

Balance After Baby Intervention

New Information Collection Request

Supporting Statement: Part B

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Program Official/Project Officer

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B. Statistical Methodology

This is a 2-arm study designed to assess the effectiveness of a web-based lifestyle intervention and weight loss program tailored to women with recent gestational diabetes mellitus (GDM). The target number of enrolled participants is 250 (total). Information will be collected at screening and the following postpartum time points: 6-weeks, 6-months, 12-months, 18-months, and 24-months. Participants randomized to the intervention group will have access to (1) standard medical care, (2) an interactive version of the BABI study website, and (3) a web-based Lifestyle Coach. Participants in the control group will have access to (1) standard medical care, and (2) a “control version” of the BABI study website that is not interactive but contains information routinely provided to women with GDM during the postpartum period. Data will be analyzed to assess whether the intervention significantly increased postpartum weight loss, and other outcomes of interest.

B1. Respondent Universe and Sampling Methods

Target Respondents

The study will be conducted with a convenience sample of provider- and self-referred women who have a recent history of a gestational diabetes mellitus (GDM)-affected pregnancy. In addition, because the study intervention is web-based, participants must have routine and ongoing access to the internet. Participants in the intervention group must have devices such as smartphones or tablets with features that allow use of the site’s interactive features and tools.

The presence of GDM as the first eligibility criterion will be based on meeting one the following criteria:

- Carpenter-Coustan diagnostic criteria in most recent singleton or twin pregnancy (Carpenter & Coustan, 1982), which indicates having two or more elevated serum glucose levels at the specified time intervals shown in the table below;

Time	Serum Glucose (mg/dl)
Fasting	>95
1 hr	>180
2 hr	>155
3 hr	>140

- a glucose value >200 mg/dL after a 50-g glucose challenge test at >12 weeks gestation;
- hyperglycemia requiring insulin during pregnancy and chart diagnoses of GDM by OB or endocrinologist caring for patient during pregnancy;

- chart diagnosis of GDM by OB or endocrinologist caring for patient during pregnancy.

Further, women must be:

- ≥ 18 years of age;
- have no personal history of Type 1 or 2 diabetes;
- have had a pre-pregnancy body mass index between 18 and 50 kg/m² and at six weeks postpartum have a body mass index between 24 and 50 kg/m² (≥ 22 for Asians);
- be English or Spanish-speaking; and capable of providing informed consent.

Initially and over the course of the study, women may be excluded from participation if they:

- prematurely deliver (≤ 34 weeks gestation);
- are diagnosed with a glucose metabolism associated disease;
- plan to or participate in a commercial weight loss program (i.e. Jenny Craig, Weight Watchers, etc);
- are taking certain prescription medications including high dose glucocorticoids, atypical antipsychotics associated with weight gain (such as risperidone (risperidone), clozapine (klozaril), olanzapine (zyprexa), quetiapine (seroquel), etc.);
- are taking weight loss medications;
- have a personal history of breast cancer or any other type of cancer other than a basal cell skin cancer;
- have a personal history of cardiovascular disease (coronary artery disease, congestive heart failure, valvular heart disease, stroke, transient ischemic attack, or intermittent claudication), kidney disease, liver disease, venous or arterial thromboembolic disease, adrenal insufficiency, depression requiring hospitalization within the past 6 months, or non-pregnancy related illness requiring overnight hospitalization in the past 6 months;
- have an underlying disease/treatment that might interfere with participation in/completion of the study (e.g., significant gastrointestinal conditions, major psychiatric disorders, and others at the discretion of the study clinician);
- have other active medical problems detected by examination or laboratory testing;
- have plans to move to a different geographic area within the next 6 months; or
- are unable to give informed consent.

The study will be conducted at 2 sites that have the appropriate medical expertise, facilities, and access to the target population in sufficient numbers to meet recruitment goals.

