol (mg/dL)	264	7.59	2.6
LDL-cholesterol (mg/dL)	264	33.83	11.7
Systolic blood pressure (mm Hg)	264	12.23	4.2
Diastolic blood pressure (mm Hg)	264	7.64	2.6
CRP (mg/dl)	264	4.50	1.5

Table 4. Power Calculations Corresponding to Aim #4.	Projected sample size for analysis	SD	Smallest detectable mean difference between arms
Aim #4: Offspring Outcomes at Delivery			
Cord glucose (mg/dl)	288	14	4.6
Cord insulin (µU/ml)	288	4.7	1.6
Cord adiponectin (µg/ml)	288	9.7	3.2
Cord leptin (ng/ml)	288	13.6	4.5
Birthweight-for-gestational age z-score [fetal growth]	288	0.93	0.3
Birthweight (g)	288	640	212
Ponderal Index (g/cm^3)	288	0.3	0.1
Birthweight-for-length z-score (WFL-z)	288	0.77	0.3
Head circumference (cm)	288	1.1	0.4
Aim #4: Offspring Outcomes at 1yr			
Adiponectin (µg/ml)	264	5.8	2
Leptin (ng/ml)	264	1.8	0.6
Weight-for-age z score (WFA-z)	264	0.98	0.3
Length-for-age z score (LFA-z).	264	0.94	0.3
Sum of skinfolds (mm)	264	4.2	1.5
Ratio of skinfolds	264	0.16	0.1
Waist circumference (cm)	264	2	0.7

D.18. Environment

In brief, Baystate Medical Center, the recruitment site, is the major medical resource in Western Massachusetts and the third largest acute-care hospital in New England, with 725 beds currently in service and approximately 4,500 deliveries per year. The School of Public Health and Health Sciences at UMASS maintains a micro computer research room for faculty, staff and students. Fifteen PC compatible microcomputers, a file server, a scanner and two laser printers are connected to the Department's Local Area Network (LAN). The LAN enables secure hard disk space for research projects that is accessible by multiple users and backed-up daily. Dr. Nader Rifai's (Department of Laboratory Medicine, Harvard University) lab at Children's Hospital, Boston, MA is a fully equipped laboratory with all of the requisite centrifuges, water baths, pipetters, etc. required to do the hormonal assays.

D.19. Timeline

This is a 5 year study. The timeline allows 12 months for study start up and protocol development, 24 months of recruitment, and follow-up of the last remaining participant (an additional 18 months from last enrollment). Data analysis will be ongoing and the last 6 months of the study will be dedicated to final analyses and manuscript writing.

D.20. Limitations and Alternatives

We chose not to utilize a group-based intervention nor more than 3 face-to-face visits in order to increase the ability of the intervention to be translated into clinical practice in underserved and minority populations. Prior reviews indicate that the time and child care pressures faced by postpartum women are barriers to attendance at groups meetings at scheduled times and that travel to and from venues would deter many.[151, 152] Indeed, retention levels in supervised group physical activity programs have been observed to fall to ~50% after 6 mos.[152, 153] In contrast, our research group,[98] as well as others,[93, 94] have found that individually-tailored lifestyle interventions delivered in person, via telephone, and via mail produce greater or comparable changes in behavior at a more cost efficient level compared with group-based interventions.

E. Protection of Human Subjects

1. Risks to the Subjects

Human Subjects Involvement and Characteristics:

The population under study includes 333 overweight pregnant/postpartum women between the ages of 16 and 45 being seen for prenatal care at Baystate Medical Center. All participants will be Hispanic. Women are generally healthy and considered ineligible if they have 1) prepregnancy BMI<25 kg/m2, 2) history of type 2 diabetes, heart disease, or chronic renal disease, 2) contraindications to participation in moderate physical activity or to a low-fat/high-fiber diet (e.g., Crohn's disease, ulcerative colitis), 3) inability to read English or Spanish at a 6th grade level, 4) <16 or >45 yrs of age, 5) >20 wks gestation, 6) current medications which adversely influence glucose tolerance, 7) not planning to continue to term or deliver at the study site, or 8) pregnant with twins or triplets. Women who have a very early preterm birth (<34 wks), a miscarriage, or a still birth after enrollment or a stillbirth will be excluded. Women who become pregnant again in the year following delivery will be censored at the time of their positive pregnancy test.