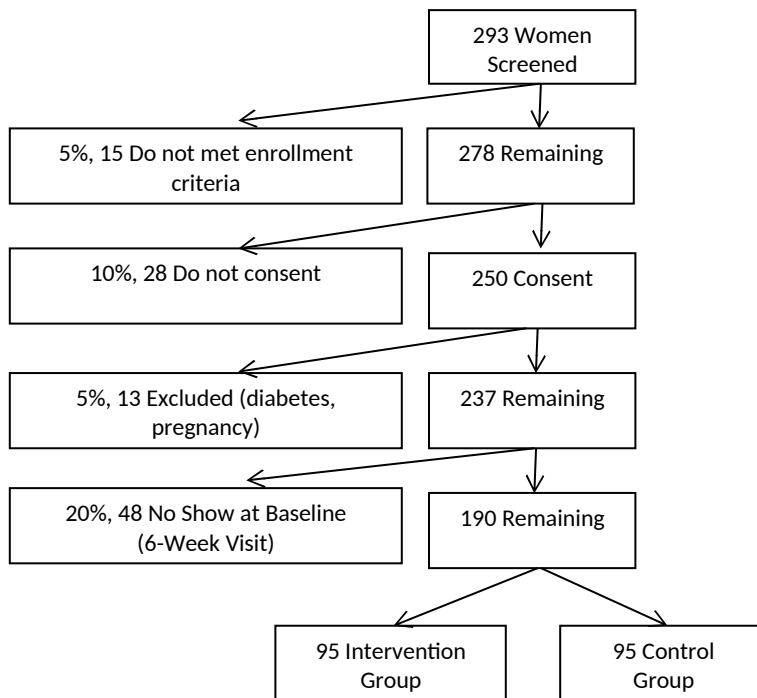
- Brigham and Women's Hospitals (BWH), located in Boston, MA, is a 779-bed hospital that averages nearly 8,000 annual births. BWH has a large research program that is

experienced in identifying and recruiting specific types of patient populations for a variety of research protocols such as the Balance After Baby Intervention (BABI).

- The University of Colorado (UCH), located in Aurora, CO. UCH is a multi-specialty community based hospital with 3,500 births annually and a 7% complication rate of gestational diabetes mellitus (GDM).

Of women found to be eligible, we estimate that 250 will consent to join the study during their third trimester of pregnancy and up to 10 weeks post-partum. The Figure below illustrates the estimated enrollment and attrition rates for the entire study. A constant 5% rate of exclusion and attrition was applied to the eligible remaining study population at the time of the previous visit to determine the number who would be eligible to return for any given current study-visit.

Figure B-1.1. Estimated Enrollment and Attrition Rate



The result of a constant application of these rates is a steady decrease in the number of subjects eligible to return for individual visits over time. It is possible that the exclusion rate may actually increase slightly over the follow-up period due to the inherent increased risk for T2DM development or pregnancy. Should this be the case, two factors have been considered that will compensate for any additional net loss: 1) greater focus in BABI on retention efforts to help ensure a decrease in the number of missed appointments or participant drop-out and 2) the perception that women who make it to the one year follow-up visit likely represent a more

committed participant that will be more likely to continue with the study for the duration of the second year.

Sample Size Determination

Based upon an effect size of .50, a desired power of at least .80, and a 2-group design (intervention/control), a power analysis ($\alpha = .05$) revealed the need for at least 130 women randomly assigned to each of the intervention and control groups. Factoring in an exclusion/attrition rate of 5% between consent and each of the subsequent study visits (6-weeks, and 6-, 12-, 18-, and 24-months), as well as an 80% show rate of eligible participants at each study visit, 250 women will be consented and 190 will be randomized, 95 in each arm. This will ensure the study is adequately powered to test for significant differences in weight change between the two groups from the 6-week, or baseline visit, to subsequent study-visits, including the 24-month post-partum visit. See **Figure B-1.1** for an illustration of this estimated enrollment and attrition process and **Table B-1.1** for a description of the number of participants predicted at each study visit.

Table B-1.1. Predicted Participants

	6 Week Post-Partum Visit	6 Month Post-Partum Visit	12 Month Post-Partum Visit	18 Month Post-Partum Visit	24 Month Post-Partum Visit
Intervention	95	90	86	81	77
Control	95	90	86	81	77
Total	190	180	172	162	154

Table B-1.2 presents the power to detect various effect sizes based on the smallest per arm sample size expected at various visit weeks. The effect sizes were derived by using the half width of the confidence interval at 12 months during analysis of the BAB Pilot (Nicklas et al., 2014). At 12 months, the calculated standard deviations in the intervention and control arms were 5.456 kg and 5.620 kg, respectively. Because the primary outcome is based on the difference in weight between baseline and 24- months, the standard deviation was approximated to be between 5 kg and 6 kg.

Table B-1.2. Power to Detect Differences between Study Arms Based on Change between Baseline and Various Study Visits*

	Difference between Baseline and Various Study Visits between the Intervention and Control Arms (Effect Size)			
Sample Size Per Arm	0.33	0.40	0.50	0.60

70	49	65	83	94
65	46	61	80	92
49	36	36	52	68
29	23	32	46	61
20	17	23	33	45

* Values shown in the table represent power (in %) for testing for differences in the change in weight from baseline to various visit weeks between study subjects in the intervention and control groups.

Randomization

Following screening and consent, study subjects will be randomly assigned to either the control or intervention arm of the study at the first (baseline) study visit, which is to occur approximately 6-weeks postpartum. A computer program will randomly assign subjects to treatment groups using a permuted block scheme with randomly varying block sizes. Assignment to a particular group dictates whether a participant is given access to the interactive website lifestyle intervention although both groups will be asked to return to the clinic with the same frequency (6 weeks, 6-, 12-, 18-, and 24-months postpartum).

B2. Procedures for the Collection of Information

Recruitment

The study sites (BWH and UCH) will rely on two recruitment strategies: participant self-referral and referral by health care providers. No women will be recruited while in labor.

For self-referral study-specific fliers and brochures (**Attachment 12**) will be placed in proximity and made available to patients on postpartum floors, in the antepartum clinics, and throughout BWH and UCH and their affiliated clinic practices, making women aware of the opportunity and allowing for self-referral to the study. The content of the fliers and brochures will also be electronically posted or delivered using community Listservs or boards that target pregnant and postpartum women (e.g., ClinicalTrials@Partners, GardenMoms), and placed in offices, stores and recreational facilities that cater to new mothers and newborns (e.g., WIC, ISIS maternity, Lamaze classes, etc.). Recruitment materials will provide instructions on how to contact study staff for more information. During follow-up telephone calls, study staff will provide additional information, obtain verbal consent, and conduct initial screening using the Screener Questionnaire (see **Attachments 2 and 2s**). If a candidate meets eligibility requirements, BABI study staff will obtain permission to contact the candidate's health care provider to obtain the information needed for confirming eligibility, and will schedule the first

study visit. A signed consent form (see **Attachments 10 and 11**) will be obtained at the first study visit, approximately 6 weeks postpartum.

Referral by healthcare providers will be based on the existing treatment relationships with OB/Gyn service providers at BWH or UCH, including BABI Principal Investigators. These providers may prescreen women and refer them to BABI study staff. For these women, the recruitment process will be conducted in person in a private room by study staff trained in the protection of human research participants. After completing the Screening Questionnaire and obtained signed consent, study staff will schedule the first study visit.

In some cases, other local health care providers may contact study staff to discuss the study or potential candidates. By email, study staff will obtain the provider's written permission before telephoning the candidate for recruitment, verbal consent, and completion of the Screener Questionnaire over the phone. Participants who are recruited in this manner will be asked to sign a consent form when they arrive for their baseline study visit.