Sources of Materials:

At the time of recruitment (~10 weeks gestation), a blood sample to evaluate serum biomarkers associated with insulin resistance and other cardiovascular risk factors will be collected (termed "blood draw"). A total 700 microliters (uL) of serum will be collected which is equivalent to 1.5 milliliters (mL) or less than a teaspoon of whole blood. Physical activity, diet, and other covariates will also be assessed at recruitment. Subsequent assessments will be conducted at ~24-28 weeks gestation, after 32 weeks gestation, 6-weeks postpartum, ~6.5-months, and ~13-months postpartum. A urine pregnancy test will also be performed at the postpartum assessments. Women who are identified as having a positive pregnancy test will be removed from the study at the time of their positive pregnancy test and referred to their obstetric care provider. Measurements of compliance with exercise and diet will include activity monitors (worn for a 4-day period within each of these assessment time points), tracking the number of intervention sessions attended, number of booster calls participated in, number of assessments (e.g., questionnaires, blood samples) completed, as well as an assessment of degree of participation in physical activity and healthy dietary behaviors. No participants will be excluded from the study based on noncompliance. Assessments to measure other important covariates will also be collected at these assessment time points. Subjects will be under no obligation to complete the assessments, activity monitoring, or blood collections. Pregnancy and postpartum medical and laboratory records will be reviewed for obstetric and medical history, clinical characteristics of the index pregnancy, and laboratory results. All data will be used specifically for research purposes.

Potential Risks:

The exercise intervention focuses on increasing walking and developing a more active lifestyle as per recommendations of the American College of Obstetricians and Gynecologists for postpartum women (ACOG Committee opinion. January 2002: "Exercise during Pregnancy and the Postpartum Period") and the American Diabetes Association guidelines for women with previous GDM (The American College of Sports Medicine and the American Diabetes Association Joint Position Statement: "Exercise and Type 2 Diabetes"). These recommendations include 30 minutes or more of moderate exercise a day on most, if not all, days of the week. The overall goal of the dietary intervention is to reduce total calories via a diet with lower intake of calorie dense foods (e.g., fast food, high-fat snacks, fried foods and sugar-sweet beverages), saturated fat, and higher fruit and vegetable intake as recommended by the American Diabetes Association.

A possible risk in this study involves the social/psychological risk for an individual resulting from inadvertent disclosure of confidential medical history information. Confidentiality of the data will be ensured by assigning a subject identification number to each participant. All data collected in the study will be entered by subject identification number only into an encrypted, password protected, firewall protected server located at

UMASS Amherst. No participant data will be individually identified or released to anyone other than the study investigators. Any paperwork related to the study, identified by study number only, will be kept in a locked filing system separate from the name-address file of participants in the study. Only the Principal Investigator and the Project Manager will have access to the data in its raw state. All other authorized study staff will view coded data via forms and reports created by the data manager

Collection of blood specimen: Serum will be collected at each assessment time point. For most people, needle punctures to obtain blood specimens do not cause any serious problems. However, needle punctures may cause bleeding, bruising, discomfort, infections, dizziness, or fainting. To reduce this concern, the sample will be collected at a Baystate Reference Laboratory. A total 700 microliters (uL) of serum will be collected which is equivalent to 1.5 milliliters (mL) or less than a teaspoon of whole blood. Note: the (one-time) approximately 5ml of blood required for the child blood draw is well below the blood drawing limit of "the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week."