In all cases,

1. Informed consent will be obtained by qualified study staff who have appropriate training in the protection of human subjects, are familiar with the project, and can refer participants to the Co-Principal Investigators for additional information, if needed.
2. Subjects who prefer contemplating their participation or who wish to discuss their participation in the study with others (family members, friends, physician), will be encouraged to do so. In this case, study staff will follow up with the patient at a later date to complete the enrollment process.
3. Study staff will collect contact information as part of the screening and recruitment process.
4. Study staff will perform a medical record review on all enrolled subjects (subjects who sign the consent form) to confirm GDM diagnosis and to determine whether the subject has any conditions that exclude her from participating in the study (see above). If GDM is confirmed and no exclusion criteria/disqualifier is identified in the subject's medical records, the subject will be scheduled for the first study visit (approximately 6 weeks postpartum).

Women may be recruited during their third trimester or up to 10 weeks postpartum. Once enrolled, specific questions included in the Screener Questionnaire domains are repeated on subsequent study-visit questionnaires (e.g. medical history, internet access, etc.) to continue

monitoring subjects for exclusions that were not previously reported, or developed throughout the course of the study.

Data Collection Cycle

This is a single-time research study in which consented participants will complete as many as six questionnaires over the 24-month postpartum period. In addition to the BABI Screener Questionnaire administered to all potential participants prior to consent, enrolled participants will complete as many as five subsequent questionnaires (**Attachments 3-7**) via computer-assisted self-interview (CASI) at the time of their study assessment visits. These assessment visits are to occur at 6-weeks and 6-, 12-, 18-, and 24-months postpartum and collection of the research data has been designed to minimize participant burden through efficient use of time at the study visits. **Table B.2-1** illustrates the assessment schedule by visit.

Specific study assessment activities, such as the oral glucose tolerance testing (OGTT), have inherent associated wait times that are well-suited to the completion of the study questionnaires. The spacing of the study visits has been designed to enable collection of physical and biological data (e.g., weight, blood glucose, etc.) that will be used to assess short- and long-term outcomes. In addition, interaction with participants in both study arms at follow-up frequencies helps reduce subject attrition for reasons such as lost to follow-up or no longer interested in participation.

Table B-2.1. Study Assessment Schedule

Activity	Screening Period (Third trimester of pregnancy – 10 weeks post- partum)	Baseline Visit 6 weeks Post- Partum (6 weeks – 12 weeks post- partum)	6 Months Post- Partum Visit (5-7 months post- partum)	12 Months Post- Partum Visit (11-13 months post- partum)	18 Months Post- Partum Visit (17-19 months post- partum)	24 Months Post- Partum Visit (23-25 months post- partum)
Screeener Questionnaire	✓					
Informed Consent	✓					
Visit-specific Questionnaire		✓	✓	✓	✓	✓
Block© Food Frequency Questionnaire		✓	✓	✓	✓	✓
Weight measurement		✓	✓	✓	✓	✓
Urine pregnancy test			✓	✓	✓	✓
OGTT		✓		✓		✓
Fasting glucose			✓		✓	
Hgb A1c test		✓	✓	✓	✓	✓
Lipid profile		✓	✓	✓	✓	✓

Data Collection Procedures

At each in-person visit, BABI staff will demonstrate to participants the use of the laptop for the purpose of completing the study questionnaire. Study staff will remain available to answer participants' questions and assist with the computer assisted self-interview (CASI) technology throughout the study visit, as needed. No participant identifying information will be collected. Participants will access the CASI web-based questionnaire by logging in with their study ID, which will serve as the link to their responses. The questionnaire, an integrated module of the BABI website, will be hosted on BWH password-protected servers. Upon subject entry of their responses on the web interface, the data will be captured on the back end in a customized Research Enabled Data Capture (REDCap) database. No data will be saved or stored on the local laptop hard drive.

A strong advantage to using CASI mode for the BABI questionnaires is it promotes the capture of honest subject responses that may not otherwise be given using an interviewer-administered mode. During interviewer-administered data collection participants may feel pressure to give responses perceived to be more desirable rather than truthful. In the CASI setting, we expect that participants will feel more comfortable providing honest responses to sensitive questions.

B3. Methods to Maximize Response Rates and Deal with Nonresponse

Loss-to-follow-up among study participants and item nonresponse are two potential sources of nonresponse error in this intervention study but specific measures have been designed to reduce the likelihood of these. At enrollment, we will ensure that multiple avenues for contacting a subject are documented as well as identifying which one is preferred. This will assist in the efficient contact of women for scheduling appointments and provision of a back-up method for contacting the subject should the preferred method fail (e.g. home phone no longer in service).

We will try to be as flexible as possible when scheduling participants, offering appointment times in the early mornings and evenings as well as during the day. The two month eligibility window for study visits will provide a wider amount of choice in scheduling to help ensure the respondent can schedule at a time best suited to her own calendar and the time that may be needed for rescheduling should it be necessary. To this end, as the opening of subjects' study visit eligibility window nears, BABI staff will call to schedule and/or confirm the date and time for the visit. Additionally, the tokens of appreciation and incentives have been planned to help remove barriers to increase participation and retention throughout the study. They have been designed to help ensure that costs associated with travelling to the clinic are not a factor in a woman's willingness to participate in the study. Although the intervals and timing of the clinic

visits are driven by the study's scientific objectives, the spacing of the in-person clinic visits of approximately 6 months provides the opportunity for development of a more personal rapport between the BABI study and participants.

Capture of questionnaire responses using CASI has been selected to maximize participants' comfort and efficiency. Computer administration of the questionnaires can be less intimidating than having study staff administer the questions, especially when responding to sensitive questions. In this way, CASI provides more privacy to respondents, which is hoped to result in few numbers of item non-response as well as more truthful responses. Using skip patterns driven by the answers an individual provides to preceding questions, CASI provides for a more custom experience that eliminates the need for subjects to see and read questions to which they do not need to respond.

B4. Test of Procedures or Methods to be Undertaken

The objective of the BABI data collection is to test the feasibility and effectiveness of a web-based lifestyle intervention for women with recent gestational diabetes mellitus to reduce postpartum weight retention. We plan to randomly allocate 190 women with recent gestational diabetes mellitus to either a web-based lifestyle program (Balance after Baby Intervention) delivered over the first two postpartum years or to a control group. Primary outcomes will be change in body weight at 12 and 24 months from 1) first postpartum measured weight; and 2) self-reported pre-pregnancy weight.

B5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Drs. Ellen Seely and Jacinda Nicklas, the BABI investigators, have been responsible for the refinement of the protocol and materials for the BABI throughout. In addition, a collaborative BABI Working Group composed the investigators, representatives from CDC's Division of Reproductive Health (Ms. Shin Kim, Dr. Andrea Sharma, Ms. Carol Bruce, and Dr. Cheryl Robbins), and Westat (Dr. Howard Fishbein and Ms. Melissa King) assisted and contributed to the refinement of the visit questionnaires and protocol. Statistical consult was provided by Dr. Diane Fairclough, University of Colorado and Westat Statistician, Dr. Brandy Rutledge.

The CDC point of contact is Shin Y. Kim, MPH, Epidemiologist, (770) 488-6281, skim1@cdc.gov.

Reference List

Carpenter, M., & Coustan, D. (1982). Criteria for screening tests for gestational diabetes. *American Journal of Obstetrics & Gynecology*, 144(7), 768-73.

Nicklas, J. M., Zera, C. A., England, L. J., Rosner, B. A., Horton, E., Levkoff, S. E. et al. (2014). A web-based lifestyle intervention for women with recent gestational diabetes mellitus: a randomized controlled trial. *Obstet.Gynecol.*, 124, 563-570.