2. Adequacy of Protection Against Risks

Recruitment and Informed Consent:

A bilingual and bicultural recruiter will describe the study and its relevance to patients at the time of routine screening for GDM. Patients will be told that they are under no obligation to participate in this study. Those who agree will complete a written informed consent which describes the: purpose of research, procedures, risks and discomforts, benefits, costs & compensation, alternatives to participation, patient enrollment/length of study, confidentiality, voluntary participation, requests for additional information, and voluntary consent.

Protection Against Risk:

Prior to randomization (~12 wks gestation), and again after delivery, participants will fill out the Physical Activity Readiness Questionnaire. If they answer yes to any of the questions on the questionnaire, Dr. Markenson (Co-Investigator, and Director of Maternal/Fetal Medicine at Baystate) will evaluate the participant for study inclusion by reviewing prenatal visit records, the delivery medical records, and/or postpartum visit records. It is important to note that we conservatively scheduled the onset of the Intervention Postpartum Phase to not begin until 6 weeks postpartum, a time by which the physiologic and morphologic changes of pregnancy no longer persist for the majority of women (ACOG Committee opinion. January 2002: "Exercise during Pregnancy and the Postpartum Period"). The American College of Obstetricians and Gynecologists recommends that, in the absence of complications from delivery, a mild exercise program consisting of walking, pelvic floor exercises, and light stretching of all muscle groups can begin in the immediate postpartum period (ACOG Committee opinion. January 2002: "Exercise during Pregnancy and the Postpartum Period"). A similar recommendation was made by ACOG for exercise during pregnancy (during the Intervention Pregnancy Phase). In the case that Dr. Markenson determines there are contraindications to the lifestyle intervention, the woman will be excluded from the study and immediately contacted by the Project Coordinator by telephone and in writing.

Although the likelihood is low, our research team has well-established procedures for monitoring and responding to adverse events resulting from moderate intensity physical activity. First, during the orientation participants will be provided with contact information for study personnel and instructed to contact our team if any exercise related adverse event occurs (e.g., soft tissue injury). Additionally, we will be corresponding with the study participants over brief time periods to obtain study-related questionnaires. As part of those questionnaires, participants will be asked whether any adverse event occurred. In the case of any report, the Principal Investigator will be immediately notified, who will then notify the DSMB and Institutional Review Board. In cases of injuries that interfered with functioning (i.e., ability to move about), the participant will be asked to cease activity and obtain physician clearance before continuing.

Studies have shown the safety and efficacy of moderate exercise and weight reduction during lactation without affecting infant growth, milk composition (i.e., immunological component concentrations, vitamin B6,

essential fatty acids), or milk volume (ACOG Committee Opinion No. 361: "Breastfeeding: Maternal and Infant Aspects"). Moderate weight reduction while nursing is safe and does not compromise neonatal weight gain (ACOG Committee opinion. January 2002: "Exercise during Pregnancy and the Postpartum Period"). Health educators will encourage lactating women to follow recommended guidelines of the American College of Obstetricians and Gynecologists which include exercising after the baby has been fed or the breasts are empty to reduce discomfort; use of a good support bra and avoidance of a sports bra because of breast compression; and maintenance of adequate nutrition and hydration to support the energy demands of breastfeeding and exercise (ACOG Committee opinion. January 2002: "Exercise during Pregnancy and the Postpartum Period").

Suicidal Ideation Protocol:
A protocol has been developed for addressing possible suicidal ideations among participants. The Edinburgh Depression Scale asks "The thought of harming myself has occurred to me." All health educators and health assessors will participate in training before beginning interviews with participants, specifically in dealing with responses to this question. In evaluating individual participant's needs for information/assistance related to depression, several levels of concern have been identified. Data collectors will determine the level of concern for each participant and respond according to the categories below:

LEVEL 1 (NO REASON FOR CONCERN): This means that the data collector has no indication from the participant by means of the Edinburgh Depression Scale that this participant is experiencing suicidal thoughts.

LEVEL 2 (CONCERN LEVEL): Participants in this category exhibit some signs of suicidal thoughts. An indication would be an answer of either 'Yes, quite often' or 'Sometimes' to the question "The thought of harming myself has occurred to me" from the Edinburgh Depression Scale (question 10).

Interviewers will provide these women with a resource referral sheet. They will urge the participant to contact her clinician to let them know that she has experienced some signs of suicidal thoughts.

Health educators and / or health assessors will then inform the study physician, Glenn Markenson, MD at (413) 794-9939 and the Project Manager, Megan Ward Harvey at (413) 545-6732. If deemed appropriate Dr. Markenson will then contact the participant's health care provider.

3. Potential Benefits of the Proposed Research to the Subjects and Others

The potential benefit to society of this study could be substantial in recognizing exercise and diet as a tool to prevent excessive gestational weight gain, postpartum weight retention, and reduce subsequent risk of obesity, type 2 diabetes, and CVD. By participating in this study, participants will receive information about how to become more physically active and improve their diets. Those in the Health & Wellness comparison group will receive high-quality, standard, low-cost, self-help material currently available to the public.

4. Importance of the Knowledge to Be Gained

The importance of the study lies in the fact that changes in modifiable risk factors may reduce the risk of excessive gestational weight gain, postpartum weight retention, and subsequent obesity, type 2 diabetes, and cardiovascular disease. The intervention protocol can readily be translated into clinical practice in underserved and minority populations. Indeed, the impact of such lifestyle modifications is likely to be greatest in ethnicities, such as Hispanics, with consistently high rates of pre-pregnancy overweight/obesity and low rates of physical activity. The risks to participants in this study are judged to be minor. The anticipated benefits are great, insofar as the results will be used to further understand the unique factors related to promoting the

adoption and maintenance of a healthy lifestyle among Hispanic women among whom health disparities and associated sedentary lifestyles remain an enormous public health concern.

5. Data Safety and Monitoring Plan

This trial will be monitored in compliance with an independent Data and Safety Monitoring Board (DSMB) written in concordance with the guidelines from the National Institutes of Health. The DSMB will: 1) review the research protocol and plans for data safety and monitoring, 2) evaluate the progress of the trial with biannual assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, and reports from related studies, and 3) make recommendations to the IRB and investigators concerning continuation or conclusion of the trial. The DSMB will consist of three members including a physician who will serve as Chair (to be named), a statistician (to be named), and an outside researcher at UMASS Amherst (to be named) all of whom will be knowledgeable about the study's content but not directly involved in the study nor in a supervisory role to study personnel. The DSMB will meet biannually. Prior to each meeting, the Principal Investigator will submit a report which will include: 1) safety of the protocol participants, specifically if any adverse events have occurred; 2) validity and integrity of the data; 3) enrollment rate relative to expectation; 4) retention of participants; 5) data completeness; and 6) preliminary data analysis. The principal investigator will receive a written response regarding the DSMB's approval or suspension of the study. The report will be forwarded to the Institutional Review board. Monitoring activities by the Principal Investigator and the DSMB will continue until all participants have completed the study and are beyond the time point at which study-related adverse events would presumably be encountered.

Women and Minority Inclusion in Clinical Research

The population under study includes 333 pregnant and postpartum women between the ages 16 and 45 years being seen for prenatal care at Baystate Medical Center. The study is an intervention in the pregnancy and postpartum period among those diagnosed with abnormal glucose tolerance of pregnancy; therefore all subjects are women.

All women are Hispanic. Hispanic women are the fastest growing minority group in the U.S. and have the highest rates of sedentary behavior as well as postpartum diabetes after a diagnosis of gestational diabetes. Hispanics have, overall, been underrepresented in prior research.

Inclusion of Children:

Children between the ages of 16 and 21 will be included. Children younger than 16 will not be included for 2 reasons: 1) the study is a pregnancy and postpartum intervention among women with a history of abnormal glucose tolerance pregnancy, 2) modifiable determinants of type 2 diabetes and cardiovascular disease may differ substantively among children under age 16 therefore precluding direct applicability of hypotheses to this age group.

F. Vertebrate Animals

None

